MONITORING OF NEUROMUSCULAR FUNCTION IS IMPORTANT DURING SQUINT SURGERY

SAIAH Michèle, MD, BORGEAT Alain, MD, WILDER-SMITH Oliver, MD.

Department of Anesthesiology, University Hospital of Geneva, 1211 Genève 4, Switzerland.

Introduction. Squint surgery is associated with a high failure rate. Conventionally used anesthetic techniques for this type of surgery are based on high doses of volatile anesthetics and a single bolus of muscle relaxants in order to facilitate tracheal intubation. Any subsequent variations in muscle tension must be the result of the direct muscular relaxant properties of the anesthetic gases used together with the depth of anesthesia. Large interindividual variations in the muscle tension up to 60 % of the baseline value (1) have been demonstrated with such anesthetic techniques. The depth of anesthesia was monitored by EEG and/or end tidal volatile anesthetic concentrations in these studies. However, no reliable correlation between muscle tension and such measures of depth of anesthesia has been demonstrated to date (2). Thus such measures of depth of anaesthesia appear inadequate to stabilise muscle tensions during squint surgery and may in part explain its high failure rate. We investigated the relationship between the extensibility of oculo-motor muscles as measured by the elongation test and the degree of peripheral muscular relaxation as monitored by evoked muscular contractions of the ulnar nerve.

Patients and methods. After institutional approval and informed consent, 5 patients (ASA I or II) aged 14 to 82 being operated upon for retinal detachment were included in the study. Anesthesia was induced and maintained with propofol. Tracheal intubation was facilitated by suxamethonium. After complete recovery from neuromuscular blockade, vecuronium was administered in fractionated doses in order to perform the oculo-motor muscle elongation test at different values of T_1 (100, 50 & 0 % respectively).

Results. All patients showed variable positions of the eyes according to the degree of myorelaxation. We also found a direct correlation between oculo-motor muscle extensibility and the degree of peripheral muscle relaxation. Changes of between 1 to 4 mm were noted according to the degree of muscular relaxation (from 0 to 100 % muscular blockade).

Conclusions. These preliminary results show that close monitoring of muscular relaxation is mandatory during squint surgery in order to keep the same level of muscular relaxation (as assessed by evoked muscular contractions) during the entire surgical procedure and to thus avoid an insufficient / inadequate correction due to varying muscle tensions.

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THE EFFECT OF ALFENTANIL ON INTRACRANIAL DYNAMICS AND HEMODYNAMICS IN PATIENTS WITH BRAIN TUMOUR UNDERGOING CRANIOTOMY.

Orlando R. Hung, FRCPC, Charles E. Hope, FRCPC, Geoffrey Laney, FFARACS, Sara C. Whynot, MLT, ASCP,
Thomas J. Coonan, FRCPC, David S. Malloy, FRCSC.
Departments of Anaesthesia and Neurosurgery, Dalhousie University and Victoria General Hospital, Halifax, NS, B3H 2Y9.

INTRODUCTION: Alfentanil is an opioid analgesic with significant advantages over other opioids due to its rapid onset and short duration of action. However, several recent studies have reported conflicting findings on its effects on intracranial pressure (ICP) and have questioned its safety in neuroanaesthesia.[1-4] The goal of this study was to determine the effects of alfentanil on the intracranial dynamics and hemodynamics in patients with brain tumour undergoing craniotomy.

METHODS: After obtaining institution approval and informed consent, adult patients with supratentorial tumours were studied. Patients with evidence of intracranial hypertension, cardiovascular or respiratory diseases were excluded. Arterial, central venous and intracranial catheters (OLM Intracranial Pressure Monitor, Camino Lab, San Diego, CA) were placed in the subjects in the Neurosurgical Intensive Care Unit (NICU) the night before or not less than 4 hours prior to the operation. Baseline mean arterial pressure (MAP), heart rate (HR), central venous pressure (CVP), and intracranial pressure (ICP) were recorded. All patients were pre-medicated with 0.15 $mg.kg^{-1}$ of diazepam orally. They received 0.0175 $mg.kg^{-1}$ of droperidol 3 minutes prior to induction. Anaesthesia was induced with thiopental 3-5 $mg.kg^{-1}$ followed by pancuronium 0.15 $mg.kg^{-1}$ and maintained with 70% nitrous oxide in oxygen. Mechanical ventilation was provided via face mask. Normocarbia was maintained and confirmed by end-tidal CO_2 and arterial blood gases (ABG). 2 minutes after the injection of thiopental, an IV bolus of alfentanil, 50 $ug.kg^{-1}$, was injected over 1 minute followed by an infusion rate of 1 $ug.kg^{-1}.min^{-1}$. The patients were intubated 2 minutes after the end of the alfentanil bolus injection. Anaesthesia was maintained by 70% N_2O in O_2, 0.5% of isoflurane and alfentanil infusion rates from 0.5 to 1.5 $ug.kg^{-1}.min^{-1}$. Bolus doses of alfentanil, 7.5 $ug.kg^{-1}$ (up to 3 doses), were given at 5 minute intervals for inadequate anaesthesia (>20% increase of baseline MAP or HR). ICP and hemodynamic parameters were charted and recorded continuously on a magnetic tape for later off-line analysis. The ICP and hemodynamic parameters preoperatively in the NICU (NICU), preinduction (OR), after thiopental injection (THIO), the initial alfentanil bolus injection (ALF), intubation (ETT), head positioning (TURN), skin incision (INC), bone drilling (DRILL), and prior to extubation (EXT) were recorded. The data were analyzed by ANOVA with repeated measures and Bonferroni t-test where appropriate with $p < 0.05$.

RESULTS: 9 male and 3 female patients were studied. Their mean (±SD) age was 52.6 ± 13 years and weight 72.9 ± 9.7 kg. No complications occurred during the studies. All ABG prior to the administration of alfentanil were within normal limits. The perioperative mean with standard error of mean (SEM) of HR, and MAP are shown in Figure 1. The perioperative intracranial dynamics are shown in Figure 2. When compared with the preoperative hemodynamics in NICU, statistically significant changes of HR (**) were observed after the injection of thiopental and at extubation, whereas significant changes of MAP (**) were only seen at extubation. Head positioning, particularly axis rotation, appeared to be the only factor which significantly altered ICP (**) during surgery.

DISCUSSION: The anaesthesia technique described, with bolus/infusion alfentanil and low dose isoflurane, appears to provide stable hemodynamics without significantly affecting ICP for patients with supratentorial tumour undergoing craniotomy. Surgical head positioning appears to have a more dramatic impact on the intracranial dynamics than any of the pharmacological agents used, including alfentanil.

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Figure 1. Perioperative hemodynamics.

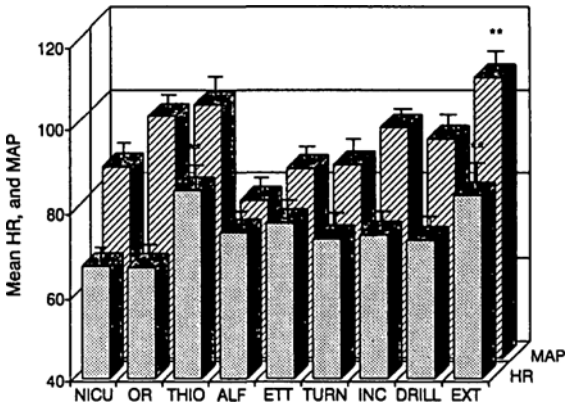
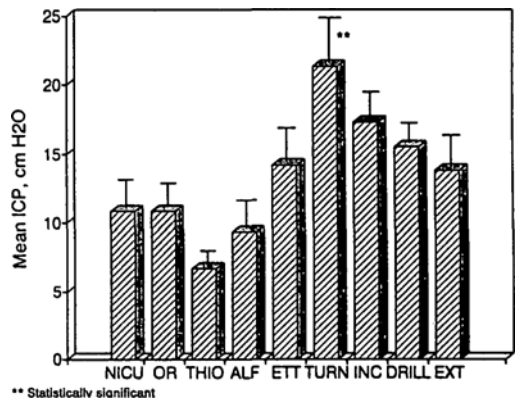


Figure 2. Perioperative ICP.



** Statistically significant

EVOKED POTENTIAL MONITORING IN POSTERIOR CIRCULATION ANEURYSM SURGERY: A COMPARISON OF TWO MODALITIES

S. PATTERSON MD,A. GELB MD,P. MANNINEN MD
Department of Anaesthesia, University Hospital, London Ontario

INTRODUCTION: A major concern in neuroanaesthesia is the monitoring of neural integrity during periods of potential ischaemia. Ischaemia may occur as a result of retraction, dissection, systemic hypotension or vascular occlusion after clipping. Focal ischaemia may occur during temporary clipping of feeder arteries, a technique which is used to facilitate aneurysm dissection and clipping. The goal of intraoperative neuromonitoring is early detection of ischaemia to prevent permanent deficits. Both somatosensory[1] (SSEP) and brainstem auditory evoked potentials[2] (BAEP) have been advocated as monitors during posterior fossa vascular surgery. This study compares these two modalities and correlates them with neurological outcome.

METHODS: Following institutional approval the charts of 48 adult patients undergoing 50 posterior fossa cerebrovascular procedures were reviewed. All patients were monitored by both SSEP and BAEP. Anaesthesia was induced according to the preference of the attending anaesthetist and maintained with air or nitrous oxide/oxygen and isoflurane with supplemental narcotics and muscle relaxants as required. SSEP's were recorded from the cortex (C_3^1 ,C_4^1 & Fpz) and C_7 or Erb's point in response to a median nerve stimulation of 15 mamp at 7.1 Hz. BAEP's were recorded from the vertex referenced to the ipsilateral earlobe using a monaural alternating click 60 db above threshold at a frequency of 21.1 Hz. The data was obtained with a Nicollet CA 1000 averager and stored to floppy disc. Bilateral potentials were recorded as controls during stable anaesthesia and continuous recordings were obtained during dissection and temporary and permanent clipping of the aneurysm. The numerical data was analyzed retrospectively and correlated with neurological status in recovery room and prior to hospital discharge. SSEP's were analyzed using both the amplitude of the cortical wave (N20) and the central conduction time (CCT, N20-N13) . Changes were considered significant if the amplitude of N20 was decreased by >50% or if the CCT was increased by over 1 ms. from control. BAEP's were analyzed using the interpeak latency (V-III) and the persistence of the IV-V complex and a change was considered significant if the interpeak latency increased by over 1 ms. or if the IV-V complex disappeared. The results were analyzed using 2x2 tables and the chi square test was used to assess for statistical significance ($p<.05$)

RESULTS: 49 BAEP and 47 SSEP were analyzed. Temporary clipping of the feeding artery was used in 32 cases. Our data (Table 1) fails to reveal any benefit to BAEP monitoring either on its own or in conjunction with SSEP's. There was no difference in the sensitivity or specificity of BAEP monitoring when comparing temporary vs permanent neurological deficits. BAEP results were not influenced by location of the aneurysm. SSEP monitoring was more sensitive ($p<.05$) than either BAEP or BAEP/SSEP combined. In addition there was no significant difference in the sensitivity, specificity or positive predictive value of SSEP's whether N20 amplitude, CCT changes or both N20 amplitude and CCT changes simultaneously were used as indices of significant change.

DISCUSSION: These results indicate that no current evoked potential monitoring modality is completely satisfactory for the posterior circulation. Despite previous case reports suggesting a role for BAEP monitoring we were unable to demonstrate a benefit either alone or in conjunction with SSEP. This may be due to the relative resilience of the brainstem to ischaemia compared to the cortex[3] or due to the limited length of the BAEP pathway compared to the SSEP. Despite this finding BAEP's remain useful in cases where direct trauma to the VIII nerve is possible. SSEP monitoring although more sensitive continues to have a disconcertingly high false negative rate of 29%. This is consistent with previous studies[1] as is the high false positive rate of 55%.

TABLE 1

	BAEP			
	neuro deficit		normal	
	true+	false-	true+	false-
Vert/Basilar	4	11	5	22
Upper Basilar	0	3	0	4

	SSEP			
	neuro deficit		normal	
	true+	false-	true+	false-
Vert/Basilar	10	4	13	13
Upper Basilar	2	1	2	2

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CORTISOL DECREASES ANESTHETIC REQUIREMENTS IN RATS

D Strum MD, B Glosten MD, MJ Spellman and EI Eger, II MD

Departments of Anesthesia at U of Pittsburgh, UC San Francisco, and U of Chicago

Introduction.Central nervous system responses to depressant drugs such as sedative-hypnotics, local anesthetics, and volatile anesthetics are rhythmic and vary as much as 10-14% related to circadian cycles (1). The mechanism underlying this response is unknown but we hypothesize that the response varies with the circadian hormone cortisol. This hypothesis is made plausible by the observation that steroid molecules with molecular structures similar to cortisol also alter anesthetic requirements (2). We asked whether a pharmacological dose of cortisol would alter anesthetic requirements in the rat. We also asked whether acute or chronic administration would make a difference if an effect were to be observed.

Methods.With approval from the animal care and use committee, we studied 45 Sprague-Dawley rats, male, each aged 2-3 months and weighing 200-250 g. The rats were divided into 3 experimental groups and one control group in order to examine the mechanism by which cortisol might have an effect. The rats were housed individually in a climate controlled room with automatically regulated light to produce equivalent periods of light and dark. Rat meal and water were available ad libitum. Isoflurane anesthesia was administered to the rats by directing a flow of 10 l/min of 100% O_2 through a vaporizer and then directing the effluent to each rat housed individually in a clear, cylindrical chamber 25 cm long and 8 cm in diameter. The rats' tails protruded through a rubber stopper at one end of the cylinder and MAC was determined for each rat using a standard tail-clamp method. All investigators were blind to the identity of each experimental group tested. Isoflurane concentrations were determined by FID gas chromatography.

The control (n=16) and experimental groups were treated similarly except for SC injections of cortisol or saline. In order to detect a gene-mediated effect of cortisol administration, 16 rats received cortisol 3.0 mg/d for 12 days before testing on day 13 (chronic group). In order to detect a direct effect of cortisol, 5 received a single large injection of 40.0 mg cortisol one hour before testing (massive acute). In order to determine whether the two mechanisms might be additive, 8 rats received chronic cortisol treatment plus an additional 3.0 mg one hour before testing (chronic + acute). In order to confirm an effect of cortisol on the rats (positive control), thymic weights were determined for each rat at autopsy to ensure the dose of cortisol chosen was sufficient to produce thymic involution. The experimental results for each group were compared using unpaired t-tests.

Results. Anesthetic requirements for isoflurane were reduced 6-9% in cortisol treated rats. Cortisol treated rats gained 7% less weight than control rats ($p=0.04$) and thymic weights were 17% lower in cortisol treated rats.

Discussion. A lessor rate of weight gain and thymic involution in cortisol-treated rats indicate significant physiological changes in these rats. The small magnitude of the decrease in MAC means that an impact on clinical practice is unlikely. However, the reduction in anesthetic requirements has provocative implications for possible mechanisms, particularly in the chronic group where the short cortisol half life virtually guarantees no cortisol would be present at the time of testing.

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Cortisol Treatment Group	n	Thymus Weight (mg)(±SD)	MAC (±SD)	Coefficient Variation MAC(%)	Body Weight on Day 12 (g)(±SD)
Control	16	624 ± 139	1.57 ± 0.11	7.0	351 ± 14
Chronic	8	404 ± 94*	1.47 ± 0.15*	9.9	327 ± 38*
Chronic + Acute	8	346 ± 83*	1.44 ± 0.13*	8.7	327 ± 38*
Massive Acute	5	--	1.42 ± 0.08*	5.3	346 ± 17

* Differs from control ($p \leq 0.05$).

CO_2 RESPONSIVENESS OF CEREBRAL BLOOD FLOW IS MAINTAINED DURING PROPOFOL ANAESTHESIA

RA CRAEN,MB.BS., AW GELB MB.ChB., JM MURKIN, MD, KY CHONG, MD. DEPARTMENT OF ANAESTHESIA, UNIVERSITY HOSPITAL, LONDON, CANADA.

INTRODUCTION: Arterial $PaCO_2$ is one of the strongest physiological modulators of cerebral blood flow(CBF). When considering the use of propofol in neuroanaesthesia, it is important to know if it alters cerebrovascular CO_2 reactivity. The purpose of this study was to evaluate the relationship between CBF and changes in $PaCO_2$ when propofol is the sole anaesthetic agent.

METHODS: Following institutional approval and after obtaining informed written consent, five unpremedicated ASA 1 and 2 patients scheduled for elective surgical procedures were enrolled. Anaesthesia was induced with propofol 2.0-3.0 mg/kg. After endotracheal intubation, maintenance of anesthesia was conducted with an air/oxygen mixture (FiO_2 0.4) and an intravenous propofol infusion at a variable rate of 100-200 ug/kg/min. The propofol infusion was commenced at 200 ug/kg/min and later decreased incrementally depending on the depth of anaesthesia as determined by clinical signs. Intraarterial pressure and nasopharyngeal temperature were monitored.

CBF was measured by the intravenous ^{133}Xenon technique using 5 scintillation counters over each hemisphere. The clearance curves were analysed by height over area analysis. CBF was measured four times: (1) when the patient was awake,(2) when the patient was anaesthesized, E_tCO_2 same as awake,(3) when E_tCO_2 was decreased to 30 mmHg, (4) when E_tCO_2 was increased to 50 mmHg. During each CBF measurement, arterial blood gases, haemoglobin, mean arterial blood pressure were determined. Concomitant with each CBF, auditory and somatosensory evoked potentials were monitored. An ANOVA for repeated measures was used for statistical analysis. A $p<0.05$ was considered significant. The results are mean ± SD.

RESULTS: Five patients, aged 32.2± 5.8 years, were studied without complications. The mean blood pressure dropped by 20% after induction of anaesthesia and remained stable thereafter. There were no changes in haemoglobin or temperature during the study. The effect of induction of anaesthesia and of manipulation of $PaCO_2$ are shown in the figure. CBF dropped significantly by 50% on induction of anaesthesia. The slope of the CBF-$PaCO_2$ relationship was 0.89ml/100gm/min/mmHg. There was no statistically significant changes in the evoked potentials at any time.

DISCUSSION: We have demonstrated that CBF responsiveness to changes in $PaCO_2$ between 27-50mmHg remains intact during propofol anaesthesia in healthy individuals.

Our absolute CBF values are similar to those previously reported during fixed dose propofol anaesthesia but are lower than those we have recorded during propofol-N_2O anaesthesia[1,2]. Similarly, the slope of CBF-$PaCO_2$ relationship is less than during propofol-N_2O anaesthesia. These differences may be explained by either the cerebrovasodilating effect of N_2O or the quantity of propofol used. During hypocapnia, CBF was low, but there were no changes clinically or in the evoked potentials to suggest ischaemia. Propofol may therefore reduce the CBF threshold for cerebral ischaemia as assessed by evoked potentials.

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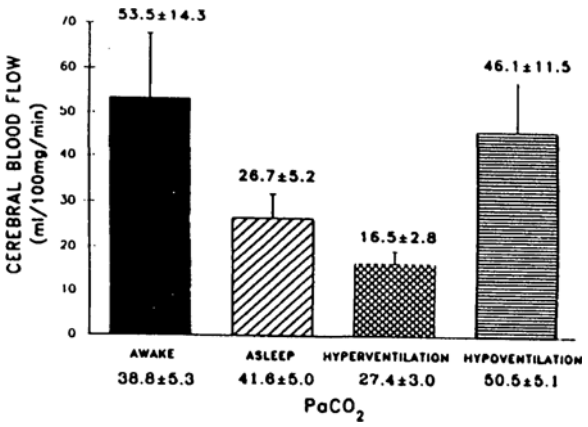
Supported by ICI Canada.



COMBINED *IN VITRO* ELECTROPHYSIOLOGICAL AND NEUROCHEMICAL ASSESSMENT DURING HYPOXIA IN THE GUINEA PIG HIPPOCAMPUS.

D. H. Penning*, H. El-Beheiry*, J. F. Brien and J. W. Goh.
Departments of *Anaesthesia and Pharmacology & Toxicology,
Queen's University, Kingston, Ontario, Canada.

Introduction

Hypoxia causes the interruption of synaptic transmission as measured in the stereotyped loss of the population spike recorded *in vitro* in the hippocampal slice preparation[1]. Extracellular glutamate concentration increases in the hippocampus during ischemia[2], which is thought to lead to neuronal death via an excitotoxic mechanism. In this study, the objective was to simultaneously monitor synaptic activity and release of the excitatory amino acid (EAA) neurotransmitter glutamate in the hippocampus of the guinea pig.

Methods

Adult Dunkin-Hartley strain guinea pigs were cooled on ice and anesthetized with 2% halothane. The hippocampus was then rapidly removed, transversely sectioned into slices 400 μm thick and placed in ice cold artificial cerebrospinal fluid (ACSF). The composition of ACSF is (in mM): NaCl 120; KCl 3.1; NaH_2PO_4 1.3; $NaHCO_3$ 26; $MgCl_2$ 2; $CaCl_2$ 2 and Dextrose 10 (pH maintained at 7.4 while bubbled with 95% O_2/5% CO_2). The slices were sandwiched between two nylon meshes and allowed to equilibrate at room temperature for 2 hours. Subsequently, the slices were placed in a submerged slice recording chamber and constantly perfused with oxygenated ACSF at a rate of 2.5 ml/min. The temperature of the chamber was increased to 35 ± 0.2°C and maintained throughout the course of the experiment. Population spikes were evoked by stimulation of stratum radiatum and recorded in the pyramidal cell body layer of the CA_1 region. ACSF was sampled (600 μl) and the glutamate concentrations were determined by a reverse-phase HPLC procedure with fluorescence detection of the thio-substituted isoindole derivatives formed by pre-column derivatization with o-phthalaldehyde and β-mercaptoethanol.

The protocol consisted of extracellular recording and ACSF sampling following the two hour equilibration period, during hypoxia of 10 minutes duration (by switching to ACSF bubbled with 95% N_2, 5% CO_2) and during reoxygenation.

Discussion

Measurement of extracellular population spikes and release of glutamate provides a combined electrophysiological and neurochemical index of the response of the CA_1 hippocampal neurons to direct exposure to hypoxia. In this study, there was rapid loss of the population spike, which was preceded by an increase in the concentration of glutamate. The presynaptic volley was maintained during 10 minutes of hypoxia. There was a 65% increase in the population spike amplitude during reoxygenation, but there was no associated increase in glutamate release.

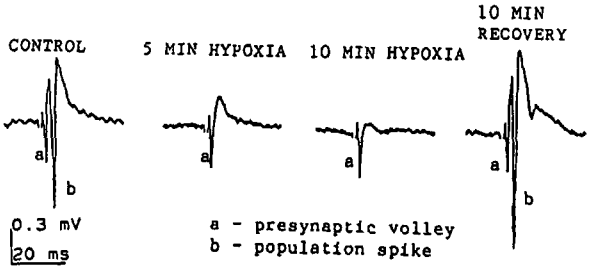
Results

TABLE

	Pop Spike (% Control) (n = 7)	Glutamate (% Control) (n = 4)
Hypoxia (min)		
1	106 ± 10	151 ± 37
3	37 ± 17	152 ± 34
5	2 ± 2	109 ± 31
10	0	82 ± 10
Recovery (min)		
1	11 ± 5	112 ± 34
3	64 ± 19	88 ± 11
5	97 ± 15	88 ± 10
10	125 ± 16	87 ± 9
20	165 ± 39	93 ± 11

Values reported are mean ± SEM

FIGURE



Conclusions

This model provides a means to temporally associate electrophysiological events and neurotransmitter release. Experiments are ongoing which will examine the effects of 1) brain maturation and 2) anaesthetic drugs in this model.

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CLINICAL CONCENTRATIONS OF HALOTHANE DO NOT INCREASE RESTING CALCIUM LEVELS IN CULTURED DRGs

R. Arellano MD, J. Correa B.Sc, L. Fedorko MD PhD
Department of Anaesthesia, University of Toronto, Toronto, Ontario

INTRODUCTION

One hypothesis of general anaesthesia proposes that anaesthetic agents depress CNS function by hyperpolarizing neurones [1]. Krnjevic has shown that intracellular injection of calcium hyperpolarizes neurones by increasing potassium conductance and therefore it has been suggested that general anaesthetic agents may increase intracellular calcium $[Ca^{++}]_i$ [2]. No study to date has measured the response of intracellular calcium in neurones exposed to clinical concentrations of inhalational anaesthetics such as halothane. Fluorescent calcium indicators such as Indo-1 AM loaded into neurones provide a method to measure intracellular calcium directly [3].

PURPOSE

This study was designed to determine whether or not clinical concentrations of halothane increase basal intracellular calcium levels in cultered rat dorsal root ganglia neurones (DRGs) using the calcium indicator Indo-1 AM.

METHODS

Dorsal root ganglia were obtained from 5-9 day old Wistar Rats. Neurones were isolated by enzymatic digestion and dispersed cells grown on coverslips for 24 hrs. Cells were loaded with 4 μm of cell permeant Indo-1 acetoxymethyl ester (Indo-1 AM) by incubation for 1 hr at 37^0C. Experiments were performed at 37^0C. Fluorescence was recorded in a Perkin Elmer LD spectroflurometer (341 nm excitation/410 nm emission). Solutions (140 NaCl, 10 HEPES, 5.0 D-glucose, 1.0 Mg Cl_2, 1.5 $CaCl_2$, 3.0 KCl pH 7.40 OSM 285-295) with or without 1.0 mM or 1.5 mM halothane (thymol free) were used to perfuse the cells during the experimental protocol. Fluorescence was calibrated by permeabilization of cells to calcium with the ionophore ionomycin (10 μm) followed by Mn Cl_2 (3mM).

RESULTS

Resting calcium levels did not increase when neurones were exposed to 1.0 mM (3.16 vol/vol %) halothane (see Table). A small but significant increase of resting calcium from 156.7 nm to 182.5 nm was observed when cells were exposed to 1.5 mM halothane (4.74 vol/vol %) ($p < 0.05$).

CONCLUSION

Halothane is capable of increasing intracellular calcium in neuronal tissue, but only in supra-clinical concentrations. Previous studies demonstrate that clinical concentrations of halothane induce neuronal hyperpolarization in vitro. Results from this study suggest that this effect is not mediated by increased intracellular calcium.

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TABLE

	Baseline $[Ca^{++}]_i$ (mean± S.D.)	Δ $[Ca^{++}]_i$ with exposure (mean± S.D.)
1.0 mM (N=6) Halothane	152.5 ± 62.8	1.0 ± 2.4
1.5 mM (N=5) Halothane	156.7 ± 57.1	25.8 ± 14.0

FDP IMPROVES PCR AND ATP RESTORATION FOLLOWING CEREBRAL ISCHEMIA\HYPOXIA

R. Arellano MD, Z. Liu MD, L. Fedorko MD PhD
Department of Anaesthesia, University of Toronto, Toronto, Ontario

INTRODUCTION

Severe cerebral ischemic\hypoxic stress induces a series of events that ultimately lead to irreversible cellular damage. During the early phase of injury intracellular phosphocreatine (PCr) and adenosine triphosphate (ATP) decline precipitously. Farias et al. (1) reported improved neurological function and neuronal histology following brief cerebral ischemia\hypoxia in rabbits pretreated with intravenous fructose-1,6-diphosphate (FDP). It has been hypothesized that elevated intracellular FDP stores sustain glycolysis and thereby increase ATP during anaerobic metabolism leading to improved neurologic outcome (2). Therefore we investigated the effects of FDP on cerebral PCr and ATP during hypoxia\ischemia and restoration of normoxia\reperfusion.

METHODS

300-500 gm Wistar rats were anaesthetized with halothane, tracheostomized and mechanically ventilated. MABP, HR and tympanic membrane temperature were continuously recorded. Both carotid arteries were exposed and anaesthesia maintained with $N_2O\backslash O_2$, 70\30% and pancuronium iv. Ischemia\hypoxia was induced by tightening carotid sutures and reducing FIO_2 to 10%. Carotid sutures were released and FIO_2 increased to 30% to establish reperfusion\reoxygenation. Animals were randomized to three treatment groups: 1) 5% FDP (50 mg\kg) iv bolus before ischemia\hypoxia, 2) an equivalent volume of saline before ischemia\hypoxia or, 3) 5% FDP (50 mg\kg) at the beginning of reperfusion\reoxygenation. PCr and ATP were measured at baseline, 30 min hypoxia\ischemia and 60 min reperfusion by HPLC analysis of lyophilized parietal cortical tissue (3).

RESULTS

PCr levels were reduced to <5% of baseline values during ischemia\hypoxia (fig 1). Pretreatment with FDP did not prevent the marked depletion of PCr however, it provided significant benefit during reperfusion; PCr levels returned to >75% of baseline whereas post-ischemia\hypoxia FDP and control groups remained depressed at <50% ($p<0.05$ for FDP pretreatment vs FDP post-treatment or control). A similar pattern evolved for ATP (fig 2). During ischemia\hypoxia, ATP levels were reduced to 10% of baseline. The FDP group also demonstrated a marked depletion of ATP. During reperfusion, pre-ischemia\hypoxia FDP treated animals recovered to >75% of baseline values whereas post-ischemia\hypoxia FDP treatment and control groups showed blunted recovery to <50% of baseline ($p<0.05$ for FDP pretreatment vs FDP post-treatment or control).

DISCUSSION

The results of this group of experiments suggest that FDP is ineffective in preventing depletion of PCr and ATP during severe ischemia\hypoxia, but is valuable in reestablishing high energy phosphate stores during reperfusion\reoxygenation.

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FIGURE 1

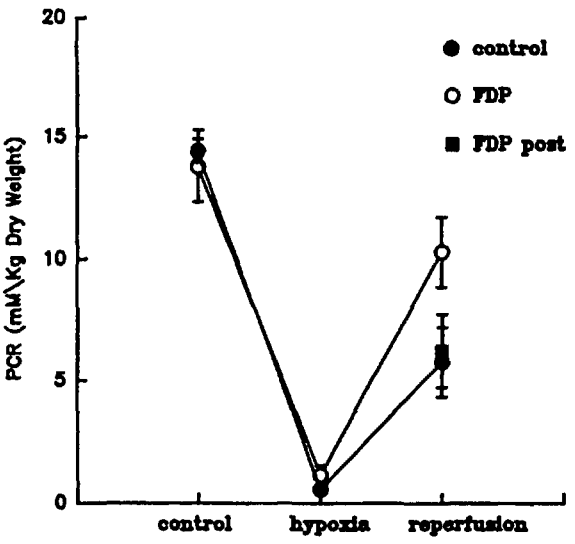
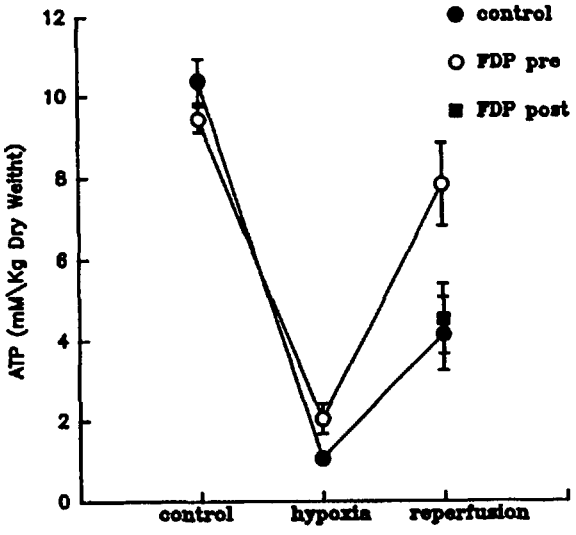


FIGURE 2



REDUCED PERIOPERATIVE BLOOD LOSS IN ORTHOTOPIC LIVER TRANSPLANTATION WITH TRANEXAMIC ACID PROPHYLAXIS

JF Boylan MB , AN Sandler MB , H Nierenberg BScN, PA Sheiner MD ,
PD Greig MD, GM O'Leary MB, SJ Teasdale MD, MFX Glynn MD
Departments of Anaesthesia, Surgery and Haematology, The Toronto Hospital, Toronto, Ontario

Introduction: Orthotopic liver transplantation (OLT) is frequently complicated by major blood loss, with the risks of massive tranfusion and reoperation. The recent documentation of accelerated fibrinolysis[1] during OLT suggests a potential therapeutic role for antifibrinolytic therapy. Aprotinin prophylaxis has already been shown to reduce fibrinolysis-related blood loss in both high-risk cardiac surgery[2] and OLT[3], while tranexamic acid (TA) prophylaxis in cardiac surgery is associated with significantly decreased blood loss.[4] We present our preliminary results with TA in a series of first-time OLT recipients. We hypothesized that TA use would be associated with decreased perioperative blood product use.

Patients and methods: Over the period March to August 1991, 20 patients undergoing first-time OLT for post-necrotic cirrhosis (NECR) resulting from chronic active hepatitis, either infective, alcoholic or cryptogenic, and 10 patients with cholestatic liver disease (primary biliary cirrhosis and sclerosing cholangitis, NON-NECR) received a TA infusion at 40 mg.kg.hr^{-1} from induction of anaesthesia to the time of hepatic revascularization, when heparin-dipyridamole infusion commenced. A standard technique of axillofemoral venovenous bypass was used in all patients. We recorded the use of red cells, plasma, cryoprecipitate and platelets in the first 24 postoperative hours.

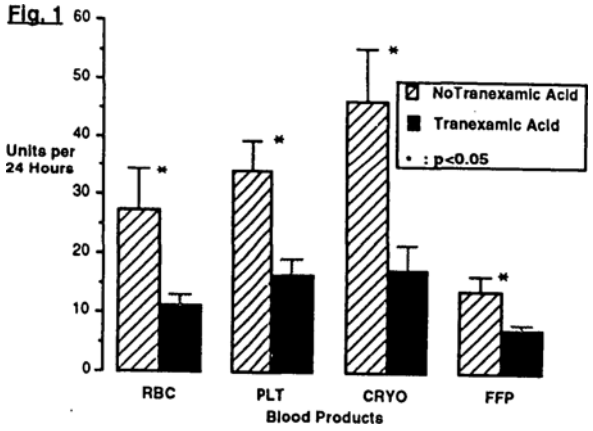
Patients receiving TA were compared with a group of 25 (19 NECR, 6 NON-NECR) consecutive patients with similar diagnoses and perioperative management who had undergone first-time OLT in the previous six months. Demographic data were analyzed using Students *t* test for unpaired data; blood product utilization was analyzed using the Mann-Whitney U test.

Results: There were no demographic differences between patients receiving TA and controls. (Table) Overall blood product usage was significantly reduced ($P < 0.05$) with TA administration. There were significant decreases in 24 hour utilization of red cells ($P < 0.05$), plasma ($P < 0.04$), platelets ($P < 0.01$) and cryoprecipitate ($P < 0.01$), in NECR patients receiving TA compared with controls. (Figure) Perioperative blood product usage was reduced from 2.5 ± 0.6 (mean ± SEM) to 1.0 ± 0.2 blood volumes ($P < 0.02$). A small, non-significant decrease in blood product usage was observed in NON-NECR patients receiving TA. No episode of hepatic arterial thrombosis was recorded with TA use. A single patient receiving TA required prostaglandin E2 therapy for impaired liver function on day 3; doppler studies suggested maintained hepatic perfusion.

TABLE 1

	TA	No TA
Age (yr)	46.4 ± 2.6	50.7 ± 2.4
Wt (kg)	71.6 ± 2.8	69.1 ± 3.4
Haemoglobin (g/L)	114 ± 4.6	105.6 ± 3.6
Preop PT (sec)	18.5 ± 1.0	17.9 ± 1.2

Fig. 1



Discussion: In contrast to the findings of other workers,[3,5] prophylactic TA administration in high-risk patients was associated with a 50% decrease in overall blood product use, similar to that reported recently with aprotinin. The use of recent controls and the absence of major changes in technique suggest that TA was a major factor in the observed reduction. A randomized double blinded study of high risk patients is in progress.

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PROPOFOL ACTIVATES INHIBITORY CHLORIDE CURRENT IN HIPPOCAMPAL NEURONS.

B.A. Orser FRCP(C), L-Y. Wang MSc., J.F. MacDonald PhD.
Dept. Anaesthesia, Sunnybrook Health Science Center,
Dept. Physiology, University of Toronto, Toronto, Ontario

Introduction: Propofol (2,6-diisopropylphenol) is a recently available alkylphenol used for induction and maintenance of general anaesthesia. Despite its clinical popularity, little is known about propofol's cellular mechanisms of action. The chemical structure of propofol is unlike any other anaesthetic and its effects on excitatory and inhibitory neurotransmitter systems remain to be defined. We used the patch-clamp method to examine the influence of propofol on ion channel activity in hippocampal neurons.

Methods: Embryonic mouse hippocampal neurons were dissociated and maintained in culture as previously described[1]. Conventional whole-cell and nystatin perforated patch recording techniques were used[2]. The extracellular solution contained: TTX 300 nM, glycine 3 μM and pipette solution (mM): Cs_2SO_4 90, CsCl 30, HEPES 10, EGTA 11, $CaCl_2$ 1, $MgCl_2$ 2, TEA 10. Propofol was prepared from Diprivan^R (propofol 10mg/ml in soya emulsion) and the vehicle solutions from Intralipid^R (100mg/ml). Cells were voltage clamped (-60mV) and currents were amplified using an AXO-PATCH amplifier. Data was filtered at 2kHz then stored on FM tape and paper-trace recorder. Drugs were applied to the external cell membrane using a rapid perfusion system. Currents were measured using the P-Clamp 5.51 (Axon Incorp.) program.

Results: Propofol studied at clinically effective doses (1μM-10mM)[3] activated an inward current in all hippocampal neurons examined (n=6) Fig.1. This effect was dose-dependent and could be depressed by the $GABA_A$ channel blocker bicuculline (100μM). The vehicle failed to elicit spontaneous currrents or potentiate GABAergic activity. The excitatory amino acid antagonist amino-phosphonovaleric acid (DL-APV) potentiated propofol activated currents. Propofol induced currents likely resulted from activation of Cl^- permeable ion channels as the reversal potential (-25mV) was close to the Cl^- equilibrium potential predicted by the Nernst Equation and similar to the reversal potential for $GABA_A$ activated inward current Fig. 2.

Discussion: The clinical effects of anaesthetics are thought to result from depression of excitatory neurotransmission (eg. glutamate) or potentiation of inhibitory transmitter systems (eg. GABA). These data indicate that propofol activates inhibitory Cl^- currents in hippocampal neurons in the absence of GABA. Under normal physiologic conditions, the opening of chloride channels produces inward Cl^- flux, cellular hyperpolarization and neuronal inhibition. It is not known if propofol binds to a site on the GABA-receptor-channel macrocomplex (similar to benzodiazipines or barbiturates) or activates a novel sub-population of channels. Propofol has been previously reported to induce chloride currents and augment $GABA_A$ currents in bovine chromaffin cells[4]. Activation of chloride channels may contribute to propofol's anaesthetic properties. Potentiation of propofol induced currents by APV suggests an interaction between excitatory amino acids and propofol mediated neuronal inhibition.

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Acknowlegements: This project was supported by a CAS Research Award and an MRC grant to the "Nerve and Synapse Group". Dr. Orser is an MRC research fellow.

Fig. 1 Propofol Induced Inward Currents.

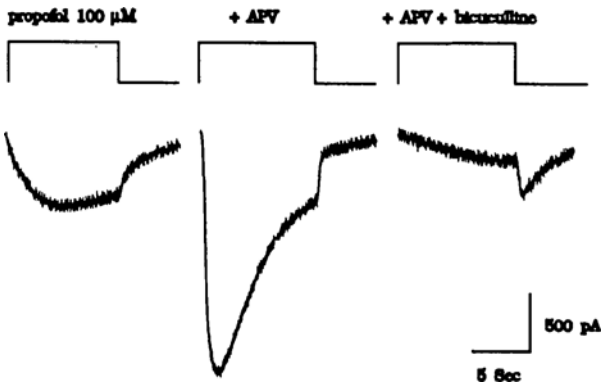
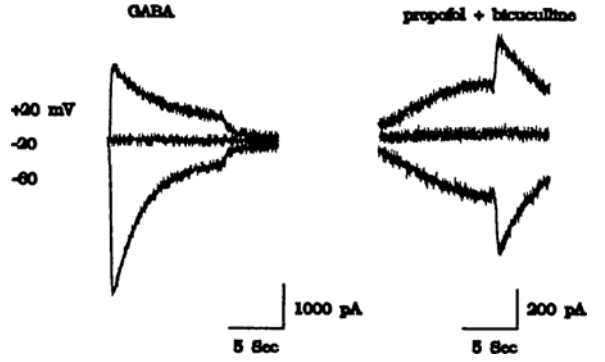


Fig. 2. Propofol and GABA Currents Reverse at the same Potential.



POTENTIATION OF INTRATHECAL (I.T.) DEXMEDETOMIDINE ANTINOCICEPTION BY I.T. METHOXAMINE IN THE RAT: EVIDENCE FOR AN ENDOGENOUS OPIOID LINK

C.W. Loomis Ph.D., K.D. Arunachalam Ph.D., D. Vyas Ph.D., B. Milne M.D.
School of Pharmacy, Memorial University of Newfoundland, St. John's, AIB 3V6 and Department of Anaesthesia, Faculty of Medicine, Queen's University, Kingston, K7L 3N6. (Supported by the Medical Research Council of Canada)

INTRODUCTION

Antinociception with intrathecal (i.t.) α-agonists is mediated by α_2-adrenoceptors in the spinal dorsal horn[1,3]. The role of spinal α_1-adrenoceptors has generally been discounted based on the weak activity of spinal α_1-selective agonists in behavioural and electrophysiological studies of nociception. However, potentiation between the antinociceptive mechanisms coupled to spinal α_1- or α_2-adrenoceptors has not been determined. To investigate this hypothesis, i.t. methoxamine (MX) and dexmedetomidine[2] (DX) were used as selective α_1- and α_2-agonists in the spinal cord of the rat. That such an interaction might involve the activation of methionine-enkephalin (Met-Enk) containing spinal neurons was also investigated.

METHODS

Under halothane anaesthesia, male, Sprague-Dawley rats (250-400 g) were implanted with i.t. catheters (L1 termination). Following recovery (minimum 4 days), rats with normal baseline responses and normal motor function were used. Drugs were injected through the i.t. catheter in a volume of 5 μl. Antinociception was determined by the tail-flick (TF) and paw pressure withdrawal (PP) tests, and data are expressed as maximum percent effect (% MPE). In a separate groups of rats treated with i.t. DX+MX (high dose twice daily for 3 days), spinal cords were fixed in situ, removed and examined by light microscopy (gross morphology and immunocytochemistry) for evidence of spinal neurotoxicity.

RESULTS

I.t. DX produced significant, reversible, dose-dependent antinociception in the PP and TF tests (Figure 1). The peak effect was observed 30 min after i.t. injection and the duration was 2 h. Addition of a fixed (10 μg) threshold (< 10% MPE) dose of i.t. MX to DX resulted in an 8-fold, parallel shift to the left of the dose-response curve (DRC; Figure 1). The interaction between MX and DX was significantly antagonized by i.t. prazosin (10 μg; α_1-antagonist) or i.t. Wyeth 27127 (0.5 μg; α_2-antagonist), and by i.t. naloxone (30 μg) (Figure 2). I.t. pretreatment with antiserum to Met-Enk, but not antiserum preabsorbed with Met-Enk, significantly attenuated the antinociceptive effect of DX+MX. In contrast, pretreatment with i.t. Schering 32615 (an inhibitor of the Met-Enk catabolic enzyme, neutral endopeptidase), produced a further 6-fold shift to the left of the DRC as compared to that in vehicle-pretreated rats (Figure 1). Animals injected with i.t. DX (10 μg) + MX (10 μg) twice daily for 3 days exhibited no inflammation, haemorrhage, or necrosis in the spinal cord, and there were no changes in substance P-, or calcitonin gene related peptide (CGRP)-like immunoreactivity in primary afferent fibers or motor neurons as compared to vehicle controls.

DISCUSSION

The results of this study indicate that a threshold dose of i.t. MX significantly potentiates the selective and reversible effect of i.t. DX in the rat TF and PP tests. This potentiation is not due to a prolonged duration of action of i.t. DX (e.g. reduced clearance of DX from the spinal subarachnoid space). Rather, it appears to be mediated, in part, by the release of Met-Enk from spinal cord neurons, consistent with the well established potentiation of spinal opioid analgesics by α_2-agonists[3]. Repeated i.t. adminstration of high dose DX+MX produced no evidence of spinal neurotoxicity. A low dose combination of an α_1- and α_2-selective agonist may prove useful in optimizing noradrenergic spinal analgesia in humans.

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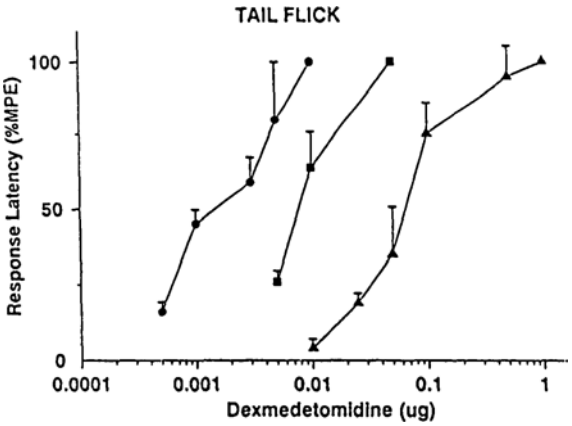

Figure 1. Dose response curves for i.t. DX alone or i.t. DX + MX (10 μg) in vehicle pretreated rats, and i.t. DX + MX (10 μg) in i.t. SCH 32615 (75 μg)-pretreated rats in the TF test. Each point represents the mean ± SD of 5-10 rats, determined 30 min after i.t. DX+MX injection.

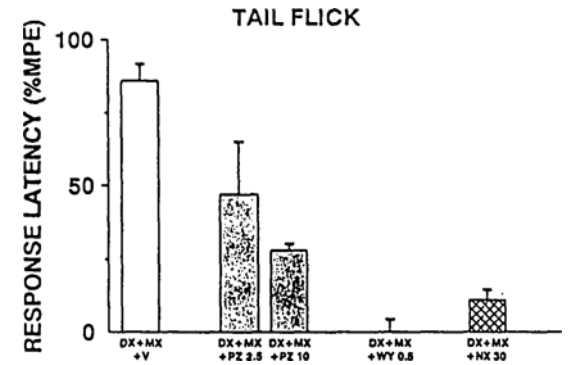

Figure 2. Effect of pretreatment with i.t. prazosin (PR; 2.5 or 10 μg), Wyeth 27127 (WY; 0.5 μg) or naloxone (NX; 30 μg) on i.t. DX (0.025 μg) + MX (10 μg)-induced antinociception in the TF test. Rats were pretreated 10 min before i.t. DX+MX, and each point represents the mean ± SD of 5-10 rats, determined 30 min after DX+MX injection.

THE EFFECT OF AMRINONE AND DOBUTAMINE ON THE OXYHAEMOGLOBIN DISSOCIATION CURVE: AN IN VITRO EVALUATION

Daniel Gagnon, M.D., Josée Lavoie, M.D., Jean-Yves Dupuis, M.D.

Centre Hospitalier Universitaire de Sherbrooke, 3001 Ave. N., Fleurimont, Québec, J1H 5N4

Amrinone is a phosphodiesterase-III inhibitor with vasodilating and positive inotropic effects. Results from a recent study suggest that the administration of amrinone at the end of cardiopulmonary bypass (CPB) following cardiac surgery may increase mixed venous oxygen saturation ($S\bar{v}O_2$)without significant effect on haemodynamics.[1] To explain this finding, we postulated that amrinone could cause a right shift of the oxyhaemoglobin dissociation curve. This assumption was based on the fact that other hypotensive agents have been found to increase affinity of haemoglogin for oxygen.[2] In order to test our hypothesis, we studied the effect of amrinone on the affinity of haemoglobin for oxygen in vitro. The effect of dobutamine, another inodilator often used after cardiac surgery, was also studied.

METHODS

The study was approved by the hospital Research Ethics Committee. Six healthy non-smoking volunteers participated in this study. Each gave 50 ml of blood which was collected through an antecubital vein, mixed with 500 units of heparin and placed on ice until utilization (≈ 30 min). For each donor, an oxyhaemoglobin dissociation curve was made in three different and consecutive in vitro conditions: 1) in absence of drug (control); 2) in presence of amrinone at a concentration of 5 µg/ml, which corresponds to blood levels found after a 0.75 mg/kg bolus during CPB; 3) in presence of dobutamine at a concentration of 250 ng/ml, corresponding to levels found during a 10 µg/kg/min infusion in heart failure patients. The sequence of the experiments was randomly modified from one subject to the other.

Aliquots of blood (5 ml) were placed in two tonometers (Instrumentation Laboratory Model IL 237). A gas mixture containing 5% CO_2 and 95% O_2 was used in one tonometer, and a mixture of 5% CO_2 and 95% N_2 was used in the other one. After equilibration for 15 minutes, variable amounts of blood were then collected from the tonometers and mixed in order to obtain samples of variable oxygen partial pressure in the range of 10 to 90 mmHg. For each sample, the PO_2 was determined using a blood gas analyzer (Model IL 1306) and the oxyhaemoglobin saturation was measured with a Co-Oximeter (IL 282). The measured PO_2 was corrected to pH 7.40 by using the equation:

$$\text{Log}_{10} P_1O_2 = \text{Log}_{10} P_2O_2 + [-0.48 \times (7.40 - \text{pH})]$$

where P_1O_2 = corrected PO_2 and P_2O_2 = observed PO_2. Nine points were used to plot each of the control and drug curves. The P_{50} and P_{70} of each volunteer were then determined from these curves.

The number of participants was selected in consideration of the standard deviation found in the study and of an arbitrary significant difference in P_{50} equal to 2.5 mmHg. This was done in order to have a power of 0.80, and an alpha of 0.05. The values found with amrinone and dobutamine were compared with the control values using the paired Students' t-test.

RESULTS

The P_{50} and P_{70} values for the control, amrinone and dobutamine groups are given as mean ± SD in the Table. No significant differences were found between drugs and control values.

DISCUSSION

These results indicate that neither amrinone nor dobutamine affect the affinity of haemoglobin for oxygen in vitro. However, the present study cannot exclude the possibility of an in vivo effect of amrinone or dobutamine on the oxyhaemoglobin dissociation curve in CPB exposed blood. Further study is needed to explain the effect of amrinone on $S\bar{v}O_2$ found in the previously quoted study.[1] A more efficient energy utilization, as suggested by the authors, or a peripheral shunt effect could also be the mechanism underlying the high SvO_2 values found by these authors after CPB.

TABLE

Groups	P_{50}	P_{70}
Control	26.3 ± .8	37.1 ± 1.3
Amrinone	26.8 ± 1.1	37.3 ± 1.3
Dobutamine	26.6 ± .7	37.2 ± 1.1
P value	N.S.	N.S.

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ALFENTANIL PHARMACOKINETICS DURING TOTAL INTRAVENOUS ANAESTHESIA WITH PROPOFOL IN PATIENTS UNDERGOING PERIPHERAL VASCULAR SURGERY

D.R. Miller, M.D., R.J. Martineau, M.D., D. Greenway, Ph.D., L. Olivaris, B.Sc., K. Hull, R.N., M. Tierney, M.Sc., J.E. Wynands, M.D.
Departments of Anaesthesia, Clinical Biochemistry and Pharmacology, Ottawa General Hospital; The Ottawa Heart Institute; and The University of Ottawa

INTRODUCTION: We have previously determined opiate requirements for patients undergoing aortic reconstructive surgery during N_2O-alfentanil anaesthesia.[1] However, administration of a variable rate alfentanil (ALF) infusion during aortic surgery must take into consideration the longer $t_{1/2}\beta$ of ALF in this older patient population (3.7±2.6 hrs).[2] Recently, it has been suggested that ALF pharmacokinetics may also be altered in the presence of a continuous infusion of propofol (PRO), resulting in lower ALF doses.[3] We undertook to study the pharmacokinetics of ALF during total intravenous anaesthesia (TIVA) using PRO, compared with ALF during balanced anaesthesia using N_2O in patients undergoing peripheral vascular surgery.

METHODS: Ten ASA Class III subjects between 50-75 years of age, who were scheduled to undergo peripheral vascular surgery, entered this study after giving written consent to the institutionally-approved protocol. Following premedication with oral diazepam 0.15 $mg \cdot kg^{-1}$, all subjects received a two-stage loading dose of ALF 50 $\mu g \cdot kg^{-1}$, followed by variable rate infusion between 0.25 and 1.25 $\mu g \cdot kg^{-1} \cdot min^{-1}$. In combination with PRO infused at 100 $\mu g \cdot kg^{-1} \cdot min^{-1}$ in O_2 or 70% N_2O in O_2, small boluses of ALF (7.5 $\mu g \cdot kg^{-1}$) were given to maintain systolic blood pressure and heart rate within 20% of each patient's baseline value. The infusion rate of ALF was progressively decreased at intervals no less than 15 minutes once a stable level of anaesthesia had been maintained, and the infusion was discontinued 15 min prior to the end of surgery. Arterial blood samples for determination of ALF serum concentrations were drawn at multiple time periods during surgery, and at 0.5, 1, 2, 3, 4, 6, 8, 10, 12, 18 and 24 hours after discontinuation of the infusion. Plasma was separated and stored for later analysis using HPLC (assay sensitivity = 2 $ng \cdot ml^{-1}$, with a coefficient of variation of 4.6% at a concentration of 175 $ng \cdot ml^{-1}$). Individual data were analyzed using non-linear regression, and were then averaged to provide between-group comparisons of pharmacokinetic parameters.

RESULTS: The groups were similar with respect to age, weight, sex distribution, and durations of ALF infusion (2.3±0.4 h and 2.3±0.5 h). The ranges and variability of ALF serum concentrations intraoperatively are displayed in the Figure (upper panel). After termination of the infusions, there was a rapid decline in ALF concentrations in both groups resulting from redistribution, followed by a slower rate of decay as drug elimination continued (lower panel). The clearance rate of ALF was less, and $t_{1/2}\beta$ was greater in the PRO group compared with the N_2O group.

DISCUSSION: Despite the older age of our study population, ALF pharmacokinetics were similar to values reported elsewhere.[4] During TIVA for peripheral vascular surgery, PRO may prolong the $t_{1/2}\beta$ of ALF by decreasing clearance. However, differences in ALF requirements or concentrations to supplement hypnosis with either PRO or N_2O could not be demonstrated.

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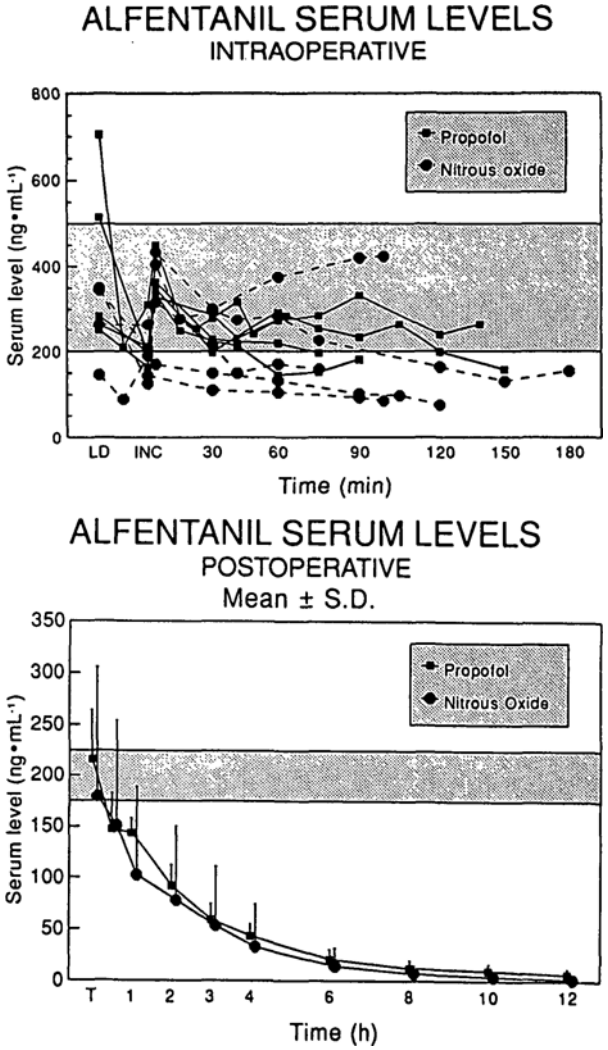
TABLE: ALFENTANIL PHARMACOKINETICS

GROUP	Propofol	Nitrous oxide
Cl ($mL \cdot kg^{-1} \cdot min^{-1}$)	2.56±0.21	4.20±0.23
Vd_{area} ($L \cdot kg^{-1}$)	0.48±0.09	0.57±0.29
$t_{1/2}\beta$ (h)	2.20±0.48	1.62±0.19



Serum concentrations of ALF intraoperatively (upper panel) and postoperatively (lower panel). The shaded area in the upper panel represents the normal therapeutic range of ALF concentrations in conjunction with 70% N_2O, and in the lower panel, the range for the threshold below which spontaneous ventilation occurs.

A COMPARISON OF ACCUMULATION PROFILES AND REVERSAL CHARACTERISTICS ASSOCIATED WITH INFUSIONS OF ATRACURIUM AND VECURONIUM DURING BALANCED ANAESTHESIA

R. Martineau, M.D., B. St-Jean, M.D., J. Kitts, M.D., D. Miller, M.D.
K. Hull, R.N., P. Lindsay, R.N., M. Curran, M.D.
Departments of Anaesthesia, Ottawa General and Ottawa Civic Hospitals, and The University of Ottawa

INTRODUCTION: Neuromuscular blocking drugs administered by infusion should ideally have limited tendency for accumulation, and should be easy to reverse upon discontinuation. The infusion requirements of both atracurium (ATR) and vecuronium (VEC) have previously been established.[1] However, despite the very different elimination half lives of these two drugs, ($t_{1/2}\beta$ = 20 and 70 minutes for ATR and VEC, respectively[2]), little attention has been focused on the relative potential for vecuronium to accumulate during prolonged infusions. A randomized, double-blind study was undertaken to compare the accumulation profiles, and reversal characteristics of prolonged infusions of ATR and VEC in an older patient population.

METHODS: Fifty patients who were free of neurologic or neuromuscular disorders, and were scheduled to undergo long surgical procedures under general anaesthesia (>2 hours duration), were enroled. All subjects were between 50-75 years of age, and gave written informed consent to the institutionally-approved protocol. Patients with neuromuscular diseases or those taking drugs known to interact with muscle relaxants were excluded. During balanced anaesthesia with alfentanil and nitrous oxide, patients in the ATR group (n=25) received a loading dose of atracurium 0.25 $mg \cdot kg^{-1}$, followed by an infusion initially set at 5.0 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Patients in the VEC group (n=25) received a loading dose of vecuronium 0.05 $mg \cdot kg^{-1}$, followed by an infusion of 1.0 $\mu g \cdot kg^{-1} \cdot min^{-1}$. During surgery, the infusions of both ATR and VEC were titrated to maintain 90-95% first twitch suppression. Supramaximal train-of-four stimuli were recorded over the first dorsal interosseous muscle using an evoked electromyogram. Upon completion of surgery, the infusions were discontinued, and the neuromuscular block was reversed with neostigmine 40 $\mu g \cdot kg^{-1}$ and atropine 15 $\mu g \cdot kg^{-1}$. Data were analyzed using repeated measures analysis of variance and the Student's *t*-test, with significance assumed when $P<0.05$.

RESULTS: The durations of infusion were similar for the two groups (164±42 and 183±67 min for ATR and VEC, respectively). The mean infusion rates of ATR remained between 4.0±0.7 and 5.0±1.0 $\mu g \cdot kg^{-1} \cdot min^{-1}$ throughout the study period (Figure). In contrast, a progressive and significant decrease ($P<0.05$) in the infusion rate of vecuronium, from 1.0 down to 0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$, was required after the second hour of infusion (Figure). Despite the progressive decrease in infusion requirements with vecuronium, the times to recover a TOF ratio >70% following administration of neostigmine were similar for the two groups (13.4±4.9 and 14.4±8.0 minutes for ATR and VEC, respectively).

DISCUSSION: Although the patterns of recovery following single doses of ATR and VEC are similar, recovery occurs primarily during the elimination phase for atracurium, while redistribution contributes more significantly to recovery for vecuronium. With larger doses or long infusions of VEC, the plasma time-concentration curve changes such that a progressively longer time to recovery will be observed.[3] This phenomenon occurs to a much lesser extent with ATR because of its shorter $t_{1/2}\beta$, and accounts for the absence of accumulation which we observed during infusion of this drug. Despite these differences, infusion of both ATR and VEC, when adjusted to maintain 90-95% twitch suppression, result in similar times to recovery following administration of neostigmine.

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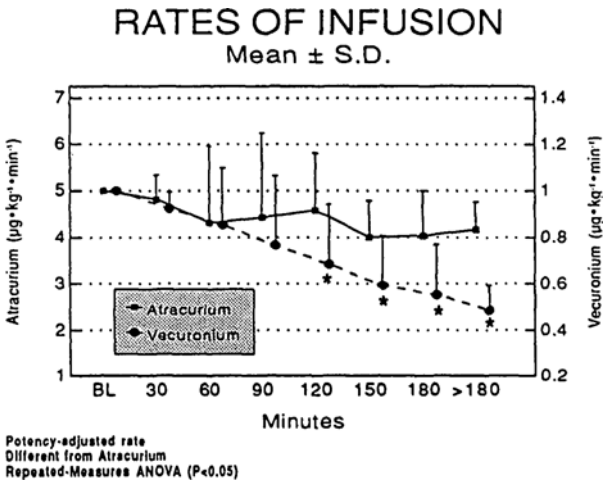
FIGURE:



The infusion rates of atracurium and vecuronium required to maintain 90-95% first twitch suppression are displayed. The between-groups comparison was calculated on the basis of the volume·min⁻¹ of muscle relaxant delivered from a coded syringe, which contained either atracurium 2.5 mg·ml⁻¹ or vecuronium 0.5 mg·ml⁻¹.

In Vitro Contracture Response to Doxorubicin in Malignant Hyperthermia Susceptible Skeletal Muscle

G.C. Allen, M.D., M.L. Crossan, R.T., P. Lindsay, R.N.

Dept. of Anaesthesia, Ottawa Civic Hospital, Ottawa, Ontario

INTRODUCTION: Malignant hyperthermia (MH) is a genetic disorder of skeletal muscle, where myoplasmic Ca^{+2} levels rise dramatically in response to certain anaesthetic agents. An abnormality of the Ca^{+2} release channel (ryanodine receptor) has been detected in MH-susceptible (MHS) muscle.[1] Doxorubicin, an anti-cancer drug, is a potent activator of Ca^{+2} release from skeletal muscle.[2,3] It appears to act directly on the ryanodine receptor in the terminal cisternae,[4] where its action is blocked by ruthenium red. Its action is similar to caffeine, except doxorubicin is 100X more potent than caffeine.[2] Significant Ca^{+2} release occurs *in vitro* at doxorubicin concentrations that are present *in vivo* during cancer chemotherapy (4-10 µM). The purpose of this study was to determine if doxorubicin induces contractures *in vitro* in MHS *vs* MH(-) muscle, and if these contractures occur at clinically relevant doxorubicin concentrations.

METHODS: After institutional approval and informed patient consent, *vastus lateralis* muscle specimens were obtained from patients undergoing diagnostic MH biopsy. Caffeine halothane contracture testing was performed according to the standards of the North American MH Group.[5] The diagnosis of MH-susceptibility was made with contracture thresholds of ≥ 0.5 g for 3% halothane or ≥ 0.3 g for 2 mM caffeine.

A stock solution of 170 µM doxorubicin (Sigma) was prepared in normal saline, then diluted in Krebs-Ringer solution to the following concentrations: 5, 10, 20, 40, 80 µM. Two or three fascicles were exposed to increasing doxorubicin concentrations. Doxorubicin concentrations were increased after 4 min, or when plateau contracture occurred. Control subject specimens were obtained from scrap surgical muscle (total hip replacement). Paired fascicles were exposed to doxorubicin or caffeine, as described above. Control muscle was not exposed to halothane.

Muscle viability was confirmed in all fascicles by the presences of predrug twitch height ≥ 0.5 g, and contractures ≥ 5 g in response to 32 mM caffeine.

Dose-response curves for doxorubicin and caffeine were determined for MHS, MH(-), and control subjects. In each subject, the single fascicle with the most abnormal contracture response was used for data analysis, to account for variability between fascicles from the same subject. Repeated measures one-way ANOVA was used to compare results within and between groups, with statistical significance at $p < 0.05$.

RESULTS: Ten diagnostic [4 MHS, 6 MH(-)] and 5 control muscle specimens were studied. All specimens showed adequate viability. MHS muscle developed larger contractures at 4 mM, but not at 2 mM caffeine (Table). There was no difference in response to doxorubicin at any concentration. All muscle specimens were normal histologically, or showed minor, nonspecific changes.

All MHS subjects had contractures > 0.5 g with 3% halothane, but only 2/4 had contractures > 0.3 g with 2 mM caffeine (5.7, 0.8 g). In these two subjects, doxorubicin 80 µM induced contractures of 1.5 and 0.7 g, respectively. One MH(-) subject showed a 0.8 g contracture at 80 µM doxorubicin.

DISCUSSION: We were unable to detect a lower contracture threshold to doxorubicin MHS skeletal muscle. Although the doxorubicin dose-response curve was shifted to the left in MHS subjects (Figure), it was not significantly different from MH(-) or control subjects. This was due in part to the variability in response between subjects.

Doxorubicin may not exert its effect directly on the ryanodine receptor, but may induce Ca^{+2} release by acting at another site. Pessah *et al.* concluded that both doxorubicin and caffeine act at a site distinct from the ryanodine receptor.[6] This would not explain why contractures were seen with caffeine, but not with equipotent concentrations of doxorubicin.

The doxorubicin concentration may have been too low to show a significant difference. The equivalent concentrations of doxorubicin were calculated from studies of skinned muscle fibres, where 100 µM doxorubicin was equipotent to 10 mM caffeine.[2] Therefore, one would have expected to see contractures > 1g at 40-80 µM doxorubicin.

Since doxorubicin did not induce contractures in MHS muscle at concentrations present during cancer chemotherapy, doxorubicin should be safe to use in MHS patients who require it. However, there are no *in vivo* studies in MHS animals to confirm the safety of doxorubicin.

In conclusion, the *in vitro* contracture response to 0.5-80 µM doxorubicin was not useful for MH diagnosis.

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Table - In Vitro Contracture Responses (X±SEM)

Caffeine

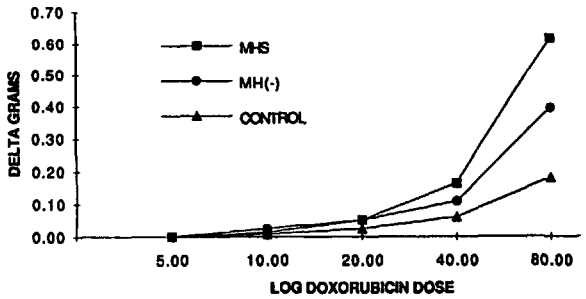
Concentration	MHS	MH(-)	Control
0.5 mM	0.04±0.04g	0g	0g
1.0	0.35±0.35	0.02±0.02	0
2.0	1.70±1.34	0.02±0.02	0
4.0	6.18±2.41*	1.68±0.41	0.96±0.39
8.0	10.80±2.70	6.73±0.85	5.36±1.55
32.0	29.75±4.01	20.94±1.91	22.52±4.83

Doxorubicin

Concentration	MHS	MH(-)	Control
5µM	0g	0g	0g
10	0.01±0.01	0.03±0.03	0.01±0.01
20	0.05±0.03	0.05±0.03	0.03±0.02
40	0.16±0.11	0.11±0.09	0.06±0.05
80	0.61±0.33	0.39±0.10	0.18±0.11
32mM caffeine	31.65±7.81	15.82±2.10	21.04±3.79

* $p < 0.05$, MHS *vs* MH(-) or controls

Figure



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THE EFFECT OF POTENCY ON ONSET CHARACTERISTICS OF NON-DEPOLARIZING NEUROMUSCULAR BLOCKING AGENTS.

RICHARD WISE, FRANÇOIS DONATI, DAVID R. BEVAN
Departments of Anaesthesia, McGill University & Royal Victoria Hospital, 687 Pine Avenue West, Montreal, Quebec H3A 1A1

INTRODUCTION: The speed of onset of non-depolarizing neuromuscular blockade depends on many factors, such as the dose administered, the sensitivity of the patient, and the method of stimulation. In addition, potency of the agent given might also affect onset time.[1] Train-of-four (TOF) fade during onset depends on which agent and which dose were administered, but its relationship to potency has not been studied.

The purpose of this study was to determine the effect of potency of non-depolarizing blocking agents on onset time and TOF fade, all other factors affecting onset being controlled. To ensure that the doses given were equipotent, only records in which maximum blockade fell within a narrow range were retained.

METHODS: Over 200 twitch records of adult patients, aged 18-75 yr, ASA physical status I or II, were examined. Anaesthesia was induced with thiopentone, 5-7 mg/kg, and fentanyl, 2-5 μg/kg, and maintained with N_2O and isoflurane (0-1% end tidal) in oxygen. Train-of-four stimulation was applied to the ulnar nerve every 10 seconds and the force of contraction of the adductor pollicis was measured.

Either d-tubocurarine (dTC), 0.36-0.4 mg/kg, rocuronium (ORG 9426), 0.12-0.24 mg/kg, pancuronium, 0.06 mg/kg, or doxacurium, 0.015-0.03 mg/kg, were given. Only patients who achieved a maximum first twitch (T_1) blockade in the range 75-95% were retained for further analysis. The time from injection to maximum T_1 blockade and maximum T_1 blockade were recorded. In addition, times from injection to the first discernible decrease in T_1 (lag time), and to 25%, 50% and 75% T_1 blockade were measured. The TOF ratio (T_4/T_1) was measured at 25%, 50% and 75% T_1 blockade.

The relationship between these variables and potency were examined by linear regression. The dose given, expressed in μmol/kg body weight was considered an inverse measure of potency. Results are expressed as means ± SEM. A p value of 0.05 or less was considered to indicate statistically significant difference.

RESULTS: The records of 63 patients were retained. Maximum block was similar for all drugs given. The lag time increased as dose decreased ($p < 0.00001$) (Table). Similarly, time to 25, 50 and 75% twitch depression increased as dose decreased or potency increased ($p < 0.00001$, $p < 0.00001$ and $p < 0.001$, respectively). However, there was no statistically significant relationship between time to maximal blockade and dose (Table). Similarly, there was no relationship between TOF ratio and dose of agent given for T_1 blockade of 25, 50 and 75% (Table).

DISCUSSION: When equipotent doses of several non-depolarizing agents are given, the onset pattern depends on potency. In particular, the earliest indicators of blockade, such as lag time, and times to 25, 50 and 75% blockade, were longer if the drug was potent. This is probably because the more potent a drug, the smaller the number of molecules available to bind to the same number of postsynaptic acetylcholine receptors. However, time to maximum blockade, which shows no relationship to potency, probably depends on rate of elimination as well. Finally, TOF fade during onset does not appear to depend on the potency of the drug.

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TABLE

	dTC	ROCURONIUM	PANCURONIUM	DOXACURIUM
Dose (μmol/kg)	.61 - .67	.20 - .40	0.08	.0135 - .027
n	20	17	12	14
Max. Block (%)	90.84 ± 1.02	83.54 ± 1.54	88.46 ± 1.67	87.08 ± 1.40
Lag Time (min.)	0.76 ± .05	1.13 ± .15	1.29 ± .12	3.30 ± .34
Time to 50% Block (min.)	1.60 ± .19	1.70 ± .17	2.51 ± .20	6.21 ± .59
Time to Max. Block (min.)	9.60 ± .81	3.68 ± .28	6.53 ± .56	12.54 ± 1.16
T_4/T_1 (%) at T_1 = 50%	52.74 ± 3.09	55.62 ± 3.39	47.49 ± 2.91	57.10 ± 3.26

CAREFUL PRE- AND INTRAOPERATIVE MANAGEMENT, NOT LOW-DOSE APROTININ, REDUCES TRANSFUSIONS IN HIGH RISK CARDIAC SURGICAL PATIENTS

J.F. Hardy, M.D., J. Desroches, M.D., J. Perrault, Ph.D., M. Carrier, M.D., D. Robitaille, M.D.
Department of Anesthesia, Montreal Heart Institute, 5000 Belanger East, Montreal, Quebec, Canada H1T 1C8

INTRODUCTION:

A high dose regimen of aprotinin (Apt) 5-6 million KIU is effective to reduce bleeding and the need for homologous blood products (HBP) associated with cardiopulmonary bypass (CPB).[1] These high doses aim to achieve plasmin and plasma kallikrein in vitro inhibitory concentrations but, theoretically, smaller doses could suffice in vivo.[2] Moreover, the potential benefit of Apt should be optimal in patients undergoing reoperations and complex surgery, since these are the patients most at risk of bleeding and being transfused.[3] Finally, Apt is an expensive drug, so efficiency requires using the smallest effective dose. Therefore, the efficacy of prophylactic Apt 1 million KIU (the maximal dose approved currently) was evaluated in this high risk patient population.

METHODS:

Following institutional review board approval and informed consent, 41 patients undergoing a reoperation and/or a complex procedure were included in a prospective, randomized, placebo controlled, double-blind study. Before skin incision, a bolus of 200,000 KIU Apt was administered in 20 min, followed by an infusion of 100,000 $KIU.h^{-1}$ during 8h. Control patients received an equal volume of saline. Dryness of operative field, chest drainage, transfusion of HBP, haemoglobin concentrations, coagulation parameters (including bleeding time), duration of stay in the ICU and in hospital were compared. Postoperative bleeding and transfusion of HBP were also compared in a group of 41 patients matched for surgical procedure performed in 1989, to control for study effect and changes in practice.

RESULTS:

There were no differences between Apt and placebo treated patients for all clinical and laboratory parameters (Table). Compared to 1989 patients, a significant reduction in the transfusion of packed red blood cells (PRBC) and fresh frozen plasma (FFP) occurred in the present sample (Table). Twenty-seven percent of patients were transfused platelets in 1989, compared to 22% in 1991 (p=0.79 by Chi-Square).

Table

	n	PRBC units	FFP units	Chest drainage ml	Post-op Hb $g.L^{-1}$
Aprotinin	22	3.0±2.8*	1.6±2.6	565±589	105±13
Control	19	2.6±2.3*	0.4±0.8*	631±423	104±13
Historic	41	5.0±4.0	2.0±2.4	502±548	106±16
p (Anova)		0.015	0.045	0.678	0.899

*$p<0.05$ vs historic by Fisher's PLSD

DISCUSSION:

Apt 1 million KIU did not reduce chest drainage and transfusions in a population at high risk of being exposed to HBP. The apparent inefficacy of Apt may be explained by the use of an insufficient dose, by a different protocol of administration (e.g. no bolus in CPB prime), or by the inability of Apt to decrease bleeding and transfusions any further. The present study suggests that improvement of the pre- and intraoperative management (such as routine preoperative discontinuation of ASA, use of membrane oxygenators, etc.) and meticulous surgical haemostasis (possibly an effect secondary to the study itself) have led to a substantial decrease in transfusion of PRBC and FFP between 1989 and 1991. The usefulness of low doses of Apt could not be demonstrated in this context.

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Effects of Glucocorticoid Supplementation During Reperfusion after Aortocoronary Bypass (ACBP) Surgery

D.M. Ansley, M.D., F.R.C.P.C., J.P.O'Connor, M.D., F.R.C.P.C., J. Dolman, M.D., F.R.C.P.C., G.E. Townsend, M.D., F.R.C.P.C., D.Ricci, M.D., F.R.C.P.C.
Departments of Anaesthesia and Medicine, University of British Columbia, Vancouver, British Columbia, Canada

Ventricular dysfunction and early post-operative myocardial ischemia are common following ACBP surgery. They may characterize 'reperfusion injury'.[1] Attempts to preserve myocardial function and prevent ischemia with preoperative steroids have been equivocal. Preoperative steroids may produce ischemic injury by increasing myocardial metabolism.[2,3] In animals, steroid administration during reperfusion enhances post-ischemic performance and modifies ischemic injury. We tested whether steroids during reperfusion are beneficial and if timing of administration after ACBP surgery influences efficacy.

METHODS: With institutional approval and informed patient consent, 28 patients (EF 57± 12%) scheduled for ACBP surgery were studied. Holter monitoring (modified V_4 and V_5) was used to detect perioperative myocardial ischemia 2-4 hours preop, intraop and 24 hours post CPB. Sufentanil/air-oxygen anesthesia was supplemented with Isoflurane prn. HR and BP were maintained to ±20% of ward control. Control hemodynamics were measured with a PA catheter. Cardiac indices and vascular resistances were calculated. Surgery included the use of hypothermic CPB, continuous aortic crossclamp (100.5 ± 33.9 min) and intermittent cold cardioplegia (4-10°C; 4935 ± 1960 ml). In a double blind randomized fashion, patients received saline (ns) or methylprednisolone (MP) 15 mg/kg at 2 time intervals: 1) initiation of rewarming, and 2) at release of aortic crossclamp (GRP I = ns/ns; n=9, GRP II = MP/ns; n=9, GRP III = ns/MP; n=10). Dobutamine 0-7 µg/kg/min, then epinephrine 0-0.4 µg/kg/min was used prn for separation from CPB and postop hemodynamic support. Hemodynamic profiles were repeated at 10, 30, and 60 min, and 3, 12, and 24 hr post CPB. Holter data and ECGs were reviewed by a cardiologist (DR). An ischemic episode was new horizontal or downsloping ST segment depression ≥ 1.5 mm at the J point + 60 msec of > 1 min duration. Myocardial infarction was diagnosed by CK-MB > 100 IU with new Q or evolving T wave changes on ECG.

Statistical analysis included repeated measures ANOVA, Student Neuman Keul's Test (SNK), χ^2, Fisher's Exact Test (FET); $p < 0.05$ was considered significant.

RESULTS: Patients were similar except for age (III > I, II) and recent MI (III > I, II). Mean dose of dobutamine, CVP, PCWP, SVR, PVR and LVSWI were similar in all groups during the study intervals. Fig.1 describes results. CI increased 10 min post CPB in each group: I = 13%, II = 29%, III = 39% (I vs III p=0.04 (SNK)). By 3 hr post CPB, CI decreased below control in I = 8/9 (89%), II = 6/9 (67%), and III = 4/10 (40%) pts (I vs III p = 0.03 (FET)). Mean CI in I was lower than CI in III by 10-25% for 3 hrs post CPB. Mean RVSWI in I decreased 27 to 58%. Mean RVSWI in III increased 9 to 24% for 3 hr post CPB. Table I describes differences in CI and RVSWI. CI and RVSWI were similar for I and II. Post CPB ischemia occurred in 4.9 (44%) pts in I, 3/9 (33%) pts in II and 5/10 (50%) pts in III (NS). Early (≤3 hr) new ischemia occurred in 3/4 ischemic pts in I, 2/3 ischemic pts in II, but no pts in III (p=0.03 (FET)). The mean time to onset of ischemia post CPB was I = 62 min vs III = 11.8 hr. MI occurred only in I = 2/9. One of these pts had early new ischemia.

CONCLUSION: Following prolonged global ischemia and high dose cardioplegia, MP 15 mg/kg given at aortic declamping preserves myocardial function by increasing RV performance and CI in response to a similar dose of inotrope, although the duration of the effect is short. The pattern, timing and outcome of ischemia may be altered by steroid treatment following ACBP surgery. On the basis of these results, a dose-response study is planned.

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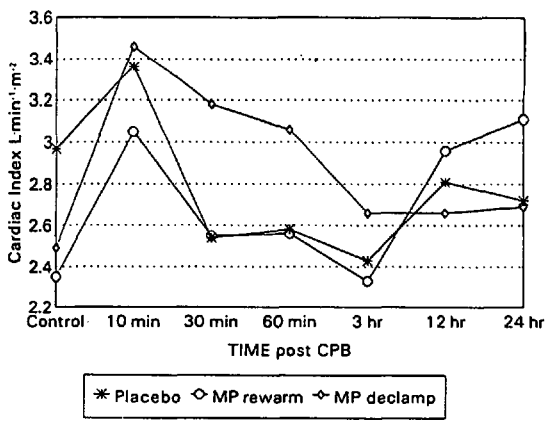
TABLE I

Gp I vs Gp III	30'	60'	3 Hr
Mean Difference CI (95% CL)	-0.65 (-1.27 to -0.02)	-0.47 (-0.92 to -0.01)	-0.27 (-0.7 to 0.16)
Mean Difference RVSWI (95% CL)	-2.6 (-4.3 to 0.89)	-1.65 (-3.66 to 0.354)	-2.48 (-3.64 to -1.31)

Figure 1.



The Effect of Clonidine on Perioperative Renal Function in Coronary Artery Bypass Grafting.

DJ Liepert, MD, PM Browne, BSC, T Hertz, M Rooney, BSP, RW Yip, MD, W Code, MD.

Dept. of Anaest., Royal University Hospital, Saskatoon, Saskatchewan, Canada, S7N 0X0

Introduction: Clonidine is an α_1 and α_2 adrenergic agonist with central and peripheral actions. It possesses diuretic and natriuretic actions due to central inhibition of ADH and a peripheral inhibition of tubular reabsorption of sodium and water.[1] Clonidine may also protect renal function during coronary artery bypass grafting based on preliminary research reported in 1990.[2] Creatinine clearance has been used to assess renal function and glomerular filtration rate.[3] Cimetidine inhibits tubular secretion of creatinine and may allow creatinine clearance to even more accurately assess glomerular filtration rate and kidney function.[4] There are no published reports of the effect of coronary artery bypass grafting on glomerular filtration rate.

Methods: 24 patients presenting for elective coronary artery bypass grafting were enrolled into this randomized, double blinded and placebo controlled trial. Patients with a left ventricular ejection fraction of less than 0.4 and/or significant aortic stenosis were excluded. Informed consents and institutional investigational approval were obtained. Three patients were excluded from the study after initial enrolment. One patient in the placebo group developed oliguric renal failure and had the cimetidine discontinued. Two patients in the clonidine group had errors in data collection. Patients were randomized into two groups receiving either 3μ/kg clonidine (range 175→275) or placebo orally, 90 minutes preoperatively. Cimetidine, 300 mg q8H was started on all patients prior to the preoperative creatinine clearance measurement and continued 3 days postoperatively. Patients received all their other regular cardiac medications pre-operatively and were otherwise premedicated at the discretion of the anaesthetist. All patients received a primarily opioid anaesthetic and membrane oxygenators were used in all cardiopulmonary bypasses. 24 hr. urine samples were collected pre-op and at days 1 and 3 post-op to determine creatinine clearances in ml/s. All creatinine clearances were standardized to body surface area.

Data were analyzed using Fisher's exact probability test, Students paired T test with the Bonferroni inequality and Students T test. Significance was defined as a p value of less than 0.05.

Results: There were no demographic differences between the two groups. Patients in the placebo group had no difference in creatinine clearance between preoperative and postoperative values. Patients in the clonidine group had significant improvements over preoperative values at both day one and day three (Table 1).

	Clonidine Creat <1 (ml/s)	**Placebo Creat.<1 (ml/s)**
Preop	1.25 ± .36	1.26 ± .34
Day 1	1.51 ± .32 $p < 0.01$	1.31 ± .33 N.S.
Day 3	1.62 ± .33 $p < 0.01$	1.37 ± .41 N.S.

* values are reported as mean ± standard deviation.

DISCUSSION: We were able to demonstrate a significant improvement in creatinine clearance and therefore glomerular filtration rate in those patients given clonidine pre-operatively in our study. We also demonstrated that patients not given clonidine had no decrement in creatinine clearance and glomerular filtration rates associated with coronary artery bypass grafting and cardiopulmonary bypass. This is in itself an interesting finding. The significant improvement in creatinine clearance and glomerular filtration rate in patients given clonidine may have clinical significance in this population. Further investigation of possible mechanisms for protection of glomerular filtration rate and renal function by clonidine are warranted.

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THE INCIDENCE OF RECALL OF INTRAOPERATIVE EVENTS FOLLOWING CARDIOPULMONARY BYPASS.

AA Phillips MB, ChB, RF McLean MD, JH Devitt MD, EM Harrington BA.
Department of Anaesthesia, University of Toronto, Sunnybrook Health Science Centre, 2075 Bayview Avenue, Toronto, Ontario. M4N 3M5.

Introduction: Recall of intraoperative events is a distressing complication of general anaesthesia. The incidence of recall after cardiopulmonary bypass (CPB) has been reported as 6 and 9% respectively in two small series of patients.[1,2] In order to provide hemodynamic stability and amnesia, large doses of narcotics and benzodiazepines are often used by anaesthetists during cardiac anaesthesia. We recently started a new cardiac surgery service in our institution. In choosing an anaesthetic philosophy, we decided as a group to avoid large doses of benzodiazepines and narcotics in the vast majority of our patients. Our aim was to attempt to reduce the recovery period and simplify management of these patients in the intensive care unit. Because of two isolated reports of recall in our first 100 patients, we decided to prospectively interview patients postoperatively in an attempt to identify episodes of recall and possible contributing factors.

Methods: All patients were anaesthetised using a balanced technique with fentanyl, benzodiazepines and volatile agents. They were premedicated with a combination of lorazepam, morphine and perphenazine. An attempt was made to visit all patients anaesthetised for cardiac surgery between March 27, 1990 and October 31, 1991. Patients were interviewed 2-3 days post discharge from the intensive care unit.(4-5 days postoperatively) A standardized questionnaire was used. The patients were asked "what is the very last thing you remember before going to sleep for your operation?" (last recall) and "what is the very next thing you remember" (first recall). Anaesthetic records were reviewed and the use of volatile agents and dosages of narcotics and benzodiazepines were recorded. Lowest nasopharyngeal temperature achieved during CPB was recorded. Recall data were stratified into three groups on the basis of the lowest recorded CPB temperature and compared using Fisher's exact test. All means are reported as ± standard deviation.

Results: Seven hundred and one out of 838 patients anaesthetised during the study period were successfully interviewed. Table 1 shows the place last remembered by patients. Table 2 shows the incidence of recall in patients stratified according to temperature. There were 9 patients with recall of intraoperative events. There was no relationship between the lowest temperature achieved and the presence of recall.

Table 1.

Last Recall	Number
Ward	387
Outside O.R.	137
Inside O.R.	177
Total	701

Table 2.

Temp°C	Recall	No Recall
<30	3	319
30-31.9	1	161
>31.9	5	212
Totals	9	692

There was no difference identified in the usage of volatile agents between patients with and without recall. Twelve of these 701 patients did not receive volatile agents intraoperatively. None of these patients reported recall. The mean dose of fentanyl was 15.9 ± 8.6 ug/kg and of diazepam was 0.09 ± 0.05 mg/kg in the 692 patients without recall. The dosages in patients with recall were similar, 14.3 ± 6.0 ug/kg and 0.08 ± 0.03 mg/kg respectively. The fentanyl was primarily given at induction and prior to sternotomy.

Discussion: Using a balanced anaesthetic technique, the incidence of recall in our patient population is 1.28%. This compares favourably with previously reported incidences. There appears to be no relationship between temperature during CPB and the incidence of patient recall.

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A TRANSIENT DECREASE IN CARDIAC OUTPUT FOLLOWS CEMENTED ARTHROPLASTY: Studies in mongrel dogs

RJ Byrick, MD, PY Wong, PhD, D Wigglesworth, BSc, JC Kay, AIMLT; Dept. of Anaesthesia, St. Michael's Hospital; Immunoassay Laboratory, Toronto General Hospital; University of To nto

INTRODUCTION: Sudden episodes of systemic hypotension and cardiac arrest are rarely reported following cemented arthroplasty (CA). Although catastrophic hypotension is rare, transient decreases in systemic arterial blood pressure (BP) is common. No studies 'in vivo' assess cardiac output changes continuously after cemented arthroplasty. Particulate fat and marrow embolism and pulmonary hypertension have been demonstrated during CA at the time of cement and prosthesis insertion.[1] We have assumed that cardiac output is reduced at this time, however, it is possible that systemic arterial hypotension is primarily caused by vasodilation with maintenance of cardiac output. The release of prostaglandins from the lung (6-keto prostaglandin $F_{1\alpha}$ and thromboxane B_2)[2] is related in time to the presence of fat emboli and systemic hypotension. Prostaglandin generation could mediate the hemodynamic changes both clinically and in the animal model.

The purpose of this study was to determine if cardiac output was maintained during these hypotensive episodes and to determine if blocking the cyclo-oxygenase enzyme by infusing ibuprofen intravenously before CA would be effective in attenuating this response. This would be interesting since many patients requiring hip arthroplasty are treated with a non-steroidal anti-inflammatory agent such as ibuprofen.

METHODS: Nine mongrel dogs were anaesthetized using pentobarbitone 30 mg/kg followed by a pentobarbitone infusion at 5 mg/kg/hr. Hemodynamic data were collected before and after bilateral CA[1,2]. Arterial (BP), right atrial (RA), left atrial (LA), and pulmonary artery (PA) pressures were continuously recorded. Cardiac output (Aortic flow) was measured continuously by placing a T_{201} ultrasonic blood flowmeter (Transonic Systems Inc) about the ascending thoracic aorta through a left fifth intercostal space thoracotomy. Arterial blood samples were obtained and the plasma concentration of 6 keto-prostaglandin $F_{1\alpha}$ (6-keto $PGF_{1\alpha}$) and thromboxane B_2 (TxB_2) were determined by radio-immunoassay after reaming of the intramedullary canals and at 1, 5 and 15 min after CA. After baseline measurements were made a bilateral cemented arthroplasty (BCA) was performed using a standardized surgical technique.[1]

Six animals were studied as a control group and three dogs were studied after pre-treatment with ibuprofen (20 mg/kg) given intravenously before CA to determine if the hemodynamic changes persisted after inhibition of the cyclo-oxygenase enzyme.

All data are reported as mean values plus or minus one standard deviation. Data were analyzed using the SAS (Statistical Analysis System) general linear model repeated measures analysis of variance procedure. When a significant F ratio was found ($p<0.05$) multiple comparisons between means were made using unadjusted pairwise comparisons as printed out by the LSMEANS comparison procedure with adjustment made on the probability of rejection using Bonferonni's correction.

RESULTS: The mean PAP increased significantly in the control dogs within 1 minute after CA (17.7 ± 3.3 mm Hg to 34.9 ± 8.1 mm Hg) and mean BP decreased within 3 min from 140 ± 11 mm Hg to 103 ± 14 mm Hg. Within 5 minutes of CA the mean BP returned to control values (142 ± 13 mm Hg). The mean PAP remained significantly elevated throughout the study (28.0 ± 4.3 mm Hg at the 5 minute measurement - $p < 0.001$). The cardiac output (aortic flow) decreased in every animal. In control dogs, mean cardiac output decreased from 3.0 ± 1.5 l/min to 2.2 ± 1.3 l/min. at the 3 min measurement, returning to 2.7 ± 1.4 l/min by 5 min after CA. No significant changes in RAP or LAP were noted during the study.

The ibuprofen pre-treated animals demonstrated similar increases in mean PAP (15.0 to 33.1 mm Hg); decreases in mean BP (152 to 125 mm Hg); and decreases in mean aortic flow (2.8 to 2.2 l/min)

The arterial plasma concentration of 6-keto $PGF_{1\alpha}$ and TxB_2 increased significantly at 1 min after CA in control dogs, however, no change from the baseline concentration was found in the ibuprofen pre-treated animals.

DISCUSSION: This study demonstrates that transient hypotension and pulmonary hypertension after CA is associated with a decrease in cardiac output (aortic flow). The transient reduction in aortic flow, increase in PAP and decrease in BP were not altered by ibuprofen-induced suppression of the prostaglandin response to CA in this model. Pulmonary hypertension may be caused by pulmonary vasoconstriction associated with fat and marrow particulate embolism after CA, however inhibition of prostaglandin generation using ibuprofen does not effectively attenuate the increased PAP.

Clinically, pre-treatment with non-steroidal anti-inflammatory agents are unlikely to alter the hemodynamic response to CA. The degree of hypotension and decreased cardiac output may be more pronounced when there is reduced cardio-pulmonary reserve. The use of a flowmeter placed around the thoracic aorta to continuously monitor cardiac output in this animal model[1,2] will permit a re-assessment of the causes of acute hemodynamic instability during CA.

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WARM HEART SURGERY:IS THE BYPASS RUN DIFFERENT THAN IN COLD HEART SURGERY?

L.A.Sinclair MD,FRCPC, J.P. Koch MD,FRCPC, K.A.Deemar CCP, G.K.Christakis MD ,FRCSC
Department of Anaesthesia, Division of Cardiac Surgery, Sunnybrook Health Science Center, University of Toronto, Toronto, Ontario, Canada

As methods of myocardial protection change,so do the physiological effects associated with their use: Warm blood cardioplegia with total body normothermia has been proposed as a more physiological means of maintaining myocardial protection. During cardiopulmonary bypass,we have observed significant differences between patients receiving cold cardioplegia/total body hypothermia and those managed with warm cardioplegia/total body normothermia. The following presentation stresses some of the more significant changes.

PATIENT POPULATION:

A long-term prospective outcome study,comparing cold versus warm cardioplegia is presently under way. We reviewed the perfusion records of 204 consecutive prospectively randomized patients undergoing aorto-coronary bypass at our institution: Myocardial protection was provided by intermittent cold blood cardioplegia in 103 patients; 101 patients were randomized to continuous warm blood cardioplegia. Both groups were similar demographically and both groups had similar pump times, cross-clamp times and number of bypasses(veins or internal mammary arteries).

RESULTS (TABLES 1&2):

Hemodynamic parameters like Cardiac Index, Systemic Vascular Resistance (SVR) and Mean Pulmonary Artery Pressure revealed no statistical differences between the cold and warm groups. SVR was similar as a result of the higher use of Phenylephrine in the warm cardioplegia group, compared with the cold cardioplegia group, in order to maintain adequate perfusion pressure. The total volume of cardioplegia in the warm group and the volume of crystalloid while on bypass were significantly greater than in the cold cardioplegia group. Secondary to this, hyperkalemia was more significant with continuous warm cardioplegia: this was of no physiological effect and therefore did not require more frequent treatment, coming off cardiopulmonary bypass.

Interestingly, and despite of the previous finding, a significantly greater number of patients had spontaneous defibrillation upon aortic cross-clamp release in the warm group when compared to the cold group.

TABLES 1&2: DIFFERENCES BETWEEN WARM & COLD BYPASS RUNS

* -p<0.05	CRYSTALLOID VOLUME (CC)	CARDIOPLEGIA VOLUME (CC)	HIGHEST SERUM K+(MMOL/L)
COLD	3114 ± 705*	2594 ± 889*	5.3 ± 0.82*
WARM	3527 ± 804*	4738 ± 1922*	5.7 ± 0.84*

* -p<0.05	PHENYLEPHRINE DOSE (µg)	SPONTANEOUS DEFIBRILLATION
COLD	591 ± 735*	34 %*
WARM	1333 ± 2384*	84 %*

DISCUSSION:

Given the relative novelty of the warm technique, this presentation remains largely descriptive in nature and stresses some of the more significant differences between the two techniques. At the present,it is not known whether warm cardioplegia will be of any advantage over the more widely used cold technique. Higher doses of vasoconstrictors are needed in the warm group in order to maintain perfusion pressure indicating more intense vasodilatation and probably the need to run the cardiopulmonary bypass with a higher hematocrit; larger fluid balances and higher serum potasssium levels are common with the continuous warm technique. It is premature to attribute the higher incidence of spontaneous defibrillation in the warm group to superior myocardial protection, pending definitive results from a future long-term outcome study. This report may provide cardiac anaesthetists with some guidelines for patient care and may instigate some further research efforts.

CGS 13080, A THROMBOXANE SYNTHETASE INHIBITOR, DOES NOT PREVENT REPERFUSION-INDUCED VENTRICULAR FIBRILLATION IN A CANINE MODEL

S. Belo PhD MD, P. Angle MD, P.Y. Wong PhD, Department of Anesthesia, St. Michael's Hospital and Department of Clinical Biochemistry, Toronto General Hospital, University of Toronto, Toronto, Canada

INTRODUCTION Several studies have suggested a role for Thromboxane A_2 (TxA_2) in the generation of arrhythmias during acute myocardial ischemia and possibly also in the development of reperfusion-induced arrhythmias (1,2). This study was designed to investigate the changes in Thromboxane levels during coronary occlusion and reperfusion in a canine model and to examine the effect of CGS 13080, a known thromboxane synthetase inhibitor (2), on the incidence of reperfusion-related ventricular fibrillation.

METHODS Fifteen mongel dogs (18-32 kg) were anesthetized with intravenous sodium pentobarbitone (30 mg/kg bolus plus 1 mg/kg/hr) and fentanyl 23 μg/kg bolus and 0.8 μg/kg/hr). Following endotracheal intubation, ventilation was controlled to maintain normocarbia. The heart was exposed through a left thoracotomy and suspended in a pericardial sling. Left ventricular and aortic blood pressures were continuously monitored. The left anterior descending artery (LAD) was dissected distal to the first major diagonal branch and an umbilical tape and snare were placed for later occlusion. Catheters were inserted into two epicardial veins draining the LAD and circumflex (CIRC) artery perfusion beds. Surface needle electrodes were placed on the thorax to continuously monitor the ECG. The animals were then divided into two groups. In the control group (n=7), the LAD was occluded for fifteen minutes then reperfused. Arterial and coronary venous blood samples for determination of Thromboxane B_2 levels (stable metabolite of TxA_2) were drawn prior to LAD occlusion (baseline) and at 1, 5, 15 and 90 min of reperfusion. DC countershock was used if ventricular fibrillation occurred. In the treated group (n=8), the animals were given CGS 13080 (0.05 -5.0 mg/kg) beginning 15 min prior to LAD occlusion and continuing throughout the occlusion period. Blood samples for TxB_2 levels were taken before and after 15 min of drug administration. Thromboxane levels were analyzed using repeated measures analysis of variance with Duncans multiple range test. A $p<.05$ was con significant. Chi squared analysis was used to test for nificant difference in the incidence of ventricular fibr

RESULTS In this model, myocardial reperfusion following 15 min of LAD occlusion was not associated with a significant increase in arterial or coronary venous Thromboxane B_2 (Table 1). CGS 13080 resulted in lower arterial and coronary venous levels of Thromboxane B_2, however there was no difference in the incidence of ventricular fibrillation (VF) between the treated and control groups (Table 2). Thromboxane B_2 levels did not correlate with the incidence of ventricular fibrillation nor did the response to defibrillation differ between the two groups.

TABLE 1

	TxB_2 (ng/mL)		
CONTROL (n=7)	**Arterial**	**CIRC**	**LAD**
Baseline	.64±.21	.73±.26	.70±.14
Reperfusion 1 min	.62±.23	.67±.17	.71±.25
5 min	.62±.27	.64±.15	.74±.21
15 min	.72±.27	.76±.42	.79±.31
90 min	.86±.22	.67±.28	.72±.25
TREATED (n=8)			
Baseline	.55±.21	.68±.17	.66±.16
CGS 13080	.48±.15	.55±.17	.55±.23
Reperfusion 15 min	.46±.20	.45±.15	.52±.09
90 min	.47±.27	.59±.08	.52±.17

TABLE 2

	Control (n=7)	CGS 13080 (n=8)
No VF	3	3
VF - defibrillated	3	2
VF - unsuccessful defibrillation	1	3

DISCUSSION These results suggest that, in this canine model, Thromboxane A_2 is not released during LAD occlusion or reperfusion and is not involved in the development of subsequent reperfusion-induced ventricular fibrillation.

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COCAINE AND ISOFLURANE ANAESTHESIA - REGIONAL ORGAN BLOOD FLOW

D Cheng MD, J Boylan MB, A Sandler MB, C Feindel MD, F Carmichael MD, P Boylen BSc

Department of Anaesthesia and Division of Cardiovascular Surgery, The Toronto Hospital, Toronto, Ontario

Introduction: Cocaine toxicity commonly causes cardiovascular and neurological morbidity and mortality. However, its effects on regional organ blood flow and potential interactions with general anaesthesia have not been documented. We report our preliminary experience with an in vivo swine model, examining the effects of cocaine on regional blood flow at two levels of isoflurane (ISO) anaesthesia.

Materials and methods: Following Institutional Animal Care Committee approval, five swine were anaesthetized with isoflurane, orotracheally intubated and mechanically ventilated to normocarbia. Anaesthesia was maintained with isoflurane in oxygen. An ear vein was cannulated for intravenous access. Electrocardiographic (ECG) leads were placed, and a left carotid arterial line, pulmonary artery catheter, coronary sinus catheter and bilateral femoral arterial lines were inserted via surgical cutdown. A median sternotomy and pericardial cradle were established and a left atrial line inserted for radionuclide-labelled (Sn^{113} and Ce^{141}) microsphere injection. After thirty minutes of steady state anaesthesia, a level of ISO of 0.75 and 1.5 MAC was delivered in random sequence for 15 minutes each. An infusion of 5% cocaine was commenced simultaneously at 0.5 mg/kg/min and continued for the remainder of the study. After 15 minutes at each level of ISO, 2×10^6 radiolabelled microspheres (diameter 15 μ) were injected via the left atrial catheter. Reference samples were simultaneously drawn from both femoral lines, beginning 15 seconds prior to microsphere injection, at a rate of 2 ml/min for 120 seconds. At the end of the experiment, the animals were sacrificed using KCl euthanasia. Autopsy-obtained tissue samples (cerebral cortex, cerebellum, spinal cord, left ventricular (LV) endo- and epicardium) were weighed and counted for isotope content using a gamma scintillation counter (Packard Instruments). Counts were referenced against intraoperative samples to correct for background and crossover effects. Cerebral (CeVR) and LV epi- and endocardial vascular resistance (CVR_{epi}, CVR_{endo}) were calculated using blood flow data and the appropriate formulae for pressure gradients. Blood flow and resistance data were compared between groups using paired *t*-tests.

Results: At steady state cocaine levels and anaesthetic dose-related decreases in cerebral and coronary perfusion pressures, cerebral, LV epi- and endocardial blood flows were similar, whereas cerebellar and spinal cord blood flow tended to increase from 0.75 to 1.5 MAC ISO. (Table 1) CeVR, CVR_{epi} and CVR_{endo} were all minimally affected. (Table 2)

TABLE 1

ORGAN BLOOD FLOW (ml/100g/min)	0.75 MAC	1.5 MAC
LV-EPI	82.9 (5.9)	87.1 (13.7)
LV-ENDO	106.0 (12.8)	102.4 (13.4)
Cerebral	49.5 (12.0)	38.5 (5.8)
Cerebellar	65.2 (9.0)	78.9 (14.3)
Spinal Cord	22.1 (1.4)	35.0 (9.6)

TABLE 2

VASCULAR RESISTANCE (ml/100g/min/mmHg)	0.75 MAC	1.5 MAC
CVR_{epi}	0.78 (0.16)	0.58 (0.18)
CVR_{endo}	0.60 (0.11)	0.55 (0.18)
CeVR	1.08 (0.58)	0.82 (0.27)

Discussion: There appeared to be a hyperaemic response to cocaine/1.5 MAC ISO relative to cocaine/0.75 MAC ISO in the cerebellar and spinal cord vasculature, while cerebral perfusion appeared to be pressure-passive. The cause for these disparate blood flow responses is unclear, but may reflect differential effects on regional brain metabolism. Despite ECG evidence for cocaine-associated myocardial ischaemia, and the presence of reduced perfusion pressures, no clear evidence was seen for a reduction in regional myocardial blood flow. Cocaine-related anaerobic myocardial metabolism may be a function of increased demand.

COCAINE TOXICITY AND ISOFLURANE ANAESTHESIA - HAEMODYNAMICS AND MYOCARDIAL METABOLISM

J Boylan MB, D Cheng MD, C Feindel MD, A Sandler MB, P Boylen BSc
Department of Anaesthesia and Division of Cardiovascular Surgery, The Toronto Hospital, Toronto, Ontario

Introduction: Cocaine abuse is an increasing problem in North America. An increasing number of patients will be expected to present for surgery with pre-existing cocaine toxicity. We present preliminary data on the effects on haemodynamics and myocardial metabolism of a steady state cocaine infusion designed to attain toxic cocaine levels, in relation to two levels of isoflurane (ISO) anaesthesia.

Materials and methods: After Institutional Animal Care Committee approval, five miniature (30 kg) swine were induced with isoflurane in oxygen. After tracheal intubation, ventilation was controlled mechanically to normocarbia. Electrocardiographic (ECG) leads were placed, and a left carotid arterial line, pulmonary artery catheter, coronary sinus catheter and bilateral femoral arterial lines inserted by cutdown. Baseline haemodynamic measurements were obtained after fifteen minutes of steady state 1.0 MAC ISO anaesthesia. An infusion of 5% cocaine was commenced at 0.5 mg/kg/minute for 30 minutes, and haemodynamics and blood samples were repeated after fifteen minutes of steady state isoflurane anaesthesia (0.75 and 1.5 MAC, in random sequence). Arterial and coronary sinus blood gases and lactate levels were measured.

Results: Sinus tachycardia occurred invariably with commencement of cocaine under ISO anaesthesia. Two animals developed ventricular bigeminy; two developed T wave inversion, and two also developed increased QRS duration. One of the latter animals' QRS changes occurred during the first (1.5 MAC) ISO phase, and resolved with onset of 0.75 MAC ISO. Maximal increase in HR and maximal decrease in systolic blood pressure and cardiac output occurred with the combination of cocaine and 1.5 MAC ISO. (Table) Myocardial lactate extraction decreased to zero or net production in two animals.

TABLE 1

	1.0MAC	COC/0.75MAC	COC/1.5 MAC
HR (beats/min)	116 ± 11	129 ± 8	140 ± 17*
SBP (mmHg)	95 ± 9	99 ± 10	75 ± 10
DBP (mmHg)	58 ± 9	77 ± 11	52 ± 9
MAP (mmHg)	69 ± 10	84 ± 11	59 ± 9
CO (L/min)	3.5 ± 0.5	3.1 ± 0.6	2.5 ± 0.4*
PCWP (mmHg)	6.0 ± 1.7	7.4 ± 1.6	6.2 ± 0.9

* $P < 0.07$

Data are means ± SEM

Discussion: Cocaine toxicity was associated with cardiac arrhythmias, ECG abnormalities, and evidence of myocardial anaerobic metabolism under ISO anaesthesia. The ECG normalization associated with lightening of anaesthesia in one animal suggests a possible potentiation of cocaine toxicity by 1.5 MAC ISO. Decreases in cardiac output and blood pressure were observed when administered in the presence of 1.5 MAC isoflurane. Possible etiological factors include cocaine-induced coronary vasoconstriction, systemic hypotension and tachycardia.

Toxic levels of cocaine interact unfavourably with deeper (but clinically common) levels of ISO anaesthesia.

ACCURACY OF MIXED VENOUS BLOOD OXYGEN SATURATION (SVO_2) MONITORING TO DETECT CRITICAL OXYGEN DELIVERY IN PATIENTS FOLLOWING HYPOTHERMIC CARDIOPULMONARY BYPASS.

L.G.R. DeLima, M.D., J.E. Wynands, M.D., H.J. Nathan, M.D., M.S. Hynes, M.D., J.Y. Dupuis, M.D., M.E. Bourke, M.D., G.N. Russell, M.D.
Department of Anesthesia, University of Ottawa Heart Institute, Ottawa Civic Hospital, 1053 Carling Avenue, Ottawa, K1Y 4E9

Introduction:
The ultimate goal of the cardiorespiratory system is to provide adequate tissue oxygenation. When oxygen delivery (DO_2) is progressively reduced oxygen consumption (VO_2) can be maintained constant by increased oxygen extraction (O_2E). With further reductions in DO_2 a critical oxygen delivery (COD) level is reached below which VO_2 falls and anaerobic metabolism ensues with increasing blood lactate levels.[1,2] We evaluated the accuracy of SVO_2 monitoring as a test enabling the clinician to detect COD in patients following hypothermic cardiopulmonary bypass (CPB).

Methods:
After institutional approval and informed consent, seventy patients were studied. Anesthesia was induced and maintained with sufentanil, midazolam and isoflurane. Patients were cooled to 28°C and rewarmed to 37°C (rectal temperatures). Neuromuscular blockade was maintained, from induction to completion of rewarming, with pancuronium and metocurine. An oximetric pulmonary artery catheter was used in each patient. Heart rate, systemic and pulmonary artery pressures, cardiac index, blood temperature, hemoglobin, SVO_2, blood gases and pH were recorded after induction of anesthesia, 10 minutes following weaning from CPB, every 10 minutes until arrival in the ICU and half hourly for two hours. Oxygen delivery index (DO_2I) and oxygen consumption index (VO_2I) were calculated. A non-linear least squares regression model was applied to the data to estimate COD. The critical point was defined as the smallest value for DO_2I for which the slope of the quadratic model was <0.1, i.e. VO_2I change of less than 1 ml/min/m² for 10 ml/min/m² DO_2I change. Oxygen delivery was considered abnormal if DO_2I was below the COD point. Three different SVO_2 cutpoints (75%, 70%, and 65%) were assessed to define a positive test. Sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) were calculated with their 95% confidence intervals for each SVO_2 cutpoint.

Results:
792 complete sets of hemodynamic measurements were recorded prior to shivering. Two subgroups were formed according to blood temperature (T_B). For patients with T_B <35.5, COD was 275 ml/min/m² with VO_2I plateau of 85 ml/min/m². For patients with T_B >35.5 COD was 490 ml/min/m² with VO_2I plateau of 125 ml/min/m². Parameters describing the accuracy of an SVO_2 cutpoint of 75% are reported in table 1. For the lower cutpoints, sensitivity and NPV were lower whereas specificity and PPV were higher.

Discussion:
Previous reports on COD in anesthetized patients[3] and following hypothermic CPB[4] did not validate the accuracy of SVO_2 to detect COD due to small sample size. Our results show that an SVO_2 cutpoint of 75% can sensitively detect DO_2 below the critical level (table 1). The low NPV in the group with T_B >35.5°C reflects the fact that few points in this group were above the COD (i.e. normal). The large difference in COD and VO_2 plateau for the two groups cannot be explained by body temperature alone but may reflect repayment of oxygen debt, awakening from anesthesia or subclinical shivering in the higher temperature group. These patients need a higher DO_2 in order to meet ongoing oxygen demand and debt. We conclude that SVO_2 is a sensitive indicator of COD in patients following hypothermic CPB. Further studies are required to validate the 75% SVO_2 cutpoint for COD in other clinical situations.

TABLE 1 Accuracy of an SVO_2 of 75% in Predicting Critical Oxygen Delivery (COD) in Patients Following Hypothermic CPB

Subgroup	N	Number of points in the critical region	*Sens.	95% CI	**Spec.	95% CI	NPV	95% CI	PPV	95% CI
SVO_2 cutpoint = 75%										
Blood temp.<35.5°C	196	80	81.3	(72.8, 89.8)	53.5	(44.4, 62.6)	80.5	(71.7, 89.3)	54.6	(45.7, 63.5)
Blood temp.≥35.5°C	596	577	77.0	(73.6, 80.4)	79.0	(55.0, 90.0)	10.1	(5.2, 15.0)	99.1	(98.2, 100.0)

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*Sensitivity, **Specificity

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Is neurolept anaesthesia stressful for patients?

Seyone C MD., Cheng D FRCPC., Chung F FRCPC

Department of Anaesthesia, Western Division, The Toronto Hospital, University of Toronto, 399 Bathurst Street, Toronto, Ontario. M5T 2S8

INTRODUCTION:

Ischaemia in the perioperative or immediate postoperative period can occur and may be silent, being discovered only electrocardiographically[1]. We undertook this study to determine the incidence of ischaemia in high risk patients and see whether general or neuroleptic anaesthesia influence the occurrence.

METHODS:

Institutional approval and informed consent was obtained. Patients with heart disease or ≥ 2 cardiac risk factors scheduled for elective retinal surgery were included in the study. Patients being treated with digitalis or those with a left bundle branch block were excluded. Routine clinical data was obtained. 12 lead electrocardiograms (EKG) were done preoperatively and on the 1st post-operative day. Creatinine phosphokinase (CPK) - Total and MB fractions were done preoperatively and at 10 hrs postop.

Continuous EKG recordings using a Holter monitor was commenced 18 hrs preoperatively on each patient, continued during the operation and removed 18 hrs postoperatively. Modified bipolar leads AVF and V_5 were monitored. Significant ST change was defined as a ≥ 1mm horizontal or downsloping S-T depression or ≥ 2mm elevation from baseline, at 60 msec after the J point, and of greater than 1 min duration. The Holter record was read by two independent investigators who were blinded to the patients' identity, history and the type of anaesthesia they received.

Intraoperatively, patients were randomized to receive standardized general (GA) or neuroleptic (LA+) anaesthesia. The patients haemodynamic profile was measured and documented at various times peri- and postoperatively.

All data were analyzed between GA and LA+ using Student's t test and Chi square where appropriate. Results are expressed as Mean ± SD. A $p < 0.05$ was considered statistically significant.

RESULTS:

Sixty six high risk patients were studied, 29 received GA and 37 LA+. There was no significant differences between the two groups with respect to their demographic data, past medical history and medications received. The heart rate (HR) 1' after commencing surgery was significantly higher in the LA+ group than in the GA group ($p < 0.05$) (Figures 1). The rate remained higher in the LA+ group right through surgery up until the end of anaesthesia. This difference however, did not reach statistical significance. Both systolic (sBP) and diastolic (dBP) blood pressures showed statistical differences between the two groups, with both pressures being significantly higher in the LA+ group at 5' post intubation/retrobulbar block ($p < 0.05$) (Figure 2). The sBP 1' after the onset of surgery, at 10', 30' and 60' post intubation/retrobulbar block also showed significant differences between the two groups with the LA+ group having higher pressures than the GA group ($p < 0.05$) (Figure 2). Patients had the Holter monitor on for 37.4 ± 6.6 hrs in the GA group and 36.4 ± 8.3 hrs in the LA+ group. Similar numbers of ST abnormalities were noted between the two groups (29.6% in GA vs 22.2% in LA+). These differences were not statistically significant. The total numbers of ST abnormalities and the duration of ST change were also not statistically significant. 10.3% of patients in the GA and 13.5% in the LA+ groups showed preoperative ischaemic changes on the Holter record. 8.1% of patients in the LA+ also demonstrated ST changes intraoperatively compared to 0% for GA. Postoperatively, there were 24.1% of patietns from the GA group with ST abnormalities versus 16.2% from the LA+ group (Table 1). CPK, both the total and MB fractions, did not show a statistical difference between the two groups.

DISCUSSION:

Although there were no differences between the two groups with respect to the incidence of ST abnormalities, there was generally a lower HR, sBP and dBP in the GA group compared to the LA+ group. This might be of potential benefit to the patient.

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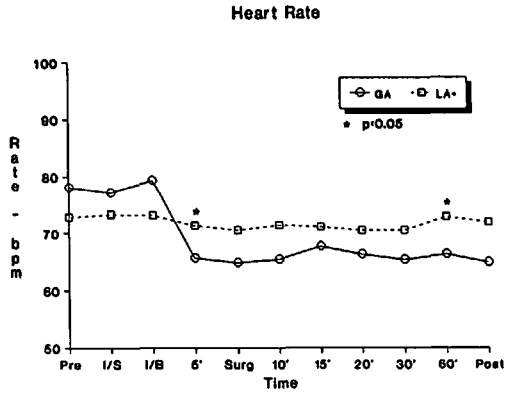

Figure 1 - Heart rate (bpm) versus time.
I/S = 1' post Induction/Sedation; I/B = 1' post Induction/Block; Sgy = 1' post surgery

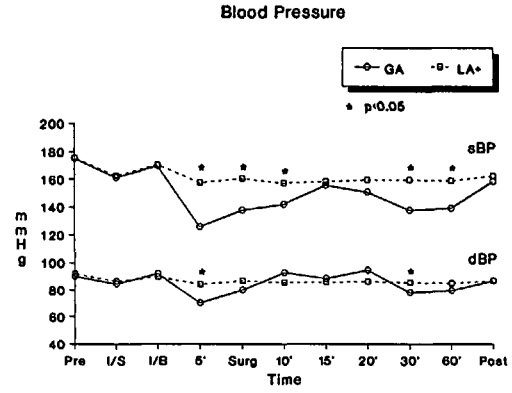

Figure 2 - Systolic and diastolic blood pressures (mmHg) versus time.
I/S = 1' post Induction/Sedation; I/B = 1' post Induction/Block; Sgy = 1' post surgery

Table 1

	GA	LA+
Dur. of Holter (hrs)	37.4 ± 6.6	36.4 ± 8.3
ST change (%)	29.6	22.2
ST number	3.2 ± 3.1	4.0 ± 3.3
ST duration (min)	83.9 ± 92.5	128.0 ± 96.3
ST preop. (% Yes)	10.3	13.5
ST intraop. (% Yes)	0	8.1
ST postop. (% Yes)	24.1	16.2

COMPUTERIZED MONITORING OF RESPIRATORY MECHANICS DURING ARTIFICIAL VENTILATION

Daniel Chartrand MD PhD, Lucie Roux MD

Hôtel-Dieu de Montréal, Department of Anaesthesia, 3840 St-Urbain street, Montréal, (Québec), H2W 1T8

INTRODUCTION

In intensive care units, many ventilators can measure the elastance (Ers) and resistance (Rrs) of the respiratory system. However, the precision of their measurements may not meet the high standards required by researchers and clinicians. Being involved in clinical research in the fields of pharmacodynamics and bronchoreactivity, we have developed a bedside computerized system for the acquisition and analysis of physiological signals. This system is able to perform reliable measurements of respiratory parameters and to analyze the mechanical behaviour of the respiratory system by four different techniques.

DATA ACQUISITION

The airway opening pressure (Pao) is measured with a piezoresistive transducer (Micro Switch 143PC01D). If required, the pleural pressure (Ppl) is estimated with an oesophageal micromanometer (Millar SPC-350). The respiratory flow ($\dot{V}$) is measured with a heated pneumotachometer (Jaeger PT-36) connected to a differential pressure transducer (Micro Switch 163PC01D). Each electrical signal provided by these transducers is amplified (Hewlett-Packard 8802A), low-pass filtered for anti-aliasing (Frequency Devices 902LPF), visualized on a digital storage oscilloscope (Gould 1604), digitized at a sampling rate of at least 200 Hz (Data Translation 2801A) and stored on the hard disk of a 10-MHz AT-compatible computer. For special purposes, up to eight analog signals (differential inputs) can be sampled. Data acquisition is controlled by programming a general purpose "scientific" software (Asyst, version 3.0).

DATA ANALYSIS

Using the preprogrammed features of the same software, we have created a customized program performing the data analysis. First of all, the flow signal is integrated over time in order to obtain the volume signal (V). The digitized signals (volume, flow and pressure) are then used to perform the analysis of the respiratory mechanics according to four different methods: the constant inspiratory flow technique, the interrupter technique, the multilinear regression analysis technique, and the multifrequency forced oscillations technique.

The three first methods are based on the general equation $(Ers \cdot V) + [(Rrs+Rt) \cdot \dot{V}] + (Kt \cdot |\dot{V}| \cdot \dot{V})$, where Rt and Kt are the Rohrer's constants of the non-linear flow resistance of the endotracheal tube. The fourth method enables us to study the respiratory input impedance but will not be described here.

With the constant inspiratory flow technique, Ers is obtained by calculating (with a linear regression analysis) the slope of the P-V relationship observed during the final part of the inspiration (0.4 to 0.9 of inspiratory time). Rrs is then estimated by the ratio $Pres/\dot{V}$, where Pres is the y-intercept of the P-V relationship previously analysed and $\dot{V}$ is the constant inspiratory flow observed during this part of the inspiratory cycle.

With the interrupter technique, the program must be able to identify the peak inspiratory pressure (Pmax), the plateau pressure (Pplat) and the PEEP, to evaluate the constant inspiratory flow and to calculate the tidal volume. The elastic pressure (Pel) is evaluated as (Pplat - PEEP). The resistive pressure (Pres) is evaluated as (Pmax - Pplat). Finally, Ers is evaluated as Pel/V and Rrs is evaluated as $Pres/\dot{V}$.

With the multilinear regression analysis technique, Ers is obtained by linear regression of ΔP over ΔV relationship for the whole respiratory cycle. After estimating $\Delta Pres$ as $(\Delta P - [Ers \cdot \Delta V])$, R (i.e.:Rrs + Rt) and Kt are obtained by multiple linear regression of $\Delta Pres$ over $\Delta\dot{V}$ and $(|\Delta\dot{V}| \cdot \Delta\dot{V})$, during the flow- decreasing part of the expiration.

DISCUSSION

With our 10-MHz AT-compatible computer equipped with a mathematics coprocessor, the analysis can be performed at a satisfactory speed. However, if the results are not required at the bedside, we still prefer to transfer the data files and to perform the analysis on a 25-MHz "486-DX" computer.

For automated monitoring of the respiratory mechanics, the constant inspiratory flow technique is usually chosen because this approach requires only a ventilator which can provide a constant inspiratory flow.

In order to validate the measurements of respiratory mechanics provided by the ventilator, we can select to perform the analysis according to the interrupter technique which is used by most ventilators. However, this second approach not only requires a constant inspiratory flow but also a stable inspiratory plateau.

Our third approach relies on the automated multilinear regression analysis technique. This technique has the disadvantage of measuring a dynamic elastance. However, this approach does not require any specific breathing pattern.

Our last approach relies on the multifrequency forced oscillations technique which enables us to study the respiratory impedance and to determine more mechanical parameters of the respiratory system. Although we prefer this approach for our research projects on bronchoreactivity, this technique requires a brief interruption of the ventilation and the use of a special breathing system producing forced oscillations.

CONCLUSION

On a physiological standpoint, monitoring of respiratory mechanics during artificial ventilation can be automated and performed at the bedside. Several techniques can and should be used: the "ideal" approach depends on the breathing pattern and on the purpose of the study.

On a clinical engineering standpoint, this monitoring system can be used by most clinicians and respiratory technicians. Furthermore, it could be easily adapted by biomedical engineers and researchers. In fact, with minor modifications (transducers and amplifiers), this custom-made computerized system can be used for the acquisition and analysis of signals in many other fields.

A LAPTOP COMPUTER BASED INTRA-OPERATIVE PHYSIOLOGICAL DATA ACQUISITION SYSTEM

S.L. Dain M.D., FRCPC, B.D. Smith, A.C. Webster M.B., FRCPC
Department of Anaesthesia, University Of Western Ontario and Saint Joseph's Health Centre, London, Ontario

Introduction

The collection of data for detailed physiological studies on anaesthetised patients is time consuming, tedious and difficult. It is difficult and potentially dangerous to simultaneously collect physiological data manually, and still be vigilant in administering an anaesthetic. Also, in order to record the small and transient perturbations in physiological parameters, it is necessary to record these parameters frequently and at regular intervals.

Methods

With the advent of laptop computers that are small enough to be unobtrusive in the very limited space within the operating room, we have devised a computerized data acquisition system. It consists of an IBM laptop computer, a Nelcor N1000 capnometer and oximeter, and a Ohmeda Finapress to continuously monitor and record oxygen saturation, end-tidal CO2, pulse rate and systolic, mean and diastolic blood pressure of patients. The laptop computer includes a 386SX microprocessor, 4MB of random access memory, a 1.44MB floppy disk and a 60MB hard disk drive.

The requirement for an intraoperative computerized monitoring system is a computer that is either powered by a DC battery or has an isolated power supply to avoid microshock. The computer must also have at least 2 serial RS-232 interfaces for the physiological monitors. Unfortunately, the IBM laptop only has 2 serial ports, which limited the number of monitors that we can acquire data from at one time. Both the Nelcor and the finapress monitors had the RS-232 ports available for connection to the computer.

Protocols which state how that data is formatted from the RS-232 port is available from the manufacturers of these monitors on request, but this information is poorly documented. Unfortunately there are no standards defining RS-232 pin assignments for medical monitors and the protocols for how the data is transmitted. This makes it extremely difficult to transfer data to the computer from the monitor without customised software.

We have written computer software to transfer this data at intervals as often as every 2 seconds and record it on the computer's hard disk. From this record on the disk, we can display and analyse the data on the Microsoft Excel or compatible spreadsheet programs.

Data acquisition software was written by one of the authors (B.D.S.) in Borland C++. The software consists of a main menu program NELLINK, which links the two modules of the program together. These are the text editor (small word-processor) and the RS-232 data acquisition modules. When the system is started, NELLINK opens the text editor module which prompts for the demographic information of the patient, date and type of surgery, anaesthetist's and surgeon's names and clinical study patient number. These prompts may be changed as per the research protocol for which this system is being used. When all the demographics have been input, program control is switched to the data acquisition module. At this time the sampling frequency is entered and the data acquisition begins.

During data acquisition, the elapsed time, the SaO_2 , the pulse rate, end-tidal CO_2, the systolic, mean and diastolic blood pressures are shown on the computer's monitor, both numerically and as a graphical trend line (figure 1). The computer's function keys, F1-F12, are defined for common anaesthetic steps, for example. induction, intubation, incision and extubation. A function key is also provided to mark times where artifactual data has been recorded such as a false desaturation due to a patient's movement or probe displacement. A template to define the function keys, placed above the keys, is provided to define each event key. which may vary between studies. This allows flexibility to use the software for different clinical studies.

After the data acquisition is completed, the text editor again appears on the screen to record any comments pertinent to the study. The data can then be analysed on any spreadsheet or database program that can read an ASCII tab delimited text file. We have chosen to use Microsoft Excel for Windows as it is easy to use.

Results

To date, our data acquisition system has been successfully used on one clinical research protocol comparing the ease of use and intra-operative and postoperative complications of endotracheal intubation and laryngeal mask airways for adenotonsillectomies in children. The major difficulty in using pulse oximeters, is to distinguish true desaturation and artifact. Artifact, usually easily recognized, represents a major problem with clinical pulse oximetry. Event markers can be included with the recorded data so that artifacts can be identified and omitted in the subsequent analysis of the data. We have found that this system is cost-effective and reliable for recording large amounts of clinical data. We are presently writing new software to allow our system to acquire data from other types and models of monitors.

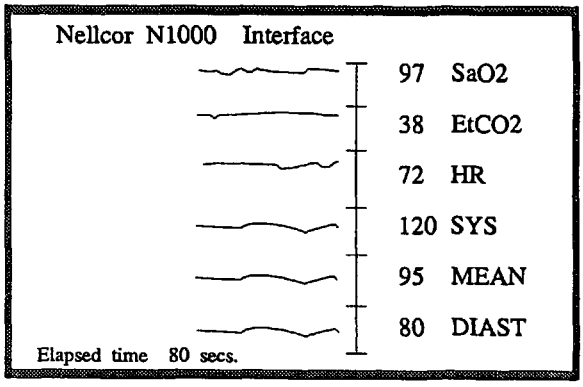

Figure 1: Computer screen output during data acquisition

The statistical analysis of a large database of anaesthetic records: A computer program to select a matched sample

DF Wigglesworth, BSc, DK Rose, MD, Department of Anaesthesia, St Michael's Hospital, University of Toronto, Toronto, Canada

INTRODUCTION

The statistical analysis of a large database of anaesthetic patient records must account for any variables which would confound the results. For example, a group of records (group A) each of which indicate the occurrence of an intraoperative event may also indicate an unusual pattern of intraoperative drug use when compared with the balance of the records in the database (group B). However, such a difference in drug use may not be relevant (i.e.: may not be causally related to the event) if group A differs from group B in other significant respects. A difference in the mean age of group A and group B could account for a difference in drug use. Then, 'age' would be said to be a confounding variable. The comparison of group A to group B must account for confounding variables.

A commonly used statistical method which reduces the effect of confounding variables (matched sample analysis) requires a matched sample. A matched sample includes the cases (group A) and, for each case, a number of unique controls (group C -- to be drawn from group B) which match the case in the confounding variables[1].

Group C is determined by criteria which describe what constitutes a match between a member of group A and a member of group B. A preliminary comparison of groups A and B will identify potentially confounding variables. The matching criteria must then be formulated accordingly. The matching criteria include a reference to each confounding variable as well as the corresponding values which define the match. For example SURGICAL PROCEDURE is a confounding variable which may have a value of TOTAL THYROIDECTOMY that may be matched to any of several values including TOTAL THYROIDECTOMY and PARTIAL THYROIDECTOMY.

The selection of a large matched sample is virtually impossible to accomplish manually. Therefore, a computer program was written which, given the criteria which define a match between a case and a control, selects a matched sample automatically.

DEVELOPMENT

The program was written using SAS-PC (Statistical Analysis Software for the IBM PC compatible computer). The matching criteria and the minimum number of matched controls required for each case were contained in the program itself. Input to the program included: (i) the database records of each case (group A), (ii) the database records of each potential control (group B). Output of the program included: (i) A list of the identity of the cases and the particular controls which matched (group C), (ii) A list of the cases for which an insufficient number of controls were matched.

A trial run of the program was executed. The case population (group A) was 217. The minimum number of controls for each case was set at 4. Therefore a control group (C) of 868 had to be drawn from a fixed population of 10,000 (group B). Initially, the criteria for a match included: AGE -- 1-10 , 11-20, 21-30 years...; SEX -- m, f; SURGICAL PROCEDURE -- (61 categories); ASA -- [1],[2],[3],[4],[5]. Given these criteria, the program was unable to find 4 matches for many cases. Thus, the criteria were too specific and had to be changed. The criteria were changed and the program was re-executed. The result was only slightly better. The whole process was repeated 8 times, adjusting the criteria at each step, until a satisfactory result was obtained. Four controls were matched to each of 210 out of the 217 cases using the following criteria: AGE -- < 60, > 60; SEX -- m, f; SURGICAL PROCEDURE -- (15 categories); ASA -- [1,2], [3,4,5].

DISCUSSION

The program can be re-executed as often as necessary to test the effect of any changes in the matching criteria. By making it possible to explore variations in the matching criteria, a good matching for a particular set of data may be more easily found.

Future improvements to this program will include a better system of matching continuous variables such as age. In the present program continuous variables must be stratified to resemble discrete variables. For example age may be stratified into 10 year age groups: 11-20, 21-30, etc. An unfortunate result of this is that a potential control which differs from a case according to the matching criteria may actually differ by as little as one day in age (eg potential control: 30, case: 31) while another potential control which matches a case according to the matching criteria may actually differ in age almost by as much as 10 years (eg control: 21, case: 30). Clearly such matches should be made in a continuous fashion. A match based on the criterion: DIFFERENCE IN AGE LESS THAN 5 YEARS, would still permit a match to be made from a group of persons spanning ten years in age but would eliminate the problems described above. However, other problems are introduced which greatly complicate the implementation of the matching program.

This program will be used in the matched analysis of our database of anaesthetic records to test the effect of drug use (pentothal vs. propofol) and outcome, where cases are matched to controls by age, sex, ASA, surgical procedure and other relevant information.

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A CRITICAL CARE DATABASE MANAGEMENT SYSTEM FOR UTILIZATION MANAGEMENT:
The user interface and data input

G. Caskennette, Phys. Tech., R.J. Byrick, MD, C. Mechetuk, HRT, Depts. of Anaesthesia, Biomedical Engineering, and Medical Records, St. Michael's Hospital; University of Toronto

INTRODUCTION A comprehensive audit of an Intensive Care Unit (ICU) requires a detailed analysis of patient case-mix (INPUT), outcome of care (OUTPUT), and resources used within the ICU (PROCESS OF CARE). We have developed a database management system to fulfil this function. Our data includes demographic information, diagnoses, procedures, complications, nursing workload measures (TISS & GRASP), severity of illness (APACHE II system) and outcome. A Health Records Technician (HRT) is responsible for abstracting and entering data.

Some investigators[1-3] have focused on isolated aspects of data acquisition but frequently overlook the design of an efficient user interface. Although the user interface includes all user accessible functions, the focus of this report is on the data input features of the program.

The usefulness of an Audit System clearly depends on the accuracy of the data entered into the system. Maintaining data integrity is an important consideration in developing the data input component of the user interface. The process of data entry is labour intensive and the potential for error is high. This function must be designed to permit fast, efficient data input with minimal processing delays and should include well designed data input screens, data validation, and error trapping routines.

METHODS A relational database[4] program (dBASE IV, Borland, Scotts Valley, CA) was used to develop our ICU database management system program (CareBase). The program is menu driven and consists of a main program and several major modules which control the operations of adding, editing, and updating records as well as report generation and routine database maintenance. There are nine primary and 14 support (lookup tables, temporary data storage etc.) databases. Eight custom designed data input screens are used to access eight of the databases.

The Prototype data input screens were developed and evaluated by assessing feedback from the HRT, observation of recurring errors during data analysis, and the programmer's assessment of performance. This information was used to develop a revised program that is more responsive to the user, less prone to data input error, and requires less interaction to control data input activities. During the re-design process, the HRT evaluated and commented on prototypes of proposed changes. This assisted the programmer in making decisions regarding options for implementing specific functions.

RESULTS Previous versions of the program required significantly more interaction on the part of the user to initiate events (via control keys), such as screen changes, during data entry. The new interface requires an estimated average of 30 control keystrokes less per patient chart entered. This was accomplished by automating screen changes, wherever possible, as long as this was consistent with leaving adequate control of the data entry process with the user. It is difficult to quantify the results of program changes (patient charts/hour or number of errors) because of the wide variation in the quantity of data per patient chart. Based on information from the HRT, a reasonable estimate would be an average 20-25% improvement on the time required to enter data.

Adjusting the sequence in which data input screens are presented resulted in significantly less paper handling, for the HRT, in cases of multiple admissions during a single hospital stay. For example, a patient with three admissions to the ICU requires three sets of datasheets. Earlier versions of the program forced the HRT to handle each set of datasheets three times during data entry. The same data entry task can now be done by handling each set of data only once

Since there is wide variability in the number of diagnoses and procedures that must be entered for each patient, these input screens were modified to provide a scrolling list of each item as it is entered. This approach provides the HRT with immediate positive feedback as data is entered. A browse screen is also available, through a Function key call, which permits scrolling and editing if it is required.

Data input, for nursing workload measures (TISS & GRASP), required nine screens each for previous versions of the program. This was inefficient because the user was required to move through all nine screens whether or not they required data input. Significant improvements were achieved by reducing the number of screens to one each for TISS and GRASP and using a dynamic search routine and lookup tables to locate items that were scored.

DISCUSSION Our experience, over the past two years, has demonstrated the value of utilizing user feedback, assessment of program performance, and analysis of system output to optimize the design of the user interface and the data input process. We have focused on the data input process because this activity consumes a substantial portion of the user's time and is one of the main sources of potential error. The time required to implement these program changes has resulted in time savings for both data entry and database maintenance, a reduction in potential sources of error, improvement in the quality of system output, and a higher level of user satisfaction.

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Computer Model for Veno-Veno Extracorporeal Membrane Oxygenation

D. John Doyle [1,2] and Wilfred DeMajo[1]
[1]Department of Anaesthesia, Toronto General Division, The Toronto Hospital
[2]Institute of Biomedical Engineering, University of Toronto

Introduction Extracorporeal membrane oxygen (ECMO) is sometimes used to treat respiratory failure refractory to more conservative measures [1]. Unfortunately, clinical experience with ECMO is limited, so that ECMO experts may disagree about its potential benefits in a particular clinical setting. This is particularly true when the patient has a high cardiac output (eg. 20 litres/min) while the ECMO pump is limited to much smaller flows (eg. 5 litres/min). In this report, we describe a computer model designed to facilitate management decisions for patients being considered for veno-venous ECMO.

Methods A mathematical model of the veno-venous ECMO situation was developed based on the shunt equation [2], the Hill model for the oxyhemoglobin dissociation curve [3] and Doyle's equation for arterial oxygen tension as a function of cardiorespiratory parameters [4]. The model was solved for various hypothetical clinical circumstances using Eureka, a commercial computer software package for solving systems of equations [Borland International, Scotts Valley, CA]. Figure 1 shows the Equation Sheet for the ECMO analysis with particular choices of cardiopulmonary parameters as indicated; this shows all the pertinent equations for the model in a simple algebraic form.

Results Some sample results are shown in Figure 2. Here, the patient parameters are: cardiac output [CO] = 5 l/min, oxygen consumption [VO_2] = 250 ml/min, hemoglobin concentration [Hb] = 15 g/dl, pulmonary shunt fraction [Q_s/Q_t] = 0.3 to 0.6 in steps of 0.1, alveolar oxygen tension [P_AO_2] = 200 mmHg, and an oxygenator oxygen tension output sufficient to result in complete hemoglobin saturation. As can be seen, for the circumstances cited, the model predicts increases in arterial oxygen tension that get progressively larger as the fraction of venous blood that goes through the oxygenator increases.

Discussion This model is an extension of previous efforts on the mathematical modelling of pulmonary gas exchange [4,5]. While the system is interesting and informative, two potential problems must be addressed. First, the equation solver requires that approximate estimates (or guesses) for the arterial oxygen tension [P_aO_2] be available for reliable "convergence" to an exact solution; this requirement can make it tedious to use the system. Secondly, the system must still be validated using actual ECMO cases - this is now being planned, and will involve both retrospective analysis of old cases and the careful study of new ECMO patients as they become available.

```
alpha=2.65 ; Hill 's constant
beta= 0.75  ; beta is the ratio of ECMO flow to cardiac output
CO=5        ; cardiac output
Hb=15       ; hemoglobin concentration
VO2=250     ; oxygen consumption
PAO2=200    ; alveolar oxygen tension
Z=0.6       ; pulmonary shunt
;P50=27      ; a reasonable value for P50
;consider oxygen added to body by ECMO machine
;addedO2 = beta*CO*10*(1.34*Hb*(1-SvO2native))
Cav=(VO2-(beta*CO*13.4*Hb*(1-SvO2native)))/(10*CO)
SvO2=SaO2 - (Cav - 0.0031*(PaO2-PvO2))/(1.34*Hb)
PaO2=PAO2 -(Cav*(Z/(1-Z)) - 1.34*Hb*(SAO2-SaO2))/0.0031
PaO2:=85
SvO2native:= 0.7
Cav:=0.8
SAO2=PAO2^alpha / (PAO2^alpha + 27^alpha) ;Hill's equation
SaO2=PaO2^alpha / (PaO2^alpha + 27^alpha) ;Hill's equation
PvO2=27*(SvO2/(1-SvO2))^(1/alpha) ;augmented mixed-venous PO2
PvO2native=27*(SvO2native/(1-SvO2native))^(1/alpha)
SvO2native=(SvO2-beta)/(1-beta)  ;SvO2 entering ECMO
PvO2>=PvO2native
PAO2>PaO2>0
SvO2>=SvO2native>0
SvO2native<1
```

Figure 1. The *Equation Sheet* for the veno-veno ECMO problem for a particular choice of physiological parameters and starting estimates for the iterative solver. The first 7 lines indicate the values of physiological parameters that are held constant. The next three lines are comments to the user, and are not used by EUREKA. Lines 11-13 and 17-21 list the basic equations to be solved. Lines 22-25 give some physiological constraints that cannot be violated (e.g., arterial oxygen tension must be less than alveolar oxygen tension). Lines 14-16 provide initial estimates for EUREKA's iterative solver.

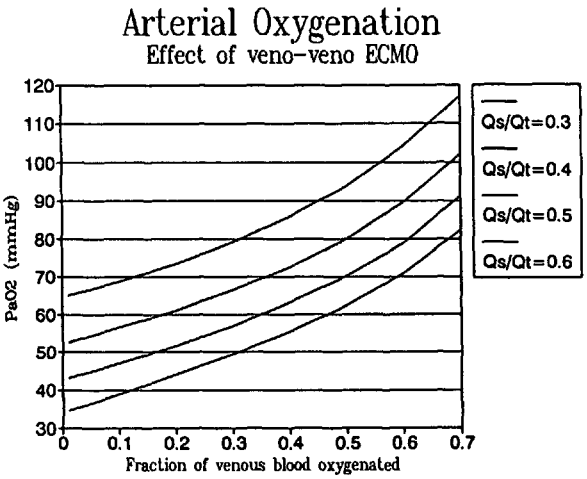

Figure 2. Plot of arterial oxygen tension (P_aO_2) as a function of the fraction of venous blood that passes through the ECMO oxygenator for various values of pulmonary shunt fraction (Q_s/Q_t).

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VENTEX: An Expert System to Advise on Ventilator Settings

D. John Doyle
Department of Anaesthesia, Toronto General Division, The Toronto Hospital
Institute of Biomedical Engineering, University of Toronto

INTRODUCTION

Expert Systems are software applications which provide guidance or advice on a specific problem (e.g. how to select a wine to go with your entree or how to workup a patient with jaundice). Expert Systems are a branch of Artificial Intelligence, a field of computer science concerned with topics varying from game playing software (e.g. computer chess) to software for theorem proving. Sample Medical Expert System applications developed by the author have included a system to interpret arterial blood gas results [1] and a system to advise on setting for a jet ventilator [2]. In this report we describe VENTEX, an Expert System to advise on ventilator settings for patients ventilated in control mode.

DESIGN

VENTEX ("Ventilator Expert") is written in GWBASIC to run on the IBM-PC family of computers. At least 256 K bytes of memory is required; however, a hard drive is not required, allowing VENTEX to be used on inexpensive machines.

At starting time, the user enters upper and lower limits for the ranges for the patient's arterial oxygen (PaO_2) and carbon dioxide ($PaCO_2$) tensions; target levels for the patient are selected to be the mid point of each range. After startup using a set of fixed ventilator settings, the user enters the patient's arterial blood gas data (pH, $PaCO_2$, PaO_2) from which VENTEX recommends new ventilator settings, if needed. The rules for VENTEX are given in Table 1. Essentially, VENTEX uses a fixed tidal volume of 10 ml/kg and varies respiratory rate to achieve a target $PaCO_2$. Adjustment of PaO_2 is more complex: both F_IO_2 and PEEP are manipulated together (Table 1, Rule 5).

DISCUSSION

VENTEX was designed to explore the concept of using a rule-based Expert System to allow nurses and respiratory therapists to "ventilate to gases". Its use is limited to patients suitable for ventilation in "control" mode; a more sophisticated set of rules would be needed, for example, to allow for changes in both tidal volume and respiratory rate or to support the use of pressure support ventilation.

At the moment, users can only alter the rules if they modify the software code written in GWBASIC. This restricts "tuning" of the system to computer programmers. A new release of VENTEX (VENTEX-Windows) is being designed to operate in the Microsoft Windows environment, and will offer several new features drawn from the list of desiderata shown in Table 2.

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TABLE 1:

MANAGEMENT RULES FOR VENTEX

1. Tidal volume and respiratory rate are set as follows
   - tidal volume = 10 ml/kg
   - respiratory rate adjusted to a target P_aCO_2 (rule 2)

2. $$\text{New respiratory rate} = \text{old respiratory rate} \times \frac{\text{old } P_aCO_2}{\text{target } P_aCO_2}$$

3. F_IO_2 and PEEP are set as follows:
   - F_IO_2 adjusted to a target P_aO_2 (rule 4)
   - PEEP adjusted based on F_IO_2 (rule 5)

4. $$\text{New } F_IO_2 = \frac{(\text{target } P_aO_2/aA\ PO_2 \text{ ratio}) + P_aCO_2}{\text{barometric pressure} - 47}$$

5. New PEEP = a x [New F_IO_2] ^{b} + c

[parameters a,b and c are suggested by consulting the "strategy advisor"; default values are a=15, b=1, c=0].

6. If "bicarb tracking mode" is used, the ventilator will ventilate the patient more when a metabolic acidosis is present:

$$\text{target } P_aCO_2 = 1.5 \times HCO_3 + 8$$

Note: a/A PO_2 ratio = P_AO_2 (alveolar) / P_aO_2 (arterial) [rule 4].

TABLE 2: Potentially Desirable Features of Medical Expert Systems Intended for Clinical Use

1) graphical user interface (eg. Windows 3.0, Presentation Manager).

2) data entry by mouse allowed for ease of data entry.

3) management strategies (algorithms) easily altered by user without need to alter program source code.

4) "how-to-use" help system to eliminate need for lengthy manuals.

5) "strategy advisor" to guide user on clinical decision making [e.g., F_IO_2 vs PEEP tradeoffs to increase P_aO_2].

6) teaches the clinician wherever possible by explaining its suggestions in a brief narritive discussion.

7) ability to use consensus-based rules where published algorthims are lacking.

Computer-Assisted Aminoglycoside Administration System

D. John Doyle [1,2], Frank van den Bosch, Wilfred DeMajo[1]
[1]Department of Anaesthesia, Toronto General Division, The Toronto Hospital
[2]Institute of Biomedical Engineering, University of Toronto

Introduction Aminoglycoside antibiotics are frequently given to critically ill patients with gram-negative sepsis. Aminoglycosides have a narrow therapeutic window outside of which the likelihood of toxicity increases. In the usual scenario, patients are given aminoglycosides in a standardized manner and adjustments are made on the basis of measured serum drug concentrations (SDCs). More recently, pharmacokinetic methods have been introduced as a more systematic method of attempting to maintain serum drug concentrations within a desired therapeutic window. Pharmacokinetics allow the prediction of drug concentration vs. time profiles for patients receiving particular dosing sequences once the parameters for that patient are known[1-3]

Another advance in recent years has been the development of intravenous infusion pump systems which can interface with a host computer. Through use of such systems, creation of complex dosing regimens is simplified and regimen delivery can be software controlled. As well, the dependency of drug therapy on clinical schedules and the probability of incorrect dosing are reduced.

The aim of this project was to develop a system which would calculate appropriate aminoglycoside dosing regimens for critically ill patients and deliver these regimens by means of a computer-controlled infusion pump. A preliminary clinical trial was run to determine where system improvements could be made.

Pharmacokinetic Methods In order to achieve the desired therapeutic result, aminoglycosides are generally administered over a period of time. In most cases, infusions are given at regularly spaced dosing intervals. Equations for multiple infusions into a single compartment model have been previously developed [3]. Given the desired upper and lower concentrations of the selected therapeutic window and the patient's volume of distribution and elimination rate constant, a dosing regimen may be calculated to specify the infusion time, infusion rate and dosing interval (the time between doses). However, such methods assume that the patient volume of distribution (Vd) and the elimination rate constant (K) are known. Currently, several methods exist for the prediction of these parameters. The methods coded in the system software are the Hull-Sarubbi method, the Sawchuk-Zaske method and the Bayesian method. Once Vd and K have been determined using one of these methods, their values are substituted back into the appropriate pharmacokinetic equations. A nomogram method, which creates dosage regimens without predicting patient's parameters, is also coded in the software.

Computer Controlled Infusion A feature which has recently become available on many infusion pumps is a communications port which allows interfacing with a host computer. This feature allows a dosage regimen calculated by the host computer to be passed directly to the infusion pump, reducing dependency of drug therapy on clinical schedules, incorrect dosing and drug wastage. One such pump is the Abbott LifeCare Model 4P. This pump accepts commands from a host computer via an RS-485/232 serial data communications interface. Computer software may establish the host-computer link by opening the serial port as a file and writing to the "file" using specified communication parameters. Pump commands consist of bytes passed as strings from the host computer. An internal microcomputer controls the pump, handles communication with the host computer and performs error checking.

Aminoglycoside Dosing Program The purpose of the Aminoglycoside Dosing Program is to facilitate the administration of aminoglycoside antibiotics. Pharmacokinetically derived dosage regimens based on patient and drug information are calculated by the computer and passed directly to the infusion pump. Use of pharmacokinetics and direct delivery of the calculated regimen may potentially reduce the frequency of SDCs which lie outside the therapeutic window.

The user may choose one of six methods mentioned above to determine the dosage regimen: Physician Experience, Nomogram, Hull-Sarubbi, Sawchuk-Zaske and Bayesian. The choice of methods was made available to allow the physician to work with a method with which he/she is familiar. The method chosen by the user is used to calculate the dosage regimen for the patient. A loading dose may be given if desired. Once the regimen is verified by the user, it is passed to the pump and the drug is delivered automatically. The maintenance dose will be given repeatedly (pausing for the remainder of the dosing interval after each infusion) until the user quits the program. The user may revise the regimen whenever the pump is paused.

During delivery of the regimen, the computer displays the current action. If the pump is infusing, the screen displays the rate of infusion, total infusion time and how long the infusion has been going on. During pause intervals, the screen displays the duration of the pause, how long the pump has been paused and the previous action.

Integrity of the pump/computer interface is checked at regular intervals using several procedures. Any error found to occur results in an alarm and display of a message describing the nature of the error.

The Aminoglycoside Dosing Program was written in QuickBASIC 4.5. Although currently configured for use on an IBM-AT, the program can operate on any IBM-compatible PC, XT, AT or 386/486 machine.

System Evaluation A preliminary clinical trial was performed to identify areas for software improvement, both in terms of proper operation and clinical acceptance. Proper operation of the software had been tested during programming and several "false" infusions into an empty jar were performed prior to actual patient use. Tobramycin regimens were then given to two patients using the system. The system was connected to the first patient for seven days during which time ten infusions were given. The second patient received 33 infusions over a period of 13 days. In both cases, patient regimens were calculated and revised using the Sawchuk-Zaske method. Physician approval was obtained before regimen administration and for any changes made to the regimen.

Results The physician was frequently hesitant to administer the calculated dosage regimen, generally opting for a lower dose. Since the physician-altered regimens will in most cases lead to peak and trough SDCs which are not equal to the desired peak and trough SDCs, the clinician may come to accept the recommended regimen with experience.

All system alarms could be explained and rectified. The software did not trigger any false alarms. This indicates that data transmission between the computer and the pump was reliable. It was necessary to ensure patency in the upper section of the infusion line to prevent alarms.

The average time from the drawing of blood samples until serum drug concentration results were returned from the lab averaged approximately 48 hours. By this time the patient condition might have altered enough to make the measured SDCs of little use. It would be preferable if the turn-around time of serum drug concentration could be reduced, tightening the feedback loop. One possible approach would be to include a concentration assay unit as part of the system. SDCs could then be known within minutes, instead of days. It would also be advantageous to obtain SDCs after each infusion, thereby tracking the drug concentration much more closely.

Finally, there were several comments about the large size of the system and amount of space it occupied next to the patient's bedside. It is suggested that a laptop computer be used for any further work.

Conclusions A computer-assisted aminoglycoside infusion system has been created. The system consists of a program which calculates optimal dosage regimens and a computer-controlled infusion pump which delivers the regimens. The program also monitors the pump for proper operation and alarms. The optimal dosage regimen is based on a one-compartment pharmacokinetic model and is calculated using patient parameters and desired serum drug concentrations as input. The program allows the regimen to be revised as updated patient information becomes available. Use of the computer-controlled infusion pump eliminates the need to round the calculated regimen to fit nursing schedules. The system has been trialed in the ICU to verify proper operation and to target areas for improvement.

The software provides six methods by which a dosing regimen can be created. All six methods were included to allow the user to pick a method with which he/she was familiar. It may be of some interest to compare the effectiveness of each method in reducing the number of SDC outliers. It remains to be shown that the use of pharmacokinetics in conjunction with a computerized delivery system will result in fewer serum drug concentrations outside the therapeutic window than current methods.

Several improvements can be made to the current system. First, a bedside SDC assay unit could be incorporated to tighten the feedback necessary to ensure that the regimen reflects the patient's current status. Without tight feedback, the system will probably not succeed in reducing the number of SDC outliers. Second, a smaller computer would reduce the space occupied by the system by the patient's already crowded bedside.

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Evaluation of AnaesthesiaTrend Display Methods by ROC Analysis

D. John Doyle [1,2] and Mark Lee [2]

[1]Department of Anaesthesia, Toronto General Division, The Toronto Hospital

[2]Institute of Biomedical Engineering, University of Toronto

INTRODUCTION In many clinical situations there is a need to make decisions based upon a limited amount of information. This information has to be presented in a form which is easily interpreted clinicially. However, the criteria by which presentation methods (displays) are evaluated may vary. One objective procedure which has gained significant acceptance for such tasks is the statistical analysis of ROC (Receiver Operating Characteristic) curves [1].

ROC curves demonstrate the relationship between the true positive (TP) rate and the false positive (FP) rate in a diagnostic task (e.g. detecting a positive CPK-MB band or detecting a change in patient BP.) Varying the definition of a positive test [operating (cutoff) point] allows one to construct an ROC curve, i.e., ROC curves are obtained by plotting the TP and FP coordinates for each of the operating points or thresholds under evaluation. Additionally, ROC curves produce information concerning detectability or discrimination and provide a method to assess the appropriate tradeoff between sensitivity (TP rate) and specificity (TN rate) for a particular clinical situation. More importantly, the area under a ROC curve (calculated by nonparametric or maximum likelihood estimation methods) serves as a mean to evaluate the performance of diagnostic and predictive test systems.

Utilizing this technique, a computer-based experimental setup to study various graphic displays was developed. We sought to obtain a set of different ROC curves for subjects using several blood pressure display methods of potential clinical value.

EXPERIMENTAL METHODOLOGY The experiment consisted of a series of different scenarios which were randomly presented to a series of 3 test subjects, who were asked to determine if there was a significant change or trend occurring in the data presented to them on a computer screen. For each scenario the correctness of the response was determined. The presentation of data was either in an alpha numeric display (Figure 1 - top) or a graphic line plot (Figure 1 - bottom). By randomizing the order of presentation, anticipatory and learned response effects were avoided. The data presented was randomly chosen from a set of three possible sequences (Steady Baseline, Step Change and Ramp Change) to which was added noise of well-defined properties so as to change the difficulty of the change detection task and thereby allow construction of the ROC curves.

The first part of the experiment was a simple discrimination test. Two signals (a random choice from the set of three) was presented to the subject with varying noise intensity (variance). That is, each signal was contaminated by a noise source with specified mean and variance levels. The objective was for the observer to determine if the two signals displayed on the computer screen were the same or different. Various noise levels and display rates were introduced to the subject to obtain a wide range of results.

To further test the display methods another parameter was later introduced. The data was now presented either in a Raw Form or Processed Form. In Raw Form the data is presented as it appears from the transducer. The Processed Form takes this raw data and applies a digital filtering technique before it is presented to the observer. The two filtering methods utilized were Trigg's Tracking Function (a special form of Kalman filtering) and Differential Filtering (linear slope detection)[2]. It was our hypothesis that the processed form of the data provide would help in detecting data changes in the presence of noise.

RESULTS AND DISCUSSION One subject was studied at length to compare the two display methods shown in Figure 1 over widely varying conditions. Figure 2 shows the ROC curves obtained. It is evident from the ROC curves that the graphic display was better than the numeric method of displaying data when the subject was asked to detect changes. Using nonparametric calculations (graphical interpolation, using polynomial fitting and bit map pixel counting) the area under the graphic ROC curve was approximately 54.5 % greater than the numeric ROC curve. Visually, the graphic display method conveys more information than the numeric display, and also shows a past history for reference. This likely enables the observer to implement their own visual trending analysis on the signal being monitored.

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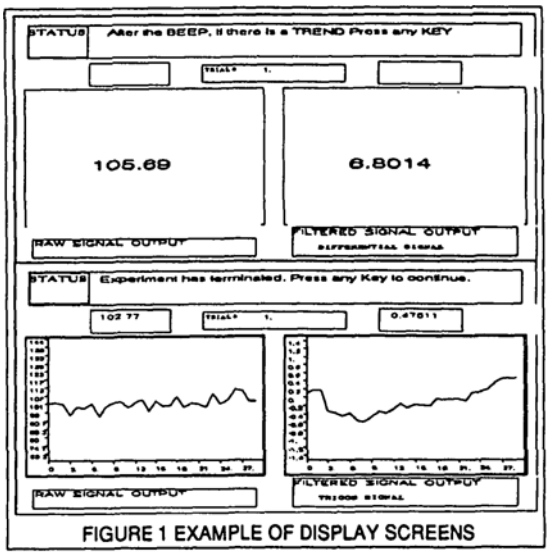


FIGURE 1 EXAMPLE OF DISPLAY SCREENS

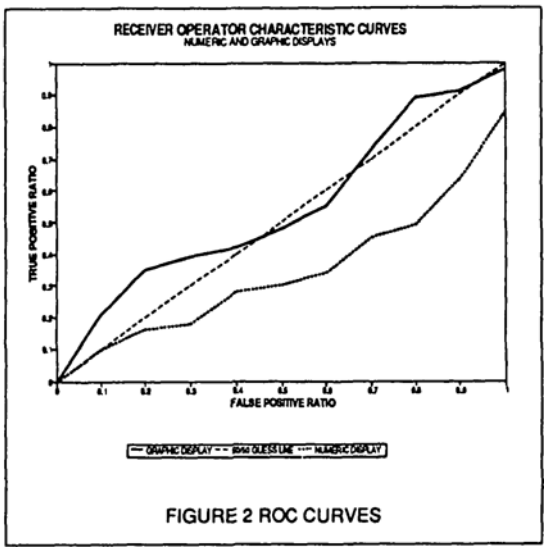


FIGURE 2 ROC CURVES

Figure 1 *(Top)* The top portion of this panel shows the numerical display, with raw data (left) and filtered data (right) displayed one point at a time. *(Bottom)* Here the data is displayed in graphical form, with raw data again on the left, and the filtered data on the right. ROC experiments indicate that monitoring performance may be superior in users of the graphical display in a monitoring for change' detection paradyme.

Figure 2. *(Bottom)* ROC curves for the numerical display (dotted) and the graphical display (solid). Curves with the most area under the curve are the best performers. The diagonal line is the '50-50 guess' line.

Blood Pressure Stability Display by Phase-Plane Methods

D. John Doyle [1,2] and Thomas Lee [2]
[1]Department of Anaesthesia, Toronto General Division, The Toronto Hospital
[2]Institute of Biomedical Engineering, University of Toronto

Patient monitoring is accomplished clinically by patient observation and scanning of patient monitors. However, such monitoring techniques may not be optimal for detecting early patient instability, for example, in blood pressure or some other monitored variable. Display methods which make more obvious changes in the behaviour of a monitored variable may facilitate timely intervention by clinicians who are dealing with unstable patients.

In this report, we propose that the concept of "phase-plane displays", borrowed from the industrial and electrical engineering arenas. We also demonstrate a microcomputer system to carryout blood pressure monitoring using this technique.

A phase-plane plot is a plot of a variable against its rate of change. The concept is illustrated in Figure 1, which shows as an example, a plot relating blood pressure (P) and its rate of change (dP/dt). Normally, blood pressure will sit near its setpoint and its rate of change will be near zero. This is illustrated in the top of Figure 1. The bottom of Figure 1, on the other hand, illustrates an unstable patient. The blood pressure is too high (far to the right of the set point) and is getting worse all the time (dP/dt highly positive). Interpretation of the regions is given in Table 1.

In essence, the patient is said to belong to one of five regions: a normal zone, two regions where the patient's pressure is unstable, and two regions where the pressure is abnormal but correcting itself. These states are called

- normal, stable
- correcting hypotension (A)
- correcting hypertension (D)
- unstable hypotension (C)
- unstable hypertension (B)

and correspond to the regions in Figure 1 and Table 1.

TABLE 1: Interpretation of Phase-Plane Regions

Normal Zone:	Zone of normal operation for a particular patient
Region A:	Blood pressure is low (below set point) but dP/dt is positive, so the situation is correcting itself at the moment [correcting hypotension].
Region B:	Blood pressure is high (above setpoint) and dP/dt is positive, indicating that the blood pressure is getting higher still. This is an unstable patient. [Unstable hypertension].
Region C:	Blood pressure is low and dP/dt is negative, indicating that the blood pressure is getting lower still [unstable hypotension].
Region D:	Blood pressure is high and dP/dt is negative, so the hypertension is correcting itself at the moment [correcting hypertension].

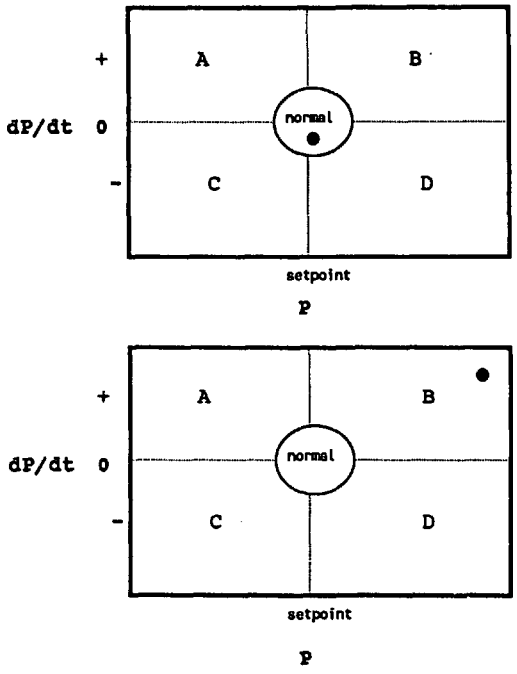
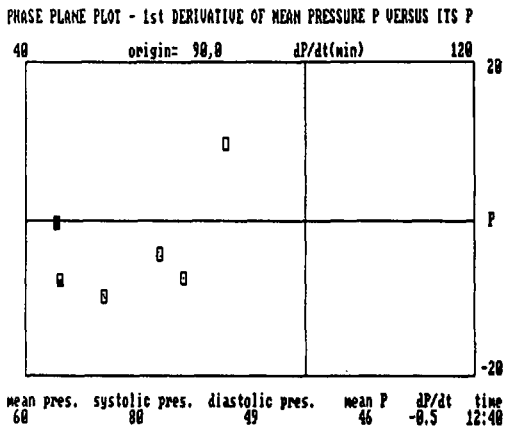


Figure 1. Illustration of the phase plane concept.
Top: Normal, stable situation
Bottom: Unstable hypertension

Figure 2. Sample phase-plane display from an ICU patient hooked up to the phase-plane monitor as developed at our laboratory. Pressure and pressure change data is shown for the last six blood pressure measurements taken at 1 minute intervals.



PATIENT A

THE RESIDENTS' COMPETITION - A 25 YEAR REVIEW

K. M. McClenaghan and C. D. Mazer, MD FRCPC, Department of Anaesthesia, St. Michael's Hospital, University of Toronto, Toronto, Ontario M5B 1W8

INTRODUCTION:

The Residents' Competition has been held at the Annual Meeting of the Canadian Anaesthetists' Society for the past 25 years. According to the "Rules of Competition" printed in the Canadian Anaesthetists' Society Journal in 1968, the purpose of the Residents' Competition was and still is to "encourage scientific excellence in physicians training in the specialty of anaesthesia in Canada".[1] The papers to be presented were to be of "research, clinical or review character", and they were to be judged by the chairs of the Canadian university departments of anaesthesia (or their delegates) "according to the material described, visual aids, and question period".[2] The purpose of this study is to review the Society's experience over the past 25 years of the Residents' Competition to decide if these goals have been achieved.

METHODS:

The data from all participants and their presentations at the Residents' Competition for the years 1967 to 1991 were collected and entered in a database program. The names of competitors, the titles of the papers, and the order of presentation were obtained from past Canadian Anaesthetists' Society meeting annual programs. The names of the award winners (first, second and third) were obtained from records from the Canadian Anaesthetists' Society. A questionnaire was sent to all participants (if address was available) to determine: 1) if his/her presentation was followed-up with a published paper, 2) the total number of his/her publications, and 3) if s/he subsequently practiced in an academic (university affiliated) setting. A separate questionnaire was sent to the program directors of anaesthesia from all 16 universities in Canada to determine the total yearly number of anaesthesia residents in their program, and to fill in missing data regarding the sex and academic affiliation of each competitor who attended that university. All entries in Residents' Competition were reviewed to determine if the work presented was primarily clinical (human research, case report or clinical review) or laboratory (animal study, technology assessment) in nature. Data was analyzed using chi-square or unpaired t tests where appropriate with $P<0.05$ being considered significant.

RESULTS:

The total number of papers presented over the 25 year period was 226. Although the Residents' Competition was originally limited to eight entries, it has ranged in size from 6 in 1972 to 13 in 1987. Sixteen program directors (100%) and 145 participants (64%) returned the completed questionnaire. Of the 226 competitors, significantly more were male (87%) than female (13%) - $p<0.0001$. However, the proportion of male entrants who were winners of first, second or third prize was similar to that of the female entrants who were winners (33.3% male vs 34.5% female). Sixty-two of the papers presented (27%) were laboratory reports. Laboratory reports accounted for 44% of the first prize winners, and 31% of the first, second or third prize winners.

The proportion of participants whose ultimate profesional practice included academic anaesthesia, and the publication profile of the competitors is shown in Table 1. Sixty percent of all participants who answered the questionnaire published a follow-up article of the material presented at the Residents' Competition, and over seventy percent have published one or more papers during their career.

DISCUSSION:

Since its inception in 1967, the Residents' Competition has provided a forum for the presentation of scholarly work by residents or fellows in Canadian anaesthesia training programs. Most of the participants have contributed to the scientific knowledge base of our specialty, and many have had distinguished academic careers. Our data would suggest that, over the last 25 years, the Residents' Competition has been successful in encouraging scientific excellence in those training in the specialty of anaesthesia, and is an important and unique aspect of the annual meeting of the Canadian Anaesthetists' Society.

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Table 1

	Follow-up article published	Mean (±SD) number of articles published	Academic Practice
All participants	60.3%	11 ± 18	78.8%
Award recipients (1st, 2nd, or 3rd)	70.2%	13 ± 17	91.6% *
First prize winners	73.7%	16 ± 19	95.7% ▲

$p < 0.05$ for award recipients vs. non-award recipients (*), or first vs. non-first prize winners (▲).

MATERNAL POSITIONING AFFECTS FETAL HEART PATTERN CHANGES AFTER EPIDURAL ANALGESIA FOR LABOUR

R. Preston MD, E.T. Crosby MD, D. Kotarba MD, H. Dudas RN, R.D. Elliott MD
Ottawa General Hospital, University of Ottawa, Ottawa, Ontario, Canada, K1H 8L6.

Introduction: Adverse changes in fetal heart patterns develop commonly during initiation of epidural block for labour analgesia and have been attributed to fetal uptake of local anesthetic.[1,2] An alternate hypothesis is that the wedged supine position (WSP), used to nurse women in labour, fails to adequately prevent aortocaval compression, thus compromising uterine blood and fetal oxygen supply. The purpose of this study is to investigate the role of maternal position on fetal heart patterns during epidural analgesia. Our hypothesis is that the full lateral position (FLP) will provide better prophylaxis than the WSP against aortocaval compression during onset of an epidural block and result in a reduced incidence of abnormal fetal heart patterns consequent to the block. The study will also examine the effects of the FLP on the efficacy of the epidural block.

Methods: Following ethics committee approval and informed consent, 88 ASA Class I or II parturients requesting an epidural, were randomized into: Group I, nursed in the WSP, and Group II, nursed in the FLP, during induction of epidural block. Continuous external fetal heart rate monitoring was initiated before block induction. Each patient received a standardized dose of local anesthetic via the epidural catheter. The duration of the study was the first 30 minutes after initiation of epidural block. The fetal heart rate strips were analyzed at the conclusion of the study for clinically important changes in the fetal heart pattern by a blinded obstetrician. The quality and efficacy of the block were assessed using VAS pain scores, a motor block score, and sensory levels. The data for the two groups were analyzed using the Chi-square and Fisher's exact tests with $P<0.05$ considered significant.

Results: 15 patients were excluded because of incomplete data, technical failure or failure to complete the protocol, leaving 38 patients in Group I and 35 in Group II. There were no differences between the two groups with respect to epidural block characteristics.(Table I)

Fetal heart pattern changes were not different with respect to the total number of events reported.(Table II) However, fetal heart pattern changes considered severe (decelerations to <100 bpm for >60 sec) occurred more frequently in Group I (13%) compared with Group II (0%), $P<0.05$.

Discussion: This study demonstrates that use of the FLP significantly decreases the incidence of ominous fetal heart pattern changes seen with onset of the block but does not adversely affect the efficacy of the epidural block compared with WSP. We attribute this result to the more effective prevention of aortocaval compression by the FLP compared with the WSP. Clinically, the study is relevant in that it shows not only that there is an alternative position in which labouring women with epidural blocks may be nursed, but also that the FLP may be the preferential position for prevention of adverse fetal heart rate changes associated with epidural analgesia.

References:

1) Anesthesia and Analgesia 1975; 54:779-82.
2) Anesthesia and Analgesia 1982; 61:638-44.

Table I.

Characteristic	WSP	FLP	P
Number of patients	38	35	
Initial VAS score			
4 - 7	18	15	NS
8 - 10	20	20	NS
Motor block			
None	24	25	NS
Partial	13	10	NS
Full	1	0	NS
Uneven block	2	5	NS
Repositioned	13	13	NS
Unilateral block (30 min)	1	0	NS
Supplement at 30 min	2	3	NS
Final VAS score			
0 - 3	35	31	NS
4 - 7	3	4	NS

Table II.

	WSP	FLP	P
FHR Strips Evaluated	38	33	
FHR Changes	13	7	NS
Decreased Variability	2	0	NS
Decelerations	10	6	NS
Tachycardia	3	1	NS
Severe Changes	5	0	$p < 0.05$

CEREBRAL AUTOREGULATION IS MAINTAINED DURING PROPOFOL-NITROUS OXIDE ANAESTHESIA IN HUMANS.

J. Enns, A.W. Gelb, P.H. Manninen, J.M. Murkin, J.K.Farrar
Department of Anaesthesia, University Hospital, London, Canada.

INTRODUCTION: In normal individuals, cerebral autoregulation maintains cerebral blood flow(CBF) constant despite changes in mean blood pressure between 50-150 mmHg. It is important that autoregulation not be deranged by anaesthetics else a change in BP, even within the normal range, could result in cerebral ischaemia or haemorrhage. The aim of this study was to establish whether autoregulation is maintained in humans during propofol-nitrous oxide anaesthesia.

METHODS: Following institutional approval and after obtaining informed written consent, eight ASA 1 patients scheduled for elective surgical procedures were anaesthetized with propofol 3.0 - 3.5mg/kg. After tracheal intubation, anaesthesia was maintained with oxygen/nitrous oxide (30%/70%) and a propofol infusion at a rate of 300 ug/kg/min which was reduced to 200 ug/kg/min after 10 minutes and then to 150 ug/kg/min 30 minutes post induction.

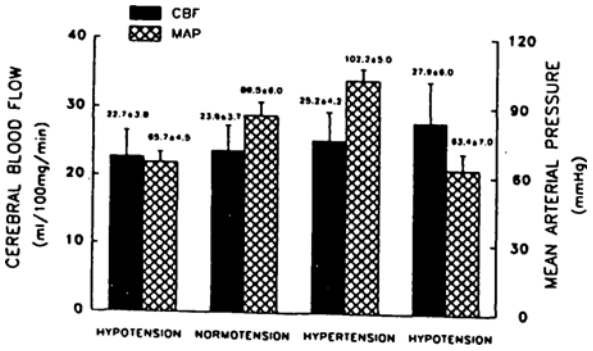
A radial arterial catheter was placed after induction of anaesthesia and BP continuously recorded. Ventilation was controlled and normocapnia maintained using continuous end-tidal capnometry. Normothermia was maintained with a heating blanket.

CBF was determined from the average clearance of intravenously injected ^{133}Xenon and measured by ten external scintillation detectors, five located over each cerebral hemisphere. End tidal gas sampling was used to correct for recirculation. The resulting clearance curves were assessed by non-compartmental height over area analysis. CBF measurements took place within 90 minutes of induction. $PaCO_2$, temperature, mean BP and haemoglobin were measured with each CBF determination.

CBF was measured during steady state at low, normal, and high BP. Induction of propofol anaesthesia results in approximately a 25% reduction in BP(low BP). BP was then increased with a phenylephrine infusion (0.25 - 1.0 ug/kg/min) to 85mmHg (normal BP) and then to 105mmHg (high BP). Finally, phenylephrine was discontinued and CBF was again determined once BP returned to a constant level.

RESULTS: BF did not change significantly despite significant changes in BP(fig 1). There were no significant changes in PaCO2, temperature or haemoglobin.

DISCUSSION: These results show that cerebral autoregulation remains intact despite changes in BP from 65mmHg to 105mmHg during propofol-nitrous oxide anaesthesia in humans. Phenylephrine could theoretically produce cerebral vasoconstriction and so mask an increase in CBF but this is unlikely as intravascular vasopressors do not have direct effects on the cerebral vasculature.



CONTINUOUS SPINAL VERSUS CONTINUOUS EPIDURAL ANAESTHESIA FOR TOTAL KNEE REPLACEMENT

David L. Muzyka, MD, L. Philip Lin, MD, Ms. Susan Fossey, Brendan T. Finucane, MD, FRCPC

Department of Anaesthesia, University of Alberta Hospitals, Edmonton, Alberta, T6G 2B7

INTRODUCTION: Continuous spinal anaesthesia (CSA) has superceded continuous epidural anaesthesia (CEA) by almost four decades [1]. However, until very recently, with few exceptions [2,3], CEA was considered preferable by most clinicians. The unacceptably high incidence of postdural puncture headache associated with CSA has given CEA the distinct advantage for many years, however, this advantage is nullified in older age groups. There is only one report in the literature which compares CSA with CEA and that was a retrospective review [4]. The purpose of this study was, to prospectively compare these two techniques, using the following parameters: technical ease, efficacy, complications.

MATERIALS AND METHODS: Following ethics approval and written informed consent, 30 patients were randomly assigned to two groups (CSA or CEA) using random numbers. Patients of either gender, scheduled for Total Knee Replacement (TKR) were considered eligible for the study. Inclusion criteria: age ≥ 50 years, ASA I-III, no contraindications to regional anaesthesia. All patients received 1 litre of Ringer lactate prior to the procedure. All procedures were performed in a sitting position in the L3-4 interspace. A 17 gauge Tuohy needle was used for both procedures. The following is a brief description of each procedure including dosage regime:

CSA: The 17 gauge Tuohy needle was advanced until CSF was obtained. Then a 20 gauge catheter was advanced 3 to 4 centimetres and taped securely. Patients were then placed supine and 1.5 ml of 0.75% bupivicaine was injected. Additional 0.5 ml increments were injected every 15 minutes until anaesthesia was detected at the T6 dermatome.

CEA: A 17 gauge Tuohy needle was advanced using the loss of resistance technique. A 20 gauge catheter was then advanced 3 to 4 centimetres into the epidural space and taped securely. The patient was then placed in the supine position and a 3cc test does of bupivicaine 0.75% was injected. Following a 3 minute period and a negative test dose, 10cc of 0.75% bupivicaine were injected over a 2 minute period. An additional 3 ml were injected every 15 minutes until anaesthesia was detected at the T6 dermatome.

MEASUREMENTS: The following parameters were measured and compared in each group: age, weight, height and gender; 5 minute vital signs; time from first injection until endpoint reached (CSF, loss of resistance); number of attempts; time from first attempt until main injection; onset and duration of sensory and motor blockade; incidence of significant hypotension (25% decrease SBP); and bradycardia (heartrate less than 60); and incidence of headache and urinary retention. Statistical analysis was performed comparing the two groups and a p-value of less than 0.05 was considered statistically significant.

RESULTS: Patient characteristics were comparable in both groups. CSA was technically easier to perform and the onset of action of both motor and sensory anaesthesia was significantly faster ($P < 0.05$ Table 1). The overall quality of anaesthesia was better with CSA compared with CEA. Blood loss was similar in both groups. The incidence of hypotension and bradycardia and urinary retention were comparable in both groups. There was one headache reported in the CSA group. There were three failures in the CSA group compared with two in the CEA group.

DISCUSSION: There has been a renewed interest in continuous spinal anaesthesia in recent years due mainly to technologic advances in needle and catheter design. With modern technology it is now possible to pass a 32 gauge catheter through a 26 gauge needle [5], thereby opening this technique up to obstetric patients. However, recent reports have suggested that the use of microcatheter techniques may contribute to the maldistribution of local anaesthetics in the subarachnoid space, which in some cases results in Cauda Equina Syndrome [6]. The technique of CSA using larger catheters has been an option in older patients for 50 years, yet few clinicians have selected it. CEA has been perceived by most clinicians to be a safer technique overall, yet there are few if any prospective studies comparing these two techniques. In this preliminary study it would appear that CSA has many advantages over CEA in patients older than 50 years of age. The onset and quality of surgical anaesthesia is superior. Technical difficulties are fewer and the incidence of complications including hypotension, headache and urinary retention are no different. Based on these data, CSA has definite advantages over CEA in patients aged > 50 years.

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[3] Anesth Analg 1987; 66: 791-4.
[4] Anaesthesia 1989; 44: 47-50.
[5] Anesth Analg 1990; 70: 97-102.
[6] Can J Anaes 1991; 38: 908-11.

TABLE 1

PARAMETER	CSA	CEA
No. of attempts	1.7 ± 1.0 **	3.0 ± 1.7
Procedure time (mins)	7.5 ± 4.9 **	9.0 ± 5.2
Sensory onset to T6 (mins)	14.0 ± 13.1 **	23.8 ± 18.5
Motor onset	8.1 ± 7.0 **	15.0 ± 6.7

values are means ± SD
** p value < 0.05

Superior Laryngeal Nerve Block: An Anatomical Study

M. Stockwell, S. Lozanoff, S. Lang and J. Nyssen

The Departments of Anaesthesia, Anatomy, and Pathology
University of Saskatchewan, Saskatoon, Saskatchewan S7N OXO

INTRODUCTION: Superior laryngeal nerve block is a frequently used technique facilitating awake intubation. As the cough reflex is not diminished with this block, it may be particularly useful in the patient requiring awake intubation who has a full stomach since airway protection (ie. the cough reflex) remains intact.[5] However, the anatomical basis of this block has not been adequately described. The purpose of this study, in part, is to determine the anatomical basis of the superior laryngeal nerve block, particularly as pertinent to injection of an aliquot of local anaesthetic.

Typically, this technique is described using a standard bevel needle for injection.[1-4,6] We modified the technique to use a short bevel 22 gauge needle since, in our experience, tactile feedback in performing the block is greatly increased. The second purpose is to determine whether our modified superior laryngeal nerve block technique can be successfully administered as simulated in cadavers.

METHODS: Fifteen cadavers were selected at the time of autopsy. Subjects were only included if the relevant anatomy of the neck could be adequately palpated and if no neck trauma was evident. Superior laryngeal nerve block was performed bilaterally using a ten ml syringe with a short bevel 22 gauge needle. Three ml of dilute methylene blue (0.02%) was used to simulate the local anaesthetic. Transcutaneous injection was made midway between the thyroid cartilage and the hyoid bone one to two centimeters ventral to the greater cornu of the hyoid all as identified by palpation. The needle was inserted until firm resistance to its passage was encountered. This was assumed to be the thyrohyoid membrane and the solution was presumably deposited external to it by withdrawing the needle a fraction of a mm. This technique was described by Schultz.[4]

Immediately following injection, gross dissection of the larynx and laryngopharynx was performed in order to identify the anatomical structures stained by the dye. Success was defined when dye stained the internal laryngeal nerve (the sensory branch of the superior laryngeal nerve) as it perforated the thyrohyoid membrane. In two subjects the larynx was removed and fine dissection was performed to further identify the relevant anatomy. Additional dissections were performed on formalin-fixed cadavers. In this case, the needle was placed as described above and the tissues surrounding the needle dissected.

RESULTS: A needle inserted in the position described passes through, or near, a number of structures after skin, sub-cutaneous connective tissue, and the strap muscles: Thyrohyoid Membrane: extending from the hyoid bone to the thyroid cartilage. This structure was thickened anteriorly and posteriorly. However, the intermediate region was thin and its fibers separated rather easily. This structure was stained by the local anaesthetic in its entirety. However, the dye was completely contained internal to this membrane, not external to it as had been expected. Subthyrohyoidal Compartment: a small space deep to the thyrohyoid membrane bounded anteriorly and laterally by the thyrohyoid membrane, medially by the laryngeal mucosa, superiorly by the hyoid bone and inferiorly by the conus elasticus. It contained the fat body of the larynx. This region was completely stained with dye. Internal Laryngeal Nerve: identified from its source at the vagus nerve, this nerve pierced the thyrohyoid membrane and entered the subthyrohyoidal compartment from the posterosuperior aspect. It coursed inferoanteriorly through the fat body as it arborized. This nerve was heavily stained with dye. Lateral Glossoepiglottic Fold: as the needle traversed the subthyrohyoidal compartment, it entered the submucosa of the larynx along the lateral wall of the piriform recess. Firm resistance to passage of the needle was provided by the dye-stained lateral glossoepiglottic fold not, in fact, the thyrohyoid membrane. Quadrangular Membrane: the mucosa overlying the false vocal folds was teased away and the quadrangular membrane identified. This membrane was thin and delicate. It was traced superiorly connected to the epiglottic cartilage as well as the connective tissue underlying the lateral glossoepiglottic fold. The region of the false vocal fold and the ventricle of the larynx were stained. Conus Elasticus: this thick connective tissue structure was observed to extend from the vocal ligament to the cricoid cartilage. No stain was seen below the true vocal fold.

Of 30 injections performed, 29 were deemed successful for a success rate of 97%. In light of the unexpected findings of the dissections, success was redefined as the dye being localized within the subthyrohyoidal compartment. As mentioned, the internal laryngeal nerve traverses this space and was heavily stained within the compartment.

DISCUSSION: Many descriptions of superior laryngeal nerve block involve perforating the thyrohyoid membrane after its location is identified by walking a needle off either the thyroid cartilage or the hyoid bone.[2,3] Injection is then made deep to the membrane. We had chosen to use the technique described by Schultz (see methods) in our previous work for two main reasons. The first is that walking a needle off the thyroid cartilage or the hyoid bone caused significant discomfort due to stimulation of the perichondrium or periosteum respectively. Secondly, a basic misunderstanding of the anatomy led us to be concerned that perforating the thyrohyoid membrane would allow the possibility of injecting anaesthetic into the airway, a situation we wished to avoid in our research.

By modifying Schultz' technique to use a short bevel 22 gauge needle we had hoped to improve tactile feedback and thus improve the sensitivity of identifying the thyrohyoid membrane. In retrospect this may have been so as a slight "pop" was felt in most, but not all, subjects as the needle passed between the hyoid bone and the thyroid cartilage. This sensation had been attributed to the needle passing through the fascia of the strap muscles but probably represented perforation of the thyrohyoid membrane. The improved tactile feedback did, however, improve sensitivity in performing the block as the lateral glossoepiglottic fold was reliably identified by the firm resistance it presented to the passage of the needle. This resistance is, in our experience, orders of magnitude greater than the resistance presented by the thyrohyoid membrane. Thus the correct depth of needle placement is easily identified and injection made in the subthyrohyoidal compartment were the internal laryngeal nerve arborizes.

Our report success rate of 97% is consistent with the rates reported by those who have used a technique that involved injection deep to the thyrohyoid membrane (thus in the subthyrohyoidal compartment). From 93 to 98% success rates have been reported in over 500 subjects.[1-3]

Despite our initial lack of understanding of the anatomy of this block, the technique we have described presents a simple and reliable method of internal laryngeal nerve anaesthesia which, in our clinical practise and research experience, presents minimal discomfort to the subject.

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Comparison of 25G Whitacre vs 24G Sprotte Needles for Caesarean Section

DC Campbell MD, MJ Douglas MD, TJG Pavy MD, ML Flanagan MD, GH McMorland MD

Department of Anaesthesia, Faculty of Medicine, The University of British Columbia & Grace Hospital, Vancouver, British Columbia

Introduction: Post-spinal headache (PSH) is still a frequent complication of spinal anaesthesia. It has been documented that the incidence of PSH correlates well with the size of the spinal needle used[1,2] and shape of the needle tip.[3] It has been demonstrated that the new non-cutting, pencil point spinal needles can reduce the amount of CSF leakage from the dural puncture site.[3] The incidence of PSH following the use of the 24G Sprotte needle was reported at less than 1%.[4,5] The 25G Whitacre needle has a similar shape, but the port is smaller and placed closer to the needle tip.

The purpose of this prospective, randomized, blinded study was to compare the incidence of PSH following the use of these two needles for spinal anaesthesia in Caesarean sections. Additionally, the effectiveness of anaesthesia and other complications were evaluated.

Methods: Following institutional Ethics Committee approval and informed consent, 91 ASA 1 and 2 women undergoing spinal anaesthesia for Caesarean section were recruited. The patients were randomized into two groups having spinal anaesthesia performed with either the Sprotte (n=43) or Whitacre (n=48) needle. Patients were blinded as to which needle was utilized.

Patients were positioned in the right lateral or sitting position and lumbar puncture performed between the L2-3 or L3-4 interspaces. Hyperbaric 0.75% Bupivicaine (9.0-11.25 mg), Morphine 0.25 mg and Fentanyl 10 mcg were administered to provide anaesthesia to the T4 dermatone. The dose of Bupivicaine was administered at the discretion of the anaesthetist conducting the procedure. Each patient received at least a 2 litre bolus of a balanced salt solution prior to subarachnoid blockade. Difficulty of insertion, dose of Bupivicaine, effectiveness of anaesthesia, and whether hypotension resulted were documented.

Post-partum, the patients were assessed every 24 hours for 5 days by an investigator blinded to the needle utilized. The patients were questioned with respect to the presence of headache, its character, location, severity, duration and any treatment was documented. A PSH was one which was aggravated by upright positioning and relieved in the supine position.

Data were analyzed using the unpaired T-Test, Chi Square and Fisher's Exact test where appropriate. Data were expressed as mean $\pm$ standard deviation and $P < 0.05$ was considered significant.

Results: There were no statistically significant differences between the two groups with respect to the demographic data (Table 1), difficulty of insertion, bupivicaine dose, occurrence of transient hypotension or effectiveness of anaesthesia (Table 2). 3 failed insertions were reported, 2 with the Whitacre (4%) and 1 with the Sprotte (2.3%). 2 (4.6%) failed blocks were reported with the Sprotte following successful first attempt dural puncture and free flow of CSF. 20 non-spinal headaches were reported postpartum (22%), 14 (33%) with the Sprotte and 6 (12%) with the Whitacre. 2 PSH were documented, both with the Sprotte (4.6%), one of which required a subsequent blood patch.

Discussion: Although the incidence of PSH following the use of the 24G Sprotte has been reported as low as 0.02%[5], it appeared higher at our institution. Therefore, this prospective, randomized, blinded study was undertaken to compare the 24G Sprotte with the 25G Whitacre spinal needle.

The results of this ongoing study indicate both needles have a similar ease of insertion, with a low incidence of insertion failure, and similar effectiveness in providing anaesthesia. However, 2 failed blocks were reported with the 24G Sprotte needle. This problem has been previously documented and appears to be related to the more proximal position of the needle's large orifice allowing inadvertent injection into the epidural space.[4,6]

The 2 PSH reported with the 24G Sprotte represented an incidence of 4.6% (2/43). One headache subsequently required a blood patch and the other was mild, not requiring analgesics. No PSH were observed with the 25G Whitacre needle (0/48).

Although more data is currently being collected, the 25G pencil point Whitacre appears to comply with the necessary requirements for technical ease of insertion and paucity of failed blocks and PSH. The Whitacre needle is also less expensive than the Sprotte needle.

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TABLE 1 DEMOGRAPHIC DATA

	SPROTTE (n=43)	WHITACRE (n=48)
AGE (yr)	31.7 $\pm$ 4.6	32.1 $\pm$ 5.8
HEIGHT (cm)	158.8 $\pm$ 7.5	158.3 $\pm$ 6.8
WEIGHT (Kg)	73.7 $\pm$ 13.3	74.6 $\pm$ 11.6
MULTIPARITY	32	37
ASA I	40	44

TABLE 2 RESULTS

	SPROTTE (n=43)	WHITACRE (n=48)
EASE OF INSERTION 1st or 2nd Attempt Failed	 41 (95%) 1 (2.3%)	 40 (84%) 2 (4%)
BUPIVICAINE (mg)	10.30 $\pm$ 0.88	10.10 $\pm$ .95
TRANSIENT HYPOTENSION	21 (49%)	27 (56%)
EFFECTIVENESS No Supplementation Failed Block	 35 (81%) 2 (4.6%)	 46 (96%) 0
HEADACHE Non-Spinal Headache PSH	 14 (33%) 2 (4.6%)	 6 (12%) 0
BLOOD PATCH	1	0

"DRUG ALLERGIES" IN THE SURGICAL POPULATION

Orlando R. Hung, FRCPC, Colin Bands, MB ChB, Geoffrey Laney, MB ChB, FFARACS, Catherine Lipsett, BSc, David Drover, MD, Mark Stafford-Smith, FRCPC, Sarah Stevens, MD, Kate Shields, MD, Michael J. MacSween, FRCPC

Departments of Anaesthesia and Medicine, Dalhousie University, Halifax, NS, B3H 2Y9

Introduction: Many patients are "labelled" as having allergies to medications. They are frequently denied the administration of these medications even though the histories of the "allergic reactions" were incompatible with allergic phenomenon. The objective of this study is to determine the incidence of reported drug allergies in a surgical population, and the validity of these drug allergies.

Method: After obtaining institutional approval, prospective preoperative evaluations of patients past history of allergy were obtained. A detailed assessment of drug allergies, symptoms and signs, family history, history of atopy, and history of laboratory investigations were recorded. An immunologist was consulted to verify the claimed drug allergies using the information obtained from the history and the patients' charts. The claimed drug allergies were placed in three different groups. High probability of allergy was considered if one or more of the following was present with or without family history of similar drug allergies, and history of atopy: (1) cutaneous manifestations; (2) respiratory difficulties; (3) cardiovascular effects; (4) positive laboratory investigations. Low probability of allergy was considered if one or more of the following symptoms and signs were present without the presence of the above: (1) gastrointestinal disturbances; (2) CNS disturbances; (3) nonspecific symptoms such as feeling strange or funny. The allergy status was considered to be unknown if the patient could not recall any symptoms and signs of drug reactions.

Results: 1411 patients were assessed of which 50.8% were females and 49.2% were males. 399 patients (28.3%) claimed to have one or more allergies to drugs with a total claim of 536 drug allergies. More females (60%) reported to have drug allergies than males (40%). Older patients appeared to have more reported allergies than younger patients (Figure 1). In patients under 30 years of age 16.7% claimed to have drug allergies compared to 38.4% in patients older than 70 years of age. There is no evidence that patients who receive more medications have more reported drug allergies. Antibiotics (ATBC) accounted for approximately 51%, whereas opioids, non-steroidal anti-inflammatory agents (NSAIA), and sedatives/hypnotics (SED/HYP) together accounted for 37.5% of all claimed drug allergies. A variety of other drugs accounted for the remainder of the reported drug allergies. Within the ATBC group, more than 60% were related to the penicillins and 20% were related to the sulfa drugs. For the opioid group, codeine (45%) appeared to be the most common reported drug allergy followed by meperidine (25%) and morphine (20%). Figure 2 shows the validity of claimed drug allergies for different classes of drugs utilizing the predefined criteria.

Discussion: More than one quarter of the surgical patients (28.2%) claimed to have had one or more drug allergies. The majority of ATBC allergies (71%) appear to be associated with a high probability of drug allergy. However, the majority (72%) of the remaining drug allergies (including opioids, NSAIA, and SED/HYP) are associated with low probability of allergic reactions. Overall, only 50% of the reported drug allergies have clinical histories which are compatible with true allergic reactions. Our findings, which are similar to those found in other hospitals, suggest a serious problem in the "labelling" of the drug allergies in our patients.[1] As physicians, we have the responsibility to take an active role in the evaluation of patients history of drug allergies. To avoid unnecessary "mislabelling" of patients with drug allergies, we must educate patients and other health care personnel in the differences between predictable adverse drug reactions and true allergic reactions.

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Figure 1.

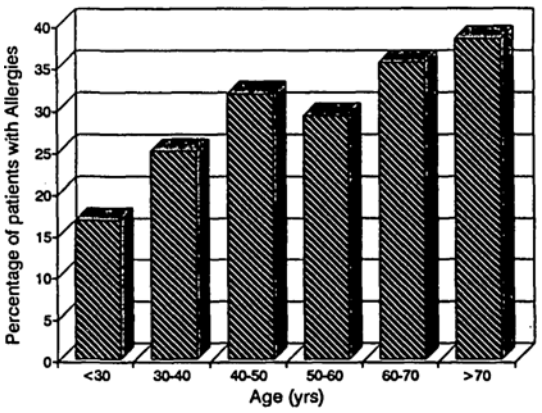
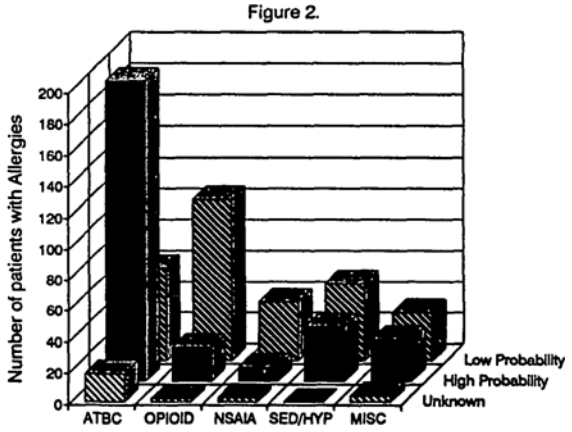


Figure 2.



RECOVERY AFTER ORAL MIDAZOLAM PREMEDICATION IN CHILDREN: INTRAVENOUS VS INHALATION INDUCTION

J.D. McAllister MD, P. K. Morley-Forster FRCPC, A.K. White FRCSC, M.D. Taylor,
H.M. Vandenberghe PhD, D. Knoppert MSc Phm
Department of Anaesthesia, St. Joseph's Heath Centre, University of Western Ontario, London, Ontario, Canada

INTRODUCTION: With its rapid onset, painless administration, low incidence of adverse effects, and short duration of action, oral midazolam approaches the ideal paediatric premedication. Previous controlled studies after oral [1], nasal [2] and rectal [3] midazolam premedication using halothane for induction and maintenance showed no increase in postoperative drowsiness. The pharmacokinetics of oral, intramuscular and rectal midazolam during halothane anesthesia have been well described [4]. However, no study to date has examined the clinical recovery characteristics and pharmacokinetics of oral midazolam following an intravenous thiopental induction.

This is the report of a prospective, randomized study to determine if midazolam premedication in children prolongs recovery after thiopental induction compared to halothane induction.

METHODS: Following institutional ethics approval and informed, written parental consent, 100 ASA 1 or 2 outpatients, aged 1 to 10, entered the study. All were scheduled for elective ENT surgery of 30 to 60 minutes duration. Each subject received midazolam (0.5 mg/kg) and atropine (0.03 mg/kg) orally, mixed with 5 - 10 cc double-strength Kool-Aid to disguise the bitter flavour. The 5 mg/ml concentration of midazolam was chosen to minimize the volume required. Twenty minutes after premedication the child was separated from the parents; anaesthesia was induced within 40 - 60 minutes of midazolam administration.

The ease of parental separation was graded by a surgical day care nurse on a 3-point scale. The level of sedation was graded on a 5-point scale at baseline (pre-midazolam) and 15 minutes post-midazolam by the nursing staff, and immediately pre-induction by the anaesthetist. The child's acceptance of the mask was graded. (see Appendix)

In the O.R., patients were randomly assigned to one of two groups: Group 1 received an inhalation induction with halothane, nitrous oxide and oxygen; Group 2 received intravenous thiopental (5 mg/kg). The children were cooperative enough to allow awake placement of all basic monitors. Intubation was accomplished with atracurium (0.4 mg/kg) and anaesthetic maintained with halothane 0.5 - 1.0%, N_2O:O_2, 70:30 with controlled ventilation.

At the end of surgery, halothane was discontinued, the muscle relaxation reversed, and intramuscular meperidine (1 mg/kg) given. The patients were extubated awake, making purposeful attempts to remove the endotracheal tube. The time from discontinuing the halothane to extubation was recorded.

The recovery room nurses, blinded to the induction technique, assessed level of sedation and standard PARR scores (see Appendix) on admission, at 30 minutes and, at discharge. Side effects, and additional morphine requirements were noted. Discharge was permitted at the discretion of the nursing staff following usual criteria.

In the last thirty patients, a #20 angiocath was inserted into the cephalic vein immediately after induction. One cc of blood was withdrawn for serum analysis every 10 minutes intraoperatively and on arrival and discharge from the PARR. Serum samples were analyzed by gas chromatography with an electron capture detector.

Data was analyzed by repeated measures ANOVA for parametric data, and chi-square for analysis of proportions. The t 1/2 ß was calculated by linear regression. A $p < 0.05$ was considered significant.

RESULTS: Five subjects were excluded for failure to follow the study protocol, leaving 47 in Group 1 and 48 in Group 2 for analysis. Each group was similar with respect to age (4.8 ± 1.9 years), sex, weight (19.7 ± 5.5 kg), type, and duration of surgical procedure (43 ±10 minutes), maintenance halothane concentration (0.6 ± .1%) and O_2 saturation preoperatively (97 ± 1.2%).

The ease of parental separation, and acceptance of the mask were described as good to excellent in 95% of patients. One child, though not visibly upset, reported visual hallucinations The time to extubation between the two groups was significantly different. (Group 1, 7.1 ± 3 minutes, vs Group 2, 8.8 ± 4 minutes, $p<0.05$). The sedation and PARR scores were lower in the thiopental group on arrival in the recovery room (Figures 1 and 2). However, there was no difference in the duration of recovery room stay (Group 1, 57 ± 18 minutes, Group 2, 59± 27 minutes), and, at discharge, sedation scores were equal.

The elimination half life was the same in both groups (Group 1, 1.9 ± .8 hrs vs Group 2, 1.8 ± .7 hrs). In those patients who had serum levels drawn on discharge from PARR, all were below 40 ng/ml, the level reported to produce sedation[4].

DISCUSSION: This study confirms the efficacy, safety and rapid uptake of oral midazolam, 0.5 mg/kg, as a premedication in young children. Although the thiopental group demonstrated a slightly prolonged emergence, the differences are not clinically important. Due to its rapid metabolism in children, it can be used for brief surgical procedures in combination with either thiopental or halothane induction without fear of prolonging recovery room stay.

APPENDIX:
Separation Scale: (1=crying 2=good, slightly anxious, 3=excellent)
Sedation Scale: 1=combative, 2=anxious, 3=calm, 4=drowsy, but awake, 5=asleep) **Mask Acceptance Scale:** (1=poor, 2=fair, somewhat fearful, 3=good easily calmed, 4=excellent, unafraid)
PARR Score: (10-point scale must be >7 for discharge)

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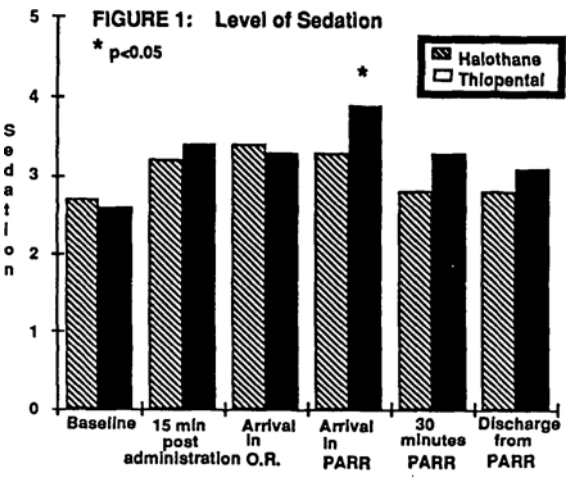

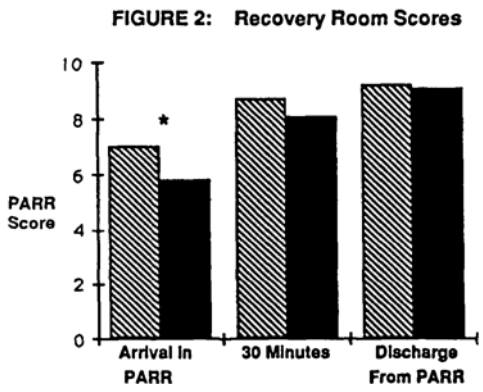

A COMPARISON OF CLONIDINE vs MORPHINE/GLYCOPYRROLATE PREMEDICATION FOR AWAKE DIAGNOSTIC FIBEROPTIC BRONCHOSCOPY

H. Reimer, MD, P.C. Duke, MD, C.H. Kehler, MD, M.W. Kepron, MD, V.A.Taraska, MD
Departments of Anaesthesia and Respiratory Medicine, University of Manitoba, Winnipeg, MB, CANADA R3E 1X2

Introduction: Fiberoptic bronchoscopy is commonly used for diagnostic purposes and for airway management. While the procedure is usually well tolerated, adverse hemodynamic and respiratory responses can occur [1]. Typical premedication consists of a narcotic/anticholinergic combination, selected for its sedative, antitussive, and antisialogogue effects. However, these agents have adverse effects including tachycardia and respiratory depression. Clonidine (C), an α-2 receptor agonist with sedative, anxiolytic, and antisialogogue properties has been shown to blunt hemodynamic responses to intubation[2]. These properties suggest that it may be a more efficacious premedicant for bronchoscopy. We therefore tested this hypothesis in a double blind prospective study, comparing clonidine to morphine/glycopyrrolate(M/G).

Methods: After institutional approval and informed consent, 40 patients were enroled in the study and randomly divided into 2 groups. Following application of a 2 channel Holter monitor (leads II and CB_5) and baseline blood pressure and heart rate determination, patients received either oral C, 5μgms/kg, 90 min pre-bronchoscopy, or IM M/G, .15mg/kg and 6μg/kg respectively, 60 min pre-bronchoscopy. All patients were also given a corresponding PO or IV placebo. 5ml/kg of ringer's lactate was administered, followed by a maintenance infusion. Prior to the procedure, salivation was measured as described by Mirakhur[3], sedation was assessed by observer on a 5 point scale, anxiety was assessed by visual analogue scale and multiple adjective checklist, and control heart rate and blood pressure were obtained. Awake diagnostic bronchoscopy was performed with topical lidocaine anesthesia. ECG and SaO2 were monitored continuously during the procedure and blood pressure was measured non-invasively every minute by oscillometry. A single measurement of ETCO2 was made through the bronchoscope with the tip positioned at the carina. New ST segment elevation or depression greater than 1 mm from baseline and lasting > 1 min was considered significant. Statistical analysis was by ANOVA for repeated measures, unpaired t-test, and Fisher's exact test as appropriate for the data being analyzed, with statistical significance assumed when $p < .05$. Data is expressed as mean $\pm$ SD.

Results: The groups were similar with respect to age, pre-existing hypertension, vasoactive drug therapy, and cough. There was a higher female/male ratio and more patients with pre-existing ischemic heart disease (4/19 vs 0/21) in the M/G group. There were no differences between groups in anxiety or sedation scores, cough during bronchoscopy, arrythmias, or ST segment abnormalities prior to the procedure. In the M/G group the volume of salivary secretions was lower, and the ETCO2 was higher. During the procedure, there was a higher incidence of ST segment abnormalities in the M/G group which persisted even when patients with pre-existing ischemic heart disease were excluded from analysis. At all measurement intervals, including baseline, there were significant differences in heart rate and blood pressure between groups. There was a small decline in SaO_2 over time, but no difference between groups. Three patients in the clonidine group developed clinically significant hypotension with postural symptoms.

Discussion: M/G premedication causes a significant hyperdynamic response which is minimally accentuated by topicalisation and bronchoscopy. This is associated with new ST segment abnormalities which may be indicative of myocardial ischemia. Clonidine premedication produces a smoother hemodynamic profile and less respiratory depression, but is associated with hypotention in some patients. It is also a less potent antisialogogue, though this difference is small.

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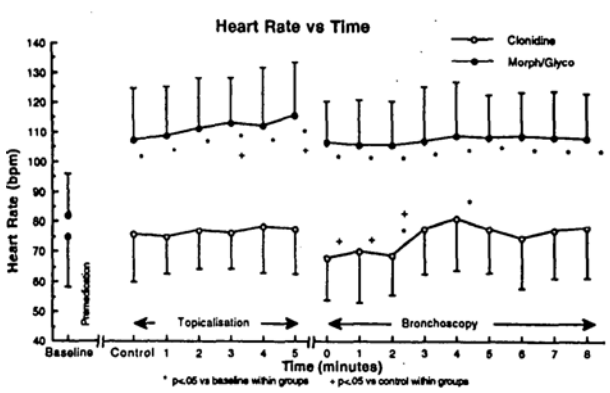
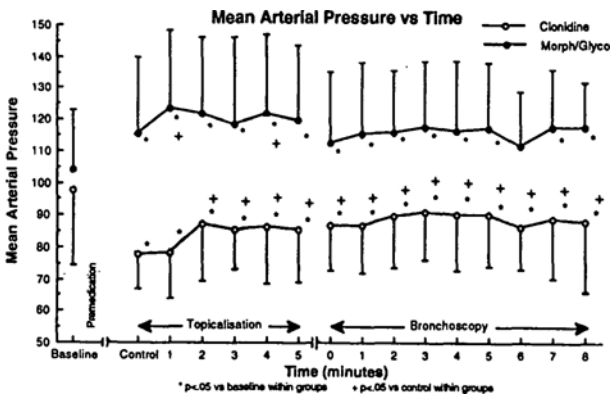
Table

	Clonidine	Morph/glyco
Salivary volume (ml)	.12±.6*	-.44±.4*
$ETCO_2$	37±6.6*	41±4.5*
ST abnormalities pre-bronchoscopy	2/20	3/14
ST abnormalities during topicalisation & bronchoscopy	0/20*	5/14*

ST data excludes 2 inadequate Holters and all patients with known ischemic heart disease *p < .05





NITROUS OXIDE IN LABOUR: SAFETY AND EFFICACY ASSESSED BY A DOUBLE-BLIND, PLACEBO CONTROLLED STUDY

J Carstoniu MD, P Norman MD FRCP(C), AN Sandler MB FRCP(C), J Katz PhD
Departments of Anaesthesia and Psychology, Toronto General Division, The Toronto Hospital and Departments of Anaesthesia and Behavioral Science, University of Toronto, Toronto, Ontario

INTRODUCTION Trials attesting to the safety and efficacy of an intermittently administered mixture of 50% nitrous oxide and 50% oxygen [N_2O/O_2] for analgesia during labour have been reported [1,2] but there is a dearth of well controlled studies in the literature despite over 60 years of clinical experience. Recently, diffusion hypoxia has been invoked to explain reported desaturation following N_2O/O_2 administration during labour [3,4] but these studies lacked adequate controls as well. The goal of this ongoing randomized, double-blind, placebo controlled prospective study was to determine whether N_2O/O_2: (1) leads to hypoxemia following contractions and (2) provides superior analgesia to compressed air when administered during labour contractions.

METHODS After obtaining institutional ethics committee approval and informed written consent, 11 women in active labour were randomized into two groups. Group I [N=5] self administered N_2O/O_2 [Ohmeda Nitronox Hospital Model #91120053] during each of 5 consecutive contractions. A 5 minute "washout" period followed and then compressed air was self administered via a hose and demand valve assembly identical to that on the Nitronox machine. Group II [N=6] received the gases in reverse order. Patients and the investigator were blinded to treatment order. Continuous monitoring with a pulse oximeter [Nellcor N-100C and D-25 oxisensor] was instituted at the start of each trial. Patients were instructed in the use of a visual analogue scale [VAS] to rate the pain of contractions. VAS scores after each contraction were recorded, as was the lowest oxygen saturation (SaO_2) reached between each contraction. Baseline VAS and lowest SaO_2 were recorded at the start of each trial. At the end of the trial patients were asked to identify whether they received N_2O/O_2 or air during the previous 5 contractions. Demographic data and patients' ability to identify N_2O/O_2 were analyzed using Student's t tests or chi square tests. A three factor [groupXtreatmentXcontraction], repeated measures analysis of variance [ANOVA] was performed on VAS and SaO_2 values. Statistical significance was denoted by $p<.05$.

RESULTS No differences were found between groups in terms of parity, duration of labour, cervical dilation, baseline SaO_2, baseline VAS scores and ability to identify N_2O/O_2. Three patients were unable to specify when they received N_2O/O_2. Results of the ANOVA revealed a significant effect of treatment on SaO_2: between contractions, SaO_2 was higher following inhalation of N_2O/O_2 than air [p=.02]. This difference however was so small that it was not of clinical significance. Figure I shows the means of the lowest SaO_2 recorded after each contraction. The lowest SaO_2 recorded for any patient was 91%. This followed inhalation of compressed air and was reached for only a few seconds. Analysis of VAS scores failed to reveal any effect of N_2O/O_2 on pain. Figure II shows mean VAS scores for each contraction.

DISCUSSION This ongoing study has so far shown that inhalation of N_2O/O_2 during labour contractions does not appear to predispose parturients to desaturation any more than does inhalation of compressed air. Furthermore the dangerously low SaO_2 values reported previously [3,4] were not reproduced in this study. No analgesic effect of N_2O/O_2 was found either but the small sample size precludes firm conclusions until further trials are completed.

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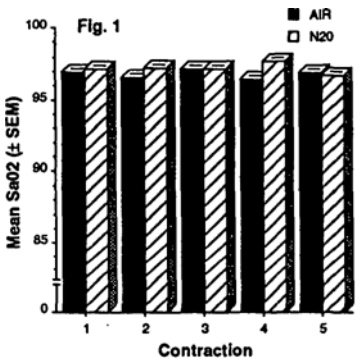

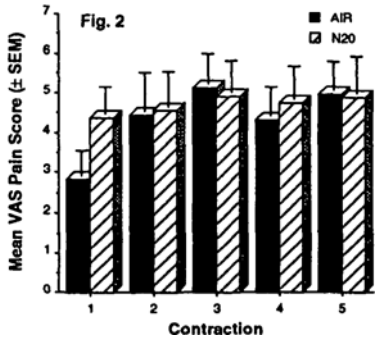

COMPARISON OF TWO TECHNIQUES TO INFLATE THE BRONCHIAL CUFF OF THE UNIVENT(R) TUBE

Medhat Hannallah, M.D., F.F.A.R.C.S.

Georgetown University Medical Center, Washington, D.C. 20007

Introduction: The Univent(R) Tube is an endotracheal tube with a movable bronchial blocker that is available for one-lung ventilation(1). The blocker's cuff has been reported to exhibit high-pressure characteristics when inflated to seal any adult bronchus(2). It is important, therefore, to avoid cuff overinflation. Two techniques have been recommended to optimally inflate that blocker to seal the bronchus, based upon creating either negative(2) or positive* pressure within the breathing system. This study was designed to measure the bronchial sealing volume and to compare the quality of lung collapse when these two techniques of cuff inflation were used.

Methods: With IRB approval, 8 adult patients undergoing thoracotomy under GA were studied. Correct placement of the Unvient(R) tube's bronchial blocker was verified with fiberoptic bronchoscopy. The negative pressure technique of bronchial cuff inflation (NPT) was tested by applying suction pressure of -150 mmHg to the blocker's lumen causing loss of volume in the breathing system as evidenced by deflation of the reservoir bag (Fig.1). The blocker's cuff was then inflated until the reservior bag ceased to deflate and the sealing volume was recorded. The positive pressure technique of bronchial cuff inflation (PPT) was then tested by connecting the blocker's lumen to a beaker of water while maintaining pressure of +30 mmHg within the breathing system (Fig.2). The bronchial cuff was inflated until air bubbles ceased to appear in the beaker and the corresponding cuff volume was recorded. Bronchial sealing volume as measured by the NPT was used to inflate the blocker's cuff initially, with suction through the blocker's lumen maintained throughout the period of cuff inflation. If lung collapse was found to be incomplete and the sealing volume as measured using the PPT was larger than that measured using the NPT, the cuff was inflated to the larger volume.

Results: Fig.3 illustrates the relationship between the bronchial sealing volumes as measured by the PPT and the NPT. The volume measured by the NPT ranged between 3-5 ml. When measured by the PPT the volume range was 4-6 ml. In 5 of the 8 patients studied, the PPT failed to confirm bronchial seal when the cuff was inflated using the NPT. In 7 of the 8 patients, on the other hand, complete collapse of the blocked lung was achieved when the NPT was used.

Discussion: Being a high-pressure cuff, it is prudent to inflate the blocker of the Univent(R) tube to the smallest volume that would accomplish the indication for its use. This should minimize the chances of bronchial mucosal injury. Lung collapse for better surgical exposure is frequently the only indication for using this tube. Since that could be achieved using smaller cuff volume and pressure when the NPT is used, this technique should be used initially for cuff inflation when the tube is indicated for that purpose. If lung collapse proves unsatisfactory, then the PPT could be used. The PPT, on the other hand, is a more reliable measure of bronchial seal against known pressure gradient. It should, therefore, provide more protection of the ventilated lung and should be used if the blocked lung is a potential source of bleeding or infected material.

References: 1) Anesthesiology, 63:342-343,1985
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Figure 1
NPT of cuff inflation

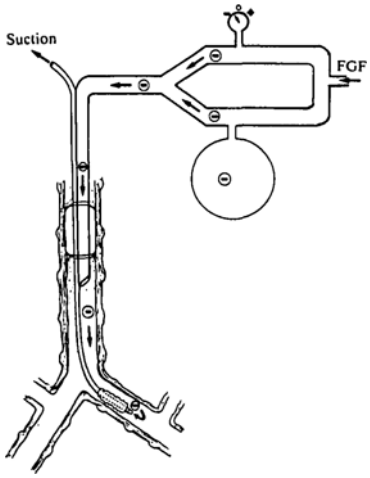


Figure 2
PPT of cuff inflation

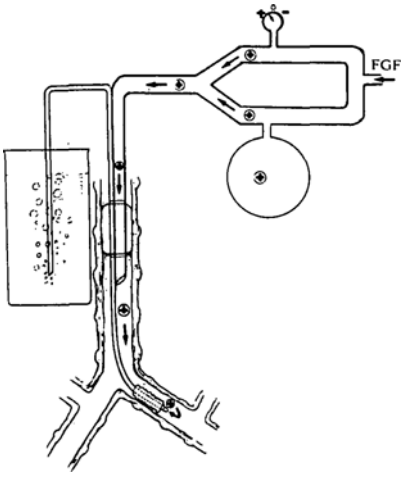
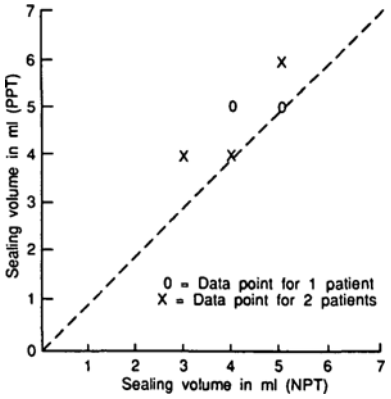


Figure 3
Bronchial sealing volume measured by PPT and NPT



VENTILATORY FUNCTION FOLLOWING LAPAROSCOPIC CHOLECYSTECTOMY.

C.M. Cooney PhD, J.B. Lyons MB, A. Hennigan, W.P. Blunnie FFARCSI, D.C. Moriarty FFARCSI.

Department of Anaesthesia and Intensive Care,
Mater Misericordiae Hospital, Dublin.

INTRODUCTION

The first case report of anaesthesia for laparoscopic cholecystectomy (Lap. Choly) was reported two years ago (1). Since then it has become the accepted method of cholecystectomy, with hospital stay times of approximately one day (2). Reported incidences of atelectasis with conventional cholecystectomies vary from 10 to 20%, probably due to decreased ability to cough. However little is known of the preservation of ventilatory function in a group of patients having laparoscopic cholecystectomy, and the range of impairment that may be found in individual patients.
The aim of this study was to determine ventilatory function at 4 and 24 hours post procedure. This was assessed by measuring Forced Vital Capacity (F.V.C.), Forced Expiratory Volume in one second ($F.E.V._1$) and Peak Expiratory Flow Rate (P.E.F.R.) post-operatively and this was expressed as a percentage of the pre-operative value.

METHODS

Twenty consecutive patients (ASA I and II), having elective laparoscopic cholecystectomies were studied. Procedures were carried out under general anaesthesia using Propofol (1 - 2 mg/kg) for induction, Fentanyl (1 - 2 mcg/kg), Atracurium (0.6 mg/kg) for intubation and ventilation, and Oxygen/Nitrous Oxide (3 l/min. with 7 l/min.) supplemented with Enflurane for maintenance of anaesthesia. Minute ventilation was 100 to 120 mls/kg/min. All patients had supplemental analgesia of aliquots of Pethidine until a pain score of less than 4 (scale 0 to 10) was recorded one hour post procedure. This was prior to being discharged from the Recovery Room.

RESULTS

The mean age of patients was 42.5 years, the male to female ratio was 1 to 19, and the mean duration of surgery was 84 minutes.

The results are expressed as mean percentage change in ventilatory parameters plus or minus standard error of the mean in parentheses. Negative values of mean percentage change indicate that the ventilatory parameter decreased relative to the pre-operative value.

Patients were divided into 2 subsets based on their post-operative P.E.F.R. values; subset 1 was a group of 10 patients which had a low mean % decrease of (- 8.9) at 4 hours. This was well separated ($p < 0.01$) from subset 2 which had a high % decrease (- 43.8) at the 4 hour time (Table 1). The mean % decrease had become less in both groups at 24 hours although there was still a very clinically significant decrease in subset 2 patients (- 35.2) at this time.

Similar trends were seen in changes in $F.E.V._1$ values (Table 2). Changes in F.V.C. however, did not follow this pattern and all decreases in patient values at 4 hours were clustered about a mean of -21.9. This decrease was also reduced to a much lower level at 24 hours (Table 3). Absolute P.E.F.R. values of less than 200 l/min. were observed in 55% of patients at 4 hours and 35% at 24 hours. Only 2 patients had P.E.F.R. values less than 100 l/min. at any stage post procedure (Table 4).

DISCUSSION

With the advent of laparoscopic cholecystectomy there is a danger that patients with poor respiratory reserve may be selected for this procedure without adequate preparation. We have shown that while many patients suffer minimal ventilatory impairment which will resolve in 24 hours, a certain sizeable sub-group will be clinically impaired at this time. The subgroup that was most impaired also had the lowest initial P.E.F.R., F.V.C. and $F.E.V._1$, values. Our patient group had a mean initial P.E.F.R. of 253 l/min. and 35% of our patients had values less than 200 l/minute at 24 hours. A P.E.F.R. of 200 l/minute is regarded by some as the minimum required to expectorate. Thus it appears that while many patients may have an early discharge from hospital after their laparoscopic cholecystectomy, it is important to try to predict pre-operatively, those who will have an impaired ventilatory function for greater than 24 hours post-operatively and manage these appropriately.

TABLE 1. % CHANGE IN P.E.F.R.

Time post lap. choly.	4 hours	24 hours
Subset 1	- 8.9 (3.3)	+ 11.0 (6.2)
Subset 2	-43.8 (4.4)	- 35.2 (5.9)

TABLE 2. % CHANGE IN $F.E.V._1$

Time post lap. choly.	4 hours	24 hours
Subset 1	- 9.3 (2.1)	- 0.2 (6.9)
Subset 2	-41.1 (4.5)	-22.7 (6.2)

TABLE 3. % CHANGE IN F.V.C. (Mean ± S.E.M.)

Time post lap. choly.	4 hours	24 hours
% Change	- 21.9 (4.4)	- 11.5 (5.4)

TABLE 4. % OF TOTAL PATIENTS

Time post lap. choly.	4 hours	24 hours
PEFR Values < 200	55%	35%
PEFR Values < 100	10%	0%

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Effects of Magnetic Resonance Imaging at 1.5T on Fentanyl Induced Respiratory Depression

WB Dobkowski[1],FS Prato[2],NA Shannon[1,2],DJ Drost[2],B Arya[1],JM Wills[2],D Bond[1],P Morley-Forester[2],[1]Department of Anaesthesia,University Hospital,University of Western Ontario; [2]Lawson Research Institute and Department of Nuclear Medicine & Magnetic Resonance,St. Joseph's Health Centre, London, Ontario, CANADA

INTRODUCTION: It has been shown in both mice and snails that exposure to magnetic resonance imaging (MRI) reduces the analgesic effect of opioids.[1,2] Opioids also decrease the sensitivity of the central respiratory centre and peripheral receptors to chemo-stimulation. Therefore, it is possible that magnetic fields could alter opioid-induced respiratory depression. Because of the extensive use of MRI in patients often given narcotics and the technical problems of respiratory monitoring of such patients, it is of clinical importance to determine if MRI exposure alters opioid-induced depression of respiration.

METHOD: After obtaining approval from the University Human Experimentation Committee and written, informed consent, 12 healthy male volunteers aged 20-25 years were studied. All subjects were studied twice within an 8 week period, once under MRI exposure conditions (1.5T static field; 63MHz RF field with amplitude modulation at ELF frequencies; gradients of 8.0mT/m with 1ms rise times repeated 21 times per second) and once under sham exposure conditions. For the sham exposure, the main magnetic field was ramped down from 1.5T to zero (a remnant field of 0.4mT remained) prior to the subject being placed in the magnet and the sound of imaging was played back through speakers to mimic the sound pressure and vibration present during an imaging procedure. On each occasion, the subjects were in the machine for a total of 135 min. during which 6 measurements were made of ventilatory response to CO_2 using a rebreathing circuit filled with 7% CO_2-93% O_2 mixture. Each measurement, lasting approximately 3-4 minutes, included a continuous recording of tidal volume and airway CO_2 concentration. Two of these measurements were done prior to a 40 min. steady infusion of a total dose of 0.006mg/kg of fentanyl (at 5min and 35 min), the third near the end of the infusion and then two more at 20 and 40 min of the recovery period while the subject remained in the magnet. A final measurement was performed 110 min after the end of the constant infusion, 60 min following removal from the magnet to a recovery area. The CO_2 concentration versus Minute ventilation was plotted and fit to a straight line using linear regression. These slopes were normalized to the preinfusion values and then image and sham values were compared using analysis of variance.

RESULTS: Only the slopes at 20 min. past infusion showed appreciable difference with the exposed group showing less respiratory depression (mean of the normalized slope for the MRI exposed was 0.518±0.11 of control (SEM) compared to 0.240±0.072 (SEM) for the sham exposed). However, significance was marginal ($p=0.04$ using an ANOVA test) Additional subjects will have to be recruited to this study to better determine significance.

CONCLUSION: The results of this study suggest and that exposure to MRI may counter the respiratory depressant effect of fentanyl. Further work will be necessary to confirm this result, especially a dose-related effect.

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FAT EMBOLISM IS ASSOCIATED WITH INCREASED PLASMA TUMOR NECROSIS FACTOR: Studies in mongrel dogs after cemented arthroplasty

RJ Byrick, MD*, PY Wong, PhD#, D Wigglesworth, BSc*, Mullen JB, MD^; * Dept. of Anaesthesia, St. Michael's Hospital; # Dept. of Clinical Biochemistry, Toronto Hospital; ^ Mt. Sinai Hospital Dept of Pathology, University of Toronto

INTRODUCTION: Acute lung injury is associated with pulmonary fat embolism after trauma and long-bone fracture. Fat emboli also have been demonstrated intra-operatively during arthroplasty procedures at the time of cement and prosthesis insertion.[1] The acute physiologic effects of fat embolism after cement and prosthesis insertion have been studied and are characterized by elevated pulmonary artery pressure (PAP), increased pulmonary vascular resistance (PVR), and reduced systemic arterial oxygen tension[2]. The determinants of acute lung injury after fat embolism are important because pulmonary edema can be caused by increases in the microvascular hydrostatic pressure and/or permeability of the alveolar capillary membrane.

Mediators such as tumor necrosis factor (TNF_α), have been implicated as a cause of a generalized inflammatory reaction[3] causing acute lung injury in many disease states. This could conribute to increased membrane permeability after cemented arthroplasty. Elevated levels of this cytokine, TNF_α, has been demonstrated in plasma and in bronchopulmonary secretions[4] of patients with the adult respiratory distress syndrome (ARDS). We proposed to monitor the immediate hemodynamic effects of fat embolism after cemented arthroplasty and assess whether increased levels of circulating TNF_α might be detectable within 30 min of BCA in anaesthetized dogs. We also relate the increase in TNF_α at 30 min after BCA to the amount of fat in the lungs and the number of emboli in six of the dogs.

METHODS: This study was approved by the local animal care committee and all dogs were treated in accordance with the regulations of the Canadian Council on Animal Care. Eight mongrel dogs were anaesthetized using pentobarbitone 30 mg/kg followed by a pentobarbitone infusion at 5 mg/kg/hr. Hemodynamic data were collected before and after Bilateral Cemented Arthroplasty (BCA)[2] using a standardized surgical technique. Arterial (BP), right atrial (RA), left atrial (LA), and pulmonary artery (PA) pressures were continuously recorded. Arterial blood samples were obtained and the plasma concentration of tumor necrosis factor (TNF_α) was determined by radio-immunoassay (Amersham Corp.) after drilling and reaming of the intramedullary canals and at 1, 5, 15 and 30 min after BCA.

The lungs were removed en bloc and fixed in inflation with 10% buffered formalin at a pressure of 25 cm of fixative. After fixation for 72 hr, the lungs were sectioned in the mid-sagittal plane for quantitative morphometric analysis. The area and diameter was calculated for each embolus. The ratio of area occupied by fat emboli to total area of lung examined is equivalent to the volume proportion of lung tissue occupied by fat (Delesse's Principle). All data are reported as mean values plus or minus one standard deviation. Data were analyzed using the SAS (Statistical Analysis Software) general linear model repeated measures analysis of variance procedure. When a significant F ratio was found ($p<0.05$) multiple comparisons between the post-reaming baseline and subsequent time periods using Dunnett's test were made.

RESULTS: The mean PAP increased significantly in the control dogs within 1 minute after BCA (15.5 ± 4.4 mm Hg to 36.5 ± 14.8 mm Hg) and remained increased above post-reaming baseline levels for the 30 min study period. Mean BP decreased transiently within 3 min of BCA, however returned to baseline levels for the next 30 min. No significant changes in RAP or LAP were noted during the study.

The arterial plasma concentration of TNF_α increased significantly ($p<0.0001$) from baseline level (580±83 pg/ml) to 791±234 pg/ml 30 min after BCA. Although a trend toward an increase in plasma TNF_α was evident at 15 minutes, no significant change from the baseline concentration was found at the 1, 5, or 15 min measurement periods (535±131, 571±99, 654±144 pg/ml). No significant relationship was found between the post-mortem estimate of the number of vessels occluded by fat or the volume proportion of lung tissue occupied by fat and the increase in plasma TNF_α at 30 min after BCA.

DISCUSSION: Cemented arthroplasty procedures and fat embolism have been associated with coagulation abnormalities[1,2] as well as acute hemodynamic changes[3]. We hypothesized that these coagulation abnormalities and delayed pulmonary edema may be secondary to release of TNF_α. Cytokine production has been associated with ARDS and coagulation changes in humans[5]. This study documents an increase in circulating plasma TNF_α 30 min after BCA. Whether cytokine release is associated with coagulation abnormalities and pulmonary edema or is part of the normal response to surgery is not known and requires furthur study. Since circulating levels of TNF_α do not reflect local lung tissue levels, the plasma concentrations found in our study could be associated with higher local lung levels and significant lung permeability changes. During early sepsis, TNF_α, presumably derived from activated macrophages, has been detected within 30 min.[6] The delay in pulmonary edema formation after post-traumatic fat embolism could be the result of a generalized inflammatory response and increasing permeability of lung vessels mediated by cytokine release with pulmonary edema aggravated by elevated PAP initiated by the particulate fat emboli as in this model.

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Airway mucosal damage induced by high dose Ventolin® aerosol in rabbits.

I Spahr-Schopfer MD, J Lerman MD FRCPC, E Cutz MD FRCPC, M Dolovich PEng.

Departments of Anaesthesia and Pathology, The Research Institute, The Hospital for Sick Children, University of Toronto, Dept of Medicine, St Joseph's Hospital, McMaster University, Hamilton, Ontario.

INTRODUCTION

The efficiency of aerosol delivery by metered dose inhaler (MDI) to distal airways can be substantially increased by delivering the dose through a narrow gauge catheter placed within the tracheal tube.[1] This study was designed to determine whether it was possible to induce morphological changes in the tracheobronchial epithelium after delivery of Ventolin® aerosol via a narrow gauge catheter in a rabbit model and to identify the possible causative factors.

METHODS

With the Approval of the Animal Care Committee, 24 adult rabbits were randomly assigned to one of 3 groups: 9 received Ventolin® delivered by MDI (salbutamol, freon as propellant and oleic acid as surfactant), 6 a placebo spray (freon and lecithin) and 9 no treatment (control). Tracheal intubation, arterial and venous cannulations were performed under halothane anaesthesia in O_2 and mechanical ventilation to a $PaCO_2$ of 40 mmHg. A 19 gauge catheter modified to permit actuation of a MDI cannister was inserted into the tracheal tube with the end of the catheter approximating the tip of the tube. After being shaken vigorously, the MDI was actuated at the end of expiration, at 30 second intervals until 20 actuations had been delivered. Rabbits in the control group received no aerosol and were ventilated for the same duration. Heart rate, invasive blood pressure and SpO_2 were recorded continuously for the 3 hour experiment. Sections of trachea and lungs were reviewed by a pathologist who was blinded to the treatment. The sections were graded following a 4-point scale[2] at three levels in the tracheobronchial tree (trachea below the tracheal tube, main bronchi and the small intrapulmonary bronchi). Nonparametric data were analyzed using the Mann Whitney U test and the Kruskall Wallis test and $p<0.05$ was accepted as statistically significant.

RESULTS

Multiple doses of Ventolin® aerosol produced significant lesions in the epithelium of the trachea and main bronchi. The histological injury after placebo spray was similar to that in the control group and both were significantly less than that observed with Ventolin® (Figure). Cardiovascular variables remained stable throughout the experiment and the SpO_2 was >97% at all times.

DISCUSSION

Our results suggest that a high dose Ventolin® aerosol directly delivered onto the tracheobronchial mucosa may induce acute epithelial damage. The placebo spray which delivers the same pressure and produces the same cooling effect as Ventolin®, did not induce more lesions than that found in the control rabbits. These data suggest that either Ventolin® itself or oleic acid augment the acute mucosal damage observed in the control/placebo groups. Further studies are warranted to investigate the pathogenesis of this injury and its possible reversibility.

References:

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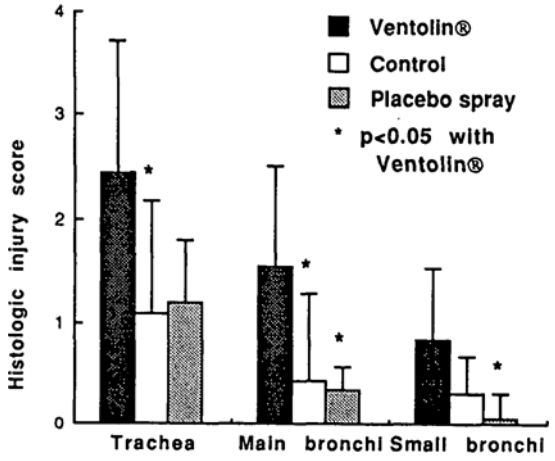
Figure



POSTOPERATIVE ANALGESIA AND PULMONARY FUNCTION FOLLOWING UPPER ABDOMINAL SURGERY: EPIDURAL FENTANYL VERSUS PCA MORPHINE.

S. Kowalski, FRCPC, B. Ong, FRCPC, D. Bell, FRCPC, T. Ostryzniuk RN, C. Serrette, MSc, T. Wasylak MN, S. Coke, MBA.

Departments of Anesthesia and Nursing, University of Manitoba, Winnipeg, Manitoba, R3E 1X2

INTRODUCTION

After upper abdominal surgery (UAS), patients have severe pain and impaired pulmonary function. Epidural fentanyl infusions (EFI) and patient controlled analgesia (PCA) have been shown to provide better postoperative (postop) analgesia than intermittent narcotic injections. It is not clear whether EFI or PCA is superior. This study compares prospectively in a randomized double blind manner the efficacy of EFI with PCA morphine on patients undergoing UAS as regards to postop pain control, pulmonary function and associated side effects.

METHODS

After approval by the University Ethics Committee and informed consent, 18 patients undergoing elective UAS were entered in this study. Patients were instructed in the use of the PCA pump preoperatively. Pulmonary function tests (PFTs) were measured at the bedside in the sitting position using a Collin's 9L water spirometer. Lung volumes measured with the constant volume technique using helium, included functional residual capacity (FRC), vital capacity (VC), and forced expiratory volume in one second ($FEV_{.1}$). Pain assessment was done using the visual analogue scale (VAS 0 no pain - 10 worst possible pain), the present pain index (PPI; 0 - no pain, 1 - mild, 2 - discomforting, 3 - distressing, 4 - horrible, 5 - excruciating) and the 15 question McGill Pain Questionnaire (McPQ - scale 0 - 45).

Preoperatively, all patients had an epidural catheter inserted and a block up to T6 was established using CO_2 - lidocaine 2% with epinephrine. They then received a "light" general anesthetic with endotracheal intubation and were maintained with N_2O/O_2 ± isoflurane. Bupivacaine 0.25% was given as needed to "top up" the epidural. Fentanyl was used intravenously up to 5 mcg/kg. No epidural narcotics were given.

Postop, the patients were randomized to receive either epidural fentanyl (group F) or PCA morphine (group M). All patients had both an epidural infusion pump and a PCA pump, but only one pump had active medication. Neither the patient nor the investigator knew which pump had active medication. Group F received a loading dose of fentanyl 1 mcg/kg and an initial infusion rate of 1 mcg/kg/hr. They could receive a second load of 0.5 mcg/kg and an increased infusion rate of 1.5 mcg/kg/hr if needed. Group M received 8 mg IV load and the PCA pump was set at a continuous infusion of 1 mg/hr with a bolus dose of 1 mg and a lockout interval of 10 minutes. A second load of morphine 4 mg and a decrease lockout interval to 5 minutes could be given if needed. Patients were assessed as needed until pain control was adequate. Pain scores were done at 2, 4, 24 and 48 hr postop. Patients were also assessed for their level of sedation, respiratory depression, nausea, pruritus and urinary retention at these times. PFTs were repeated at 24 hr, 48 hr and 1 week postoperatively.

Statistical analysis was done using Student's T-test, ANOVA for continuous variables and Wilcoxon rank sum test for non-continuous variables.

RESULTS

There were 9 patients in each group. The groups were similar in height, weight and age. There was good pain control in both groups but there was a discrepancy between the pain scores (Table 1). Using the VAS score there were lower pain scores in Group F at 4 and 24 hrs postop. Using the McPQ there was a lower pain score in Group F only at 24 hrs postop. Using the PPI there was no difference between groups at any time and pain scores were usually 2 or less. There was no difference between groups in preoperative PFTs. There was a decline in $FEV_{.1}$, FVC and FRC postoperatively (Table 2). The FEV_1 and FVC tended to be slightly higher in group F at 24 hrs postop. There was no difference between groups with regards to sedation, nausea, pruritus or urinary retention. No patient had clinically significant respiratory depression.

DISCUSSION

Pain control appears to be better in group F but all patients were satisfied with their pain management. These differences may due to the fact that PCA patients have been shown to tolerate more pain. PFTs tended to be better in the epidural group at 24 hrs. This did not reach statistical significance which may be due to the small sample size. However, even a small difference in analgesia and PFTs may be important to high risk patients. This study is still in progress and more results will be presented.

TABLE 1. PAIN SCORES * $P < .05$ ° $P < .001$

HOURS POSTOP		2	4	24	48
VAS	F	5.3 ± 2.1	4.9 ± 3.1*	2.3 ± 1.8°	2.1 ± 1.4
	M	5.3 ± 3.3	5.4 ± 2.2*	3.8 ± 2.2°	2.1 ± 1.9
PPI	F	1.8 ± 0.4	2.0 ± 1.3	1.2 ± 0.8	1.6 ± 1.5
	M	2.2 ± 1.6	1.7 ± 0.5	1.3 ± 0.7	0.8 ± 0.7
McPQ	F	8.1 ± 4.1	9.3 ± 6.3	3.2 ± 2.6*	6.2 ± 7.9
	M	13.5 ± 10.0	10.2 ± 3.6	7.2 ± 4.6*	4.7 ± 3.5

TABLE 2. PFTs AS A PRECENT OF PREOP CONTROL.

DAYS POSTOP		1	2	7
FEV_1	F	.68 ± .23	.67 ± .21	.74 ± .14
	M	.52 ± .16	.67 ± .15	.90 ± .13
FVC	F	.63 ± .21	.64 ± .22	.75 ± .15
	M	.50 ± .14	.63 ± .16	.82 ± .14
FRC	F	.73 ± .15	.75 ± .18	.87 ± .06
	M	.80 ± .25	.84 ± .14	1.05 ± .17

EFFECTS OF STELLATE GANGLION BLOCK IN BRONCHIAL ASTHMATICS

Takako Tsuda, M.D., Takashi Nakagawa, M.D., Norifumi Mabuchi , M.D., Hiroshi Ando, M.D., Osamu Nishida, M.D.. Takafumi Azami, M.D., Hirotada Katsuya, M.D., Yukio Goto,M.D.*
Department of Anesthesiology and Resuscitology, Nagoya City University Medical School, 1 Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya 467, Japan
*Department of Anesthesiology, Fukui Medical School, Fukui 910-11, Japan

INTRODUCTION:
The stellate ganglion block has been recognized as a useful treatment for allergic rhinitis. Although much attention has been focused on the effects of stellate ganglion block on immunological status as well as the autonomous nervous system, very little information is available regarding the treatment of bronchial asthmatics. The objective of this study is to evaluate the effects of stellate ganglion block in bronchial asthmatics.

MATERIALS AND METHODS:
Eight stable asthmatics (seven women and one man) between 35 and 62 years of age presenting as out patients at the Department of Anesthesia of Nagoya City University Hospital were studied. All subjects met the criteria used for definition of stable asthma published by the American Thoracic Society and informed consent was obtained from all patients. For each individual patient, the investigation was divided into pre-treatment and study periods. During the pre-treatment period of approximately 6 months, the patients were assessed on a regular basis for airway resistance, heart rate and the candle test. peak flow rate and inspiratory reserve volume being measured weekly before and after IPPB nebulization with the bronchodilator orciprenaline. The patients were similarly handled during the study period but on each out-patient visit received stellate ganglion block (SGB) injections alternatively to the left and right sides prior to challenge with orciprenaline. The dose administered was in each case 6 ml of 1% lidocaine and respiratory function testing was conducted before SGB, 30 minutes thereafter and after IPPB nebulization. Blood samples were taken immediately before starting the investigation and after performance of the SGB 20 times and the levels of histamine, as well as leukotrienes B4(LTB4) and C4(LTC4), were measured. In addition, evaluation of the autonomic nervous system was carried out at the same time-points by assessment of variation in R-R interval values.

RESULTS:
As compared to data gained before IPPB nebulization, which were arbitrarily assigned the value of 100, the results after orciprenaline application in the pre-treatment period were: for airway resistance, 83+13; heart rate, 100±5; candle test, 106±7; peak flow rate, 125±21; inspiratory reserve volume, 114±11 (n=75). In the study period the respective values 30 minutes after SGB and after IPPB nebulization were: airway resistance, 97±16 and 89±13; heart rate, 97±6 and 99±8; candle test, 102±11 and 106±12; peak flow rate, 101±11 and 111±23; Significant differences were only observed at the $P<0.05$ level for airway resistance before SGB and after orciprenaline.Over the relatively long period of the investigation a drop in actual airway resistance values was evident from an average of 6.7±2.4 $cmH_2O/l/sec$ to 5.9±2.6 $cmH_2O/l/sec$. With regard to the haematological data a significant shift was observed with LTC4 values dropping from 45.6±24.2 pg/ml (n=8) to below 10 pg/ml (n=2). In contrast LTB4 demonstrated a marked increase from 151±65.9 pg/ml (n=8) to 449±184.5 pg/ml (n=2). Histamine levels did not change (0.3±0.1 ng/ml as compared to 0.4±0.1ng/ml). R-R interval analysis revealed a tendency for improvement of the autonomic nervous system over the study period.

DISCUSSION :
In this study, a drop in actual airway resistance after repeated SGB indicated improvement of respiratory function. It has been well documented that the slow reacting substance of anaphylaxis (SRS-A) belongs to the group of compounds including leukotriene C4(LTC4), LTD4 and LTE4. LTC4 levels in peripheral venous blood from patients with bronchial asthma showed a significant increase during asthmatic attacks as compared with in times of remission (1). The observed significant decrease in LTC4 values after repeated SGB treatment may then suggest that SGB may exert protective effects against asthmatic attack. Further studies using R-R interval analysis (2) are necessary to confirm the efficacy of SGB in bronchial asthmatics. However, the results of this preliminary study clearly indicated that repeated SGB administration may be of advantage for treatment of chronic bronchial asthmatics.

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AMRINONE IS AN EFFECTIVE FIRST LINE DRUG FOR SEPARATION FROM CARDIOPULMONARY BYPASS

J.F. Hardy, M.D., N. Searle, M.D., M. Roy, R.R.T., J. Perrault, Ph.D.
Department of Anesthesia, Montreal Heart Institute, 5000 Belanger East, Montreal, Quebec, Canada H1T 1C8

INTRODUCTION:

A crucial element for weaning patients from cardiopulmonary bypass (CPB) rests on the selection of an appropriate therapeutic regimen. This seems more relevant now that cardiac surgery is performed on older, sicker patients that often have compromised ventricular function. Traditional therapy relies mainly on sympathomimetic agents, but catecholamines have drawbacks such as tachycardia, arrhythmias, and increased myocardial oxygen demand. Amrinone (Amr), a phosphodiesterase III inhibitor combines inotropic support with pulmonary and systemic vasodilatation, without increasing heart rate or myocardial oxygen consumption.[1] These characteristics should be useful in the failing heart during weaning from CPB.

METHODS:

Following institutional review board and informed consent, 15 patients were included in a prospective, open-labeled study when systolic blood pressure (SBP)<80 mmHg, and diastolic pulmonary artery pressure (DPAP) >15 mmHg or central venous pressure (CVP)>15 mmHg, during progressive separation from CPB. At that moment, CPB flow was increased to alleviate heart failure and Amr administered as a bolus of 0.75 $mg.kg^{-1}$, followed by an infusion of 10 $\mu g.kg^{-1}.min^{-1}$. Weaning from CPB was then resumed and haemodynamic parameters compared at CPB flow where failure first occurred. If necessary, norepinephrine (NE) was used subsequently to maintain SBP>80 mmHg.

RESULTS:

Failure to wean from CPB occurred at 56±26% of full pump flow. After Amr bolus, DPAP decreased significantly by 16% and CVP by 21% (Table). Subsequently, 13 patients required the infusion of low-dose NE (4-8 $\mu g.min^{-1}$) to increase SBP. Heart rate remained unchanged after the bolus of Amr, after separation from CPB, and no arrhythmias were noted. Successful weaning from CPB was possible 13±9 min after Amr bolus (10±2 min in 86% of patients). Weaning resulted in a cardiac index (CI) similar to that measured prebypass (2.56±0.6 vs 2.3±0.4 $L.min^{-1}.m^{-2}$ respectively).

Table

	Failure to wean	After Amr	After CPB
SBP mmHg	73±5	78±10	94±16
DPAP mmHg	19±4	16±4 *	21±4
CVP mmHg	14±4	11±4 *	14±4
HR $beats.min^{-1}$	80±14	80±14	83±12

All data mean±SD; * $p<0.05$ compared to failure to wean by Student's paired t-test

DISCUSSION:

Amr was used as the first line drug after an unsuccessful attempt at weaning from CPB. Failure to wean was based on objective criteria and Amr was administered therapeutically, rather than prophylactically[2] or for treatment of a low output syndrome following separation from CPB[3] as had been published previously. Separation was accomplished promptly after the bolus of Amr, with no arrhythmia or tachycardia. However, a clinically significant decrease in systemic pressure was observed, but corrected easily with low-dose norepinephrine. Amr (0.75 $mg.kg^{-1}$ followed by an infusion of 10 $\mu g.kg^{-1}.min^{-1}$) was rapidly effective during weaning from CPB and provided the necessary inotropic support during this unstable period.

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EFFECT OF HEMODILUTION ON THE CARDIOVASCULAR RESPONSE TO PROTAMINE

Charles E. Smith, MD, FRCPC, Alfred C. Pinchak, PhD, PE, MD, Joan F. Hagen, BA, Donald Hancock, AEET

Department of Anesthesia, MetroHealth Medical Center, Case Western Reserve University, Cleveland, OH 44109

INTRODUCTION
Maintenance of tissue oxygenation during acute normovolemic hemodilution (HD) is related to increased cardiac output and oxygen extraction, and redistribution of blood flow to some organs. However, conditions which depress cardiac function may impair the ability of the heart to compensate for the reduced oxygen content of arterial blood during HD. Protamine reversal of heparin anticoagulation has been associated with systemic hypotension, pulmonary hypertension and cardiac depression. It is unknown whether protamine interferes with the normal compensatory response to HD. This study evaluated the circulatory effects of protamine reversal of heparin anticoagulation during HD in dogs. The study has clinical relevance because anesthesiologists often administer protamine to hemodiluted patients after cardiopulmonary bypass.

METHODS
Twenty-three animals were randomly divided into 4 groups as follows: 1) HD followed by protamine; 2) no HD, protamine; 3) HD alone; 4) controls (no HD, no protamine). Anesthesia was with pentobarbital. After splenectomy, catheters were placed for measurement of arterial, left ventricular (Millar), central venous and pulmonary artery pressures, and cardiac output. A biaxial accelerometer (flat frequency response from 0 - 300 Hz) placed in the lower esophagus allowed measurement of peak to peak cardiac accelerations (A1x, A1y)[1]. The hematocrit was reduced from 43 to 20% by the simultaneous withdrawal of blood and infusion of a similar volume of hetastarch at a rate of 20 mL/min. The total volume exchanged was 45 mL/kg. Hemodynamics, blood gases, oxygen delivery (DO2), consumption (VO2) and extraction ratio (ER=VO2/DO2*100) were measured prior to and after HD, and 5 and 30 min after protamine infusion (3 mg/kg via the femoral vein over 10 min). Rectal temperature was maintained at 38°C. Statistical analysis was with ANOVA. A P value < 0.05 was considered significant.

RESULTS
Hemodilution resulted in decreased DO2 and increased ER, with maintenance of VO2 (Table). Compared with controls, infusion of protamine after HD reduced cardiac contractility but had little effect on oxygen metabolism.

DISCUSSION
Despite reduced contractility, there was no evidence of impaired tissue oxygenation in hemodiluted animals receiving protamine.

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Percent change in cardiovascular parameters from after HD value 5 min after protamine in groups 1-4.

	1	2	3	4
DO2 (mL/min)				
after HD	462 ± 86	635 ± 58	495 ± 82	702 ± 121
(% change)	(-12 ± 6)	(-2 ± 7)	(-4 ± 3)	(-6 ± 4)
VO2 (mL/min)				
after HD	105 ± 13	100 ± 14	112 ± 7	102 ± 4
(% change)	(-7 ± 5)	(1 ± 6)	(-6 ± 5)	(-3 ± 3)
ER				
after HD	27 ± 6	16 ± 2	27 ± 5	17 ± 3
(% change)	(6 ± 3)	(3 ± 3)	(-2 ± 3)	(3 ± 2)
dP/dt (10^3mmHg/s)				
after HD	3.9 ±.5	4.0 ±.5	3.6 ±.3	3.4 ±.4
(% change)	(-19 ± 5)*	(-6 ± 3)	(2 ± 2)	(-2 ± 2)
A1y (G units)				
after HD	.36 ±.07	.23 ±.03	.30 ±.03	.27 ±.03
(% change)	(-11 ± 9)	(-11 ± 9)	(13 ± 6)	(-7 ± 9)

Mean ± SEM * p < 0.05 vs groups 3 and 4

EFFECTS OF DIPRIVAN ON THE SYMPATHETIC NERVOUS SYSTEM

Andrei V. Krassioukov MD PhD, Lynne C. Weaver DVM PhD, Adrian W. Gelb MD
Departments of Physiology and Anaesthesia, The University of Western Ontario and
The John. P. Robarts Research Institute, 100 Perth Drive, London, Ont. N6A 5K8

INTRODUCTION

This study was done to determine if the actions of Diprivan to decrease arterial blood pressure (BP) and heart rate (HR) are mediated through depression of central neural structures involved in resting and reflex control of blood pressure. Several areas of the brainstem including the ventrolateral medulla and pontine reticular formation are thought to control resting BP and HR through actions on the sympathetic nervous system [1, 2]. The objective of our experiments was to determine the effects of different doses of Diprivan (propofol) on resting sympathetic discharge, BP and HR, on sympathetic and cardiovascular control from the pons and the ventrolateral medulla, and on the sympathetic component of the baroreceptor reflex.

METHODS

BP, HR and postganglionic discharge of renal sympathetic nerves were recorded in rats (n=17). Anaesthesia was initially induced with pentobarbital (40 mg/kg, intraperitoneally) followed by Diprivan after the jugular vein had been cannulated. Rats were paralysed with gallamine and artificially ventilated. When effects of pentobarbital anaesthesia had worn off the infusions of different concentrations of Diprivan were begun. Diprivan was infused at 18-29 mg/kg/hr (low dose), at 35-50 mg/kg/hr (middle dose), and at 60-115 mg/kg/hr (high dose). Changes of BP, HR and sympathetic activity during infusion of different doses of Diprivan were first investigated. Next tonic discharge of neurons in the pontine reticular formation and in the ventrolateral medulla was inhibited by microinjecting the inhibitory amino acid glycine into these regions. Glycine (1M) was microinjected unilaterally in small volumes (50-80 nl). Responses to this blockade were compared during infusion of different doses of Diprivan. Finally, actions of Diprivan were studied on sympathetic responses to activation of baroreceptors by bolus i/v injections of phenylephrine (1-3μg). Parametric statistical analyses of the data were perfomed.

RESULTS

Diprivan decreased renal nerve activity as well as BP and HR in a dose-dependent manner. Diprivan did not significantly change baroreceptor-induced sympatho-inhibition. In general, the haemodynamic changes, during infusion of propofol, were comparable to those found in previous studies. Infusion of Diprivan in low doses had no effect on BP, HR and renal nerve activity. After 35 min of infusion of Diprivan at the middle dose, BP decreased by 17±4 mmHg, HR by 24±4 bpm and nerve activity by 23±4%. The decreases in BP and HR began before the changes in sympathetic discharge. Infusion of Diprivan in high doses decreased BP by 45±5 mmHg, HR by 77.0±6 bpm and nerve activity by 52 ±4%.

Responses to blockade of regions of the pontine reticular formation were identical in animals before infusion of Diprivan and after the low and middle doses. Renal sympathetic activity was inhibited by this blockade by 41±4% (before Diprivan), 42±5% (low dose) and 38±7.8% (middle dose). During infusion of the large dose, this pontine blockade decreased sympathetic activity by only 12±4%. Sympathetic responses to blockade of the ventrolateral medulla were: before Diprivan, -48±4%; low dose, -49±4%; middle dose, -35±3% and high dose, -27±5%.

DISCUSSION

Diprivan, in concentrations of 35-50 mg/kg/hr, produced sufficient levels of anaesthesia and caused small decreases in renal nerve activity, BP and HR. This dose had no effect on pontine neurons responsible for resting control of BP and HR but did depress the medullary vasomotor region moderately. The pontine source of cardiovascular support was minimally depressed by doses of Diprivan less than the largest. No concentration of Diprivan affected sympatho-inhibition induced by the baroreceptor reflex. Because decreases of BP and HR occurred before changes in renal nerve activity a part of the vasodepression and bradycardia caused by Diprivan results from peripheral actions on blood vessels and the heart. However, Diprivan had moderate to large effects on tonic sympathetic control of the circulation as larger doses were administered.

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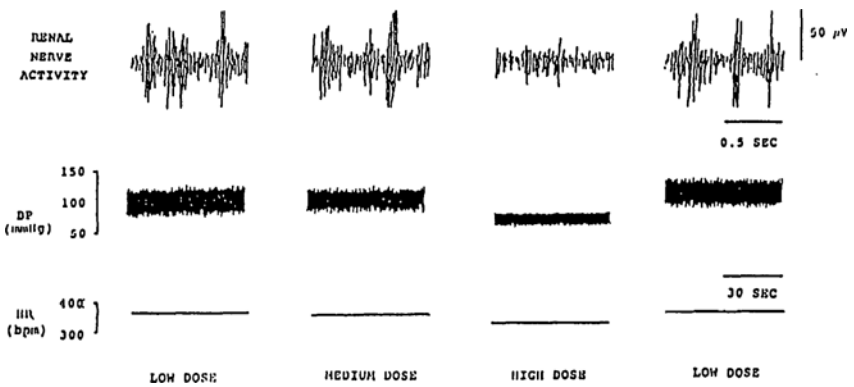


Figure. Changes in renal nerve activity, BP and HR during infusion of different doses of Diprivan. Recordings were taken 35 min after beginning each new dose.

The cerebral pressure-flow relationship during cardiopulmonary bypass with ∝-stat acid-base management in dogs

IR Sutton M.D., WAC Mutch M.D., JM Teskey M.D., IR Thomson M.D., M Rosenbloom BSc, D Thiessen BSc
Departments of Anaesthesia and Surgery, St. Boniface General Hospital, University of Manitoba

Introduction: The cerebral circulation is felt to autoregulate over an extensive range of cerebral perfusion pressure (CPP), which means cerebral blood flow (CBF) is stable with increasing CPP; in other words, the autoregulatory plateau is horizontal. However, cerebral pressure-flow curves (multiple determinations of cerebral blood flow over a broad range of CPP) have not been constructed in situations where CPP is altered independently of the need for vasopressors, vasodilators or hemorrhage. In this study we have examined cerebral pressure-flow curves at two different temperatures during cardiopulmonary bypass (CPB) with ∝-stat acid-base management. With this approach CPP was altered exclusively by changing roller pump output.

Methods: Eighteen mongrel dogs (22 ± 3 kg) were randomly assigned to two groups: Group **N** (n = 9) normothermia (37°C), Group **H** (n = 9) moderate hypothermia (28°C). All animals were anesthetized with sodium thiopental (STP) (25 mg/kg). Anesthesia was maintained with isoflurane 1.40% end-tidal (1 MAC) in O_2 during the surgical preparation. Following thoracotomy, the isoflurane was discontinued and the EEG made isoelectric with a bolus of STP (29 ± 5 mg/kg). A continuous infusion of STP at 10 mg/kg/hr was administered to maintain the EEG isoelectric during CPB. The right atrium and proximal aorta were cannulated with a 38 Fr atrial and 24 Fr aortic cannula, respectively. Mean arterial pressure (MAP) and cerebrospinal fluid pressure (CSFP) were recorded by calibrated transducers referenced to the intra-auricular line. The superior saggital sinus (SSS) was cannulated for blood sampling. Cardiopulmonary bypass was conducted utilizing a Travenol® nonpulsatile roller pump with a Bentley 10 Plus® bubble oxygenator and a Bentley® arterial line filter (25μm). The roller pump and oxygenator were primed with 2.5 - 3.0 litres of Ringer's lactate and 1 - 2 units (500-1000 ml) of canine whole blood in CPDA-1 solution. The animal was systemically heparinized to give an activated clotting time (ACT) ≥400 sec (Hemochron 400®). Throughout the experiment the animal had an intravenous infusion of Ringer's lactate at 200-250 ml/hr containing $NaHCO_3$. In Group **N**, the intravenous solution contained 25 mEq/l and in Group **H**, it contained 12.5 mEq/l. This was done to maintain a stable hemoglobin concentration and acid-base state during the experiment (∝-stat pH management). Following the initiation of CPB, the mean CPP was maintained at 90 mmHg for 15 - 20 min. to allow the animal to stabilize. The animal was then randomized to either Group **N** or **H**. Nasopharyngeal temperature was continuously monitored throughout the experiment. Once the temperature was stable, the CPP was randomly allocated to each of the following five pressures: 50, 60, 70, 80 and 90 mmHg by altering roller pump output. When CPP was stable, radioactive microspheres were injected into the arterial inflow proximal to the aortic root cannula. Approximately $2x10^6$ microspheres (15μm diameter) were injected for each flow determination. The randomly selected microspheres were labelled with ^{46}Sc, ^{85}Sr, ^{141}Ce, ^{95}Nb, or ^{113}Sn. A Harvard pump withdrew blood (25 ml) from the brachial artery for 300 sec, starting 15 sec before each microsphere injection. At the end of the experiment the entire brain was excised. Following removal of the pia mater, the brain was sectioned into specific regions (left and right frontal, parietal, occipital cortex, basal ganglia, cerebellum, and brainstem). The organ and blood samples were placed in a gamma counter after being weighed. Counts per minute were converted to regional blood flow (ml/g/min) by computer program with the use of standard equations. Regional CBF (rCBF) in ml/g/min was determined by summing weighted flows to appropriate brain regions and dividing by regional brain weight. The CPP = MAP - mean CSFP and cerebral metabolic rate for O_2 ($CMRO_2$) = cerebral cortical blood flow × (Art - SSS O_2 Content) in ml O_2/g/min. Time-related changes were evaluated by analysis of variance (ANOVA) for repeated measures. When ANOVA was significant, comparisons were made with the least-squares means test. Bonferroni's correction was applied ($P < 0.05/n$; where n = number of comparisons) when multiple comparisons were made. The corrected P-value was considered statistically significant. The cerebral-pressure flow relationship for various brain regions was determined by analysis of covariance with CPP as covariate. Data are presented as mean ± SD.

Results: The mean temperature in Group **N** was 37.0 ± 0.1°C and 27.6 ± 1.0 °C in Group **H**. The hemoglobin, $PaCO_2$, and pH were similar within and between groups at each CPP level (Table). Cerebral pressure-flow data was fit to the linear equation rCBF = mCPP + b. In both groups, CPP was a covariate for neocortical blood flow (tCortex; P = 0.004 and 0.015 for group **N** and **H** respectively). The change in tCortex blood flow/mmHg change in CPP was 1.22% and 2.06% respectively. For whole brain (tCBF) CPP also was a covariate (P = 0.012 and 0.017). The change in tCBF/mmHg change in CPP was 1.06% and 1.90% respectively. An inverse relationship of Art - SSS content difference *versus* CPP was found (P = 0.0001 for both groups). The mean Q_{10} (the ratio of $CMRO_2$ values over a 10 degree change in temperature) was 3.9 in this model (44 determinations of $CMRO_2$ in Group **N** and 45 in Group **H**).

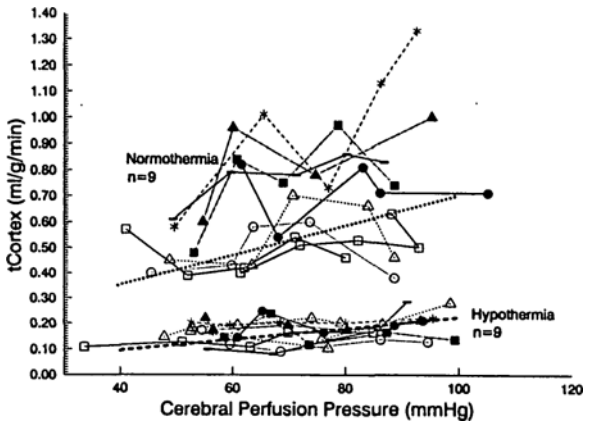
Discussion: In this canine model, the cerebral autoregulatory curve was shown to have a positive slope independent of body temperature. This was most obvious for the neocortex. That CBF increased with increasing CPP is strongly supported from our finding of an inverse relationship for Art - SSS content difference *versus* CPP. Thus, this study demonstrates that the autoregulatory plateau is not flat as commonly depicted in standard textbooks.

Table:

Variable		CPP 90	CPP 80	CPP 70	CPP 60	CPP 50
CPP (mmHg)	N	90.3±6.9	82.2±7.0*	72.5±7.4*	62.3±5.7*	51.7±6.8*
	H	92.1±6.5	82.0±6.5*	70.6±5.8*	62.4±8.2*	52.3±7.9*
Hgb (g/dl)	N	8.6±1.6	8.4±1.8	8.7±1.7	8.7±2.1	8.6±1.9
	H	8.9±2.4	8.8±1.8	8.9±2.1	8.9±1.9	8.8±1.7
$PaCO_2$ (mmHg)	N	36.3±1.6	37.2±1.7	36.3±2.1	37.3±1.8	37.4±2.1
	H	35.7±2.6	36.0±2.5	36.8±2.6	36.9±1.3	36.9±3.0
pH	N	7.30±.04	7.29±.06	7.31±.06	7.29±.05	7.28±.07
	H	7.31±.05	7.31±.05	7.32±.05	7.30±.04	7.30±.06

Mean ± SD N = Normothermia; n = 9 H = Hypothermia; n = 9
* P < 0.05 *versus* CPP 90 within groups

Figure:



tCortex Blood Flow *versus* Cerebral Perfusion Pressure for the two groups. The line of best fit for the normothermic data was tCortex = 0.005CPP + 0.160 and for the hypothermic data tCortex = 0.002CPP - 0.004.

THE ROLE OF MUSIC, POSITIVE SUGGESTIONS AND WHITE NOISE IN THE RECOVERY OF AORTO-CORONARY BYPASS PATIENTS

Nakagawa T MD., Seyone C MD., Teasdale S FRCPC., Corbin H MA., Chung F FRCPC.

Department of Anesthesia, The Toronto Hospital, University of Toronto, 399 Bathurst Street, Toronto, Ontario. M5T 2S8, Canada

INTRODUCTION:

The immediate postoperative period is a very stressful time for any patient and can be aggravated by a noisy intensive care unit (ICU) environment. This is of special concern to the surgeon and anesthesiologist, as they often influence the patient's reactions to surgical procedures and adversely affect postoperative recovery [1-4]. We undertook a study to compare the effects of different auditory stimuli on anxiety levels, hemodynamics and sedation in post-coronary artery bypass graft (CABG) patients.

METHODS:

Institutional approval was obtained. All patients scheduled for elective CABG and who had no hearing impairment were eligible to be included in the study. Patients were randomly assigned to receive one of four different sound inputs. All sounds were recorded on visually identical 60 min. casette tapes to receive either music, cardiovascular intensive care unit (CV-ICU) noise, white noise or positive suggestions. The music used was designed to be relaxing with no driving beats. The tape of CV-ICU noise consisted of a professional recording of the noise that occurs in our CV-ICU. The white noise tape contained a spectrum of frequencies with no disharmonious decibels. The positive suggestions tape consisted of 6 reinforcing suggestions every 10 min. interspersed with white noise.

All patients were seen preoperatively and informed consent obtained. Anxiety levels were assessed using the State Trait Anxiety Inventory (STAI). A standard regimen with high dose fentanyl was used for anesthesia with myocardial protection by hypothermia and potassium crystalloid cardioplegia. Postoperatively, all study patients were connected to a portable casette player via high fidelity ear-phones. The total duration of sensory input was 10 hrs. Postoperative monitoring consisted of the patients hemodynamic profile, postoperative medications within the 1st 24 hours, the time to extubation, time of discharge from the intensive care unit, incidence and type of complications, if any, and the time to discharge from hospital. The STAI test was repeated and a questionnaire completed on the 6th postoperative day to determine whether patients were able to remember any stimuli in terms of sensory input.

RESULTS:

We studied a total of 200 patients, with 50 patients allocated randomly to each of the 4 sensory modalities. There were no significant differences in the demographic distribution between these four groups. All patients received a comparable anesthetic protocol and the majority had either a triple or quadruple bypass. The time to commence sound input ranged in the 4 sensory groups from 55.7 - 61.0 min. with the total duration being from 9.9 - 10.1 hrs. Patients remained intubated postoperatively for 18.6 - 23.0 hrs. and stayed in the ICU in the majority of cases for 2 days. The total duration of stay in the hospital ranged from 8.7 - 9.2 days. None of these times were significantly different between the 4 sensory groups.

There were no significant differences observed between the 4 groups with respect to their postop. hemodynamic parameters, type or dose of medications administered, and the incidence of complications. The STAI tests administered pre. and postop. were essentially equivalent.

Patients who received the normal CV-ICU noise as their sensory modality reported a very high incidence of being able to remember events that happened preoperatively (61.3%) when compared to those who received white noise (31.6%). This difference was significantly different at a level of $p < 0.03$. 36.8 - 57.1 % of the patients had some memory of hearing something unusual during the time of sensory input but could not be more specific. This did not reach a statistically significant difference between the four groups.

DISCUSSION:

Different sounds administered postoperatively did not have a significant influence on recovery in this study of 200 patients. This lack of effect could be due to the fact that patients were adequately sedated and therefore could not hear or that the duration of sensory input too short to have an impact on recovery.

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Paraplegia following thoracic aortic cross-clamping in dogs: Better outcome with methohexital *versus* isoflurane

WAC Mutch M.D., MR Graham M.D., IR Thomson M.D., JM Teskey M.D., D Thiessen BSc, M Rosenbloom BSc
Departments of Anaesthesia and Surgery, St. Boniface General Hospital, University of Manitoba

Introduction: Paraplegia is the most dreaded complication of surgical reconstruction of the thoracic aorta. The influence of anesthesia on neurologic outcome following thoracic aortic cross-clamping (AXC) has not been examined in a randomized controlled fashion. In this study we compared two anesthetics, methohexital *versus* isoflurane, in a canine model of thoracic AXC. The severity of lower limb dysfunction was assessed at 24 hours following thoracic AXC.

Methods: Eighteen dogs (21 ± 3 kg; mean ± SD) were studied. All animals received 25 mg/kg sodium thiopental IV for induction of anesthesia. After intubation the animals were ventilated with O_2 and 1.4% end-tidal isoflurane. End-tidal CO_2, end-tidal isoflurane, temperature, proximal aortic pressure via the right internal mammary artery (MAP_p), distal aortic pressure via the right femoral artery (MAP_d), central venous pressure (CVP) and cerebrospinal fluid pressure (CSFP) were continuously monitored. The spinal cord perfusion pressure (SCPP; MAP_d minus CSFP) was derived. Through a left thoracotomy, a left atrial cannula was placed for radioactive microsphere injection in 4 animals. Following surgical intervention all animals received heparin 5000 IU IV. In each dog the thoracic aorta was occluded 2.5 cm distal to the left subclavian artery for 30 minutes. No attempt was made to control for the hemodynamic consequences of thoracic AXC. Two groups of animals were studied in a random fashion: (1) **methohexital group** (M, n = 9; the isoflurane was discontinued in this group following the thoracotomy and a bolus of M was administered until an isoelectric EEG was obtained. A continuous infusion of M at 20 mg/kg/hr was administered for the cross-clamp duration. (2) **isoflurane group** (I, n = 9; the end-tidal isoflurane was altered to yield a baseline MAP of 85 - 100 mmHg (an MAP similar to group M). In all animals hemodynamic measurements were obtained at five time periods: (1) **baseline**, (2) AXC on for 2 minutes (**AXC 2 min**), (3) AXC on for 20 minutes (**AXC 20 min**), (4) **AXC off** for 5 minutes (5) 30 minutes after volume **resuscitation**. In four animals in group M radioactive microspheres were injected at these times. With each microsphere injection, blood was drawn from the right internal mammary artery (reference organ). After resuscitation, the wounds were sutured and infiltrated with 0.5% bupivacaine. Protamine 50 mg IV has given to neutralize the heparin. The dogs were given buphenorphine (0.015 mg/kg) IM for post-op analgesia and returned to animal holding. All animals received Ringer's lactate at 100 cc/hr and supplemental oxygen by nose cone. At 24 hours an observer blinded to the anesthetic protocol assessed the dog as to severity of paraplegia using Tarlov's paraplegia scale[1]; Grade 0: no movement of the lower limbs, Grade 1: some movement of the lower limbs, Grade 2: good movement of the lower limbs but unable to stand, Grade 3: able to stand and walk, Grade 4: full recovery. The dogs were sacrificed, the brain and spinal cord were removed, weighed, and the tissue radioactivity measured by gamma counter. Blood flow in ml/g/min was determined using standard formulae. Within and between group differences for hemodynamics were tested by repeated measures ANOVA. When significant, the least squares means test was applied with Bonferroni's correction. A P-value of < 0.05 was considered statistically significant. Incidence and severity of paraplegia was assessed by the Mann-Whitney U test.

Results: No difference in temperature, $PaCO_2$, pH, or hemoglobin was seen at any time period between groups (Table). The mean dose of M given to induce an isoelectric EEG was 15 ± 4 mg/kg. The end-tidal I prior to cross-clamp was 1.6 ± 0.3 percent. In group M the SCPP was significantly higher following release of the cross-clamp. During AXC SCPP was negative in group I. Lumbar spinal cord blood flow ($SCBF_l$) was very low following cross-clamping at **AXC 2 min** and unchanged at **AXC 20 min**. Blood flow increased dramatically 5 minutes after cross-clamp removal and remained elevated at **resuscitation**. Severity of paraplegia was assessed at 24 hours in all dogs. For Group M the Tarlov scores were as follows: Grade 0 - 0 dogs; Grade 1 - 5 dogs; Grade 2 - 0 dogs; Grade 3 - 4 dogs and Grade 4 - 0 dogs. For Group I: Grade 0 - 5 dogs; Grade 1 - 3 dogs; Grade 2 - 0 dogs; Grade 3 - 1 dog; Grade 4 - 0 dogs ($P = 0.018$; Mann-Whitney U test; two-tailed).

Discussion: The incidence and severity of paraplegia was significantly less in animals anesthetized with M. When anesthetized with M all dogs had some preserved neurologic function in the lower limbs and 4/9 animals could walk. When anesthetized with I 5/9 animals had complete paraplegia. The SCPP was significantly higher in group M, following cross-clamp release. We cannot conclusively say if higher SCPP at these times has contributed to a better outcome. The $SCBF_l$ with M was no higher than that seen with thiopental or isoflurane anesthesia following AXC in previously reported findings from this laboratory[2,3]. Since $SCBF_l$ was so low a degree of spinal cord protection may have been provided by methohexital administered in doses which resulted in an isoelectric EEG.

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		Baseline	AXC 2 min	AXC 20 min	AXC off	Resuscitation
Temp (°C)	Methohexital	36.6 ± 0.4	36.6 ± 0.4	36.6 ± 0.3	36.6 ± 0.3	36.5 ± 0.5
	Isoflurane	36.9 ± 0.6	36.7 ± 0.6	36.7 ± 0.6	36.6 ± 0.5	36.5 ± 0.4
$PaCO_2$	Methohexital	37.9 ± 1.9	35.8 ± 3.4	37.6 ± 3.1	41.7 ± 3.7*	36.9 ± 2.1
	Isoflurane	37.4 ± 1.3	37.1 ± 1.2	37.8 ± 1.5	41.1 ± 4.3*	37.7 ± 1.2
Hgb (g/dl)	Methohexital	12.6 ± 2.1	12.7 ± 1.6	13.8 ± 1.5*	14.7 ± 1.8*	13.4 ± 2.2
	Isoflurane	12.2 ± 1.7	12.3 ± 1.5	14.2 ± 1.2*	14.5 ± 1.7*	13.1 ± 2.0
$MAP_{proximal}$	Methohexital	84 ± 10	124 ± 11*	148 ± 15*	108 ± 20*	108 ± 18
	Isoflurane	85 ± 11	131 ± 20*	156 ± 16*	88 ± 16†	83 ± 12†
MAP_{distal}	Methohexital	86 ± 12	12 ± 3*	17 ± 6*	111 ± 19*	110 ± 17*
	Isoflurane	87 ± 11	12 ± 3*	14 ± 2*	88 ± 13†	82 ± 15†
CVP	Methohexital	6.6 ± 2.6	9.1 ± 2.9*	8.7 ± 2.6*	6.6 ± 3.2	5.8 ± 2.2
	Isoflurane	6.3 ± 2.6	9.2 ± 2.3*	8.0 ± 2.8*	5.8 ± 2.7	6.1 ± 2.8
CSFP	Methohexital	6.4 ± 1.6	9.2 ± 2.2*	11.0 ± 2.7*	8.6 ± 2.1	6.1 ± 2.0
	Isoflurane	13.7 ± 4.2†	14.7 ± 3.8†	15.1 ± 2.5†	13.0 ± 2.5†	9.2 ± 3.7†
SCPP	Methohexital	80 ± 13	3 ± 2*	6 ± 8*	103 ± 20*	102 ± 18
	Isoflurane	73 ± 11	-3 ± 4*	-2 ± 2*	75 ± 16†	72 ± 15†
$SCBF_l$	Methohexital	0.14 ± 0.03	0.02 ± 0.02*	0.04 ± 0.02*	1.19 ± 0.35*	0.46 ± 0.19*

Mean ± SD Methohexital n = 9 Isoflurane n = 9 Except $SCBF_l$ n = 4 $SCBF_l$ = lumbar spinal cord blood flow (ml/g/min)
All pressures in mmHg * $P < 0.05$ within groups *versus* baseline † $P < 0.05$ between groups

THE FEMORAL 3-IN-1 BLOCK REVISITED

S.A. Lang, MD, FRCPC; R.W. Yip, MD, FRCPC; P. Chang, MD; M. Gerard, MD.

University of Saskatchewan, Department of Anaesthesia, Saskatoon, Saskatchewan, Canada.

INTRODUCTION: To provide anaesthesia for surgery performed in and around the knee four separate nerves must be anaesthetized - the femoral nerve, the lateral femoral cutaneous nerve, the obturator nerve and the sciatic nerve.[1] In theory, a combination of femoral 3-in-1 and sciatic nerve blocks should provide complete anaesthesia of the knee.[1] However, we have experienced several instances where patients having femoral 3-in-1 and sciatic nerve blocks required supplemental analgesia for such surgical procedures despite efficacious blocks. The present study was designed to try to elucidate the mechanism of failure of combined femoral 3-in-1 and sciatic nerve blocks in surgery near the knee.

METHODS: After approval by the University Ethics Committee consent was obtained to perform femoral 3-in-1 nerve blocks in individuals having lower extremity surgery (Table I). All femoral 3-in-1 nerve blocks were performed or supervised by the principle author (S.L.). The study was prospective but was not randomized. The initial 30 patients were allocated to the nerve stimulator group (Group I) as part of an ongoing study on sciatic nerve blockade. Subsequently, an additional 32 consecutive patients entered the study via Group 2 (paraesthesia group).

Patients crossed over from Group II to Group I if a paraesthesia could not be elicited after six attempts. These were considered failures of the paresthesia technique. There were no crossovers from Group I to Group II.

All femoral 3-in-1 nerve blocks were performed as described by Winnie[2] with 30 cc. of either 0.375% bupivacaine with 1/200,000 epinephrine or 2.0% lidocaine with 1/200,00 epinephrine.

Sensation was assessed by pin prick preoperatively and 45 minutes post-block. Motor power in quadriceps, iliopsoas and the adductors were also assessed preoperatively and 45 minutes post-block.

Only patients with complete sensory abolition in the distribution of the femoral nerve[1] and a solid femoral motor block (i.e. quadriceps) were considered for the ability of the femoral 3-in-1 technique to block the obturator and lateral femoral cutaneous nerves.

A successful obturator nerve block was defined as absence of cutaneous sensation in the classic distribution assigned that nerve[1] and evidence of adductor weakness.

A successful lateral femoral cutaneous nerve block was defined as absence of cutaneous sensation in the classic distribution assigned that nerve.[1]

A telephone survey was done by an independent observer two to six months following the blocks to look for neurological complications.

Demographic data were analyzed using student t-test and chi-quare with Yates correction for continuity. The relative success rates of Group I (nerve stimulator group) and Group II (paresthesia group) were compared using Fischer's exact probability test.

RESULTS: There were no systemic complications in either group, nor were manifestations of local anaesthetic toxicity observed.

When assessed at between 2-6 months postoperatively there was an incidence of sensory abnormalities in the operative extremity of 6.8% (3/44 patients contacted).

The original success rate with the nerve stimulator (Group I) was 96.7% (29/30 patients). The original success rate with the paraesthesia technique (Group II) was 62.5% (20/32 patients - Table II). This was statistically significant at $P<0.002$ (Fischer's exact probability test). The overall success rate in Group I (including patients who crossed over to Group I from Group II) was 89.7% (35/39 patients). The overall success rate in Group II remains 62.5% (20/32 patients) as there were no crossovers from Group I to Group II.

Only 2/55 (3.6%) patients had any indication of loss of power in their adductors. All but seven successful femoral blocks (12.7%) had complete anaesthesia of the lateral femoral cutaneous nerve.

DISCUSSION: Our study demonstrates that the femoral 3-in-1 nerve block, performed as originally described by Winnie, does not consistently produce anaesthesia of the obturator nerve as assessed by adduction. The same block does, however, reliably produce anaesthesia of the femoral and the lateral femoral cutaneous nerves.

REFERENCES

1. Cousins MJ and Bridenbaugh PO. Neural Blockade in Clinical Anaesthesia and Management of Pain. 2nd Edition JB Lippincott Co. Philadelphia, 1988: 417-41.

2. Winnie AP, Ramamurthy S, Durrani Z. The Inguinal paravascular technique of Lumbar Plexus Anaesthesia: The 3-in-1 block. Anesth Analg 1973; 52:989-96.

Table I - Demographic Data Before Crossover

	Group I n = 30	Group 2 n - 32	
Age (yrs)	44.0 ± 21.5	48.7 ± 21.5	NS[a]
Weight (kg)	82.6 ± 13.8	79.5 ± 18.9	NS[a]
Height (cm)	171.1 ± 11.4	169.6 ± 10.3	NS[a]
Sex (M:F)	1.7:1	0.9:1	NS[b]

Mean ± SD, NS = non-significant, a = Student's t-test,
b = Chi-squared with Yate's corrections for continuity.

Table II - Success Rates

	Initial Success	Failure	% Success
Group I	29	1	97%
Group 2	20	12	62.5

Fischer's exact probability test was used to compare Group I (nerve stimulator group) and Group 2 (paresthesia group). Group 1 was found to be superior when compared to group 2. Fischer's exact probability test: P = 0.002.

ALKALINIZATION OF MEPIVACAINE FOR AXILLARY BLOCK DECREASES THE INCIDENCE OF UPPER BLOCK EXTREMITY TOURNIQUET PAIN

J.E. Tetzlaff, M.D., M. Walsh, M.D., H. Yoon, M.D.

Cleveland Clinic Foundation, Dept. of General Anesthesia, Cleveland, Oh 44195 USA

INTRODUCTION: Use of pneumatic tourniquet during upper extremity surgery can complicate otherwise adequate axillary brachial plexus anesthesia due to tourniquet-induced pain. It is known to occur with different incidence, depending on regional anesthetic technique and the agent chosen.[1-3] It also has been shown to be altered by the addition of bicarbonate to mepivacaine epidural anesthesia for lower extremity surgery.[4] It is the purpose of this study to evaluate the effect of alkalinization of mepivacaine on the incidence of upper extremity tourniquet pain.

METHODS: This study was approved by the Institutional Review Board. Written informed consent was obtained from 40 patients scheduled for hand surgery. They were randomly chosen to receive axillary brachial plexus block with 40 ml of 1.4% mepivacaine and 1:200,000 epinephrine to which either bicarbonate (1 mEq/10 ml) or saline (1 ml/10 ml) were added. Transarterial technique was used. Patients with pain-free tourniquet time less than 60 minutes were excluded. Sedation was provided, excluding narcotics unless pain was encountered. Patients were questioned every 15 minutes about pain and the answers were recorded by an observer unaware of group assignment. If pain was reported, adequacy of sensory block was determined to distinguish tourniquet pain from failed block. Fentanyl was used to treat pain. Incidence of tourniquet pain was compared with Fischer's Exact Test and considered significant at $p < 0.05$.

RESULTS: The pH of alkalinized mepivacaine was 7.30-7.35. One patient (bicarbonate) was excluded for pain-free tourniquet time less than 60 minutes. Both groups were comparable for sex, age, ASA status, and duration of tourniquet. There was significantly more tourniquet pain in the saline group (Table 1).

DISCUSSION: Alkalinization of mepivacaine favors penetration of nerve cell membranes. It may be that a higher concentration is available at the level of those small, C-fibers thought to transmit tourniquet pain leading to a denser or longer lasting interruption of transmission. In addition to shortening latency to onset, pH adjustment of local anesthetics may alter the quality of neural block.

REFERENCES:

1. Anesthesia and Analgesia 67:828-832, 1988.
2. Anesthesia and Analgesia 65:1181-1185, 1986.
3. Anesthesia and Analgesia 67:833-837, 1988.
4. Can J Anaesth 37:561, 1991.

TABLE 1

	Pain	No Pain	Total
Bicarbonate (B)	2	17	19
Saline (S)	9	11	20
Total	11	28	39
	Fischer's Exact	P = 0.031 S>B	

AN EVALUATION OF pH ADJUSTMENT OF MEPIVACAINE FOR AXILLARY BRACHIAL PLEXUS ANESTHESIA

M. Walsh, M.D., J.E. Tetzlaff, M.D., H. Yoon, M.D.

Cleveland Clinic Foundation, Dept. of General Anesthesia, Cleveland, Oh 44195 USA

INTRODUCTION: Alkalinization of local anesthetics has been shown to decrease the latency to onset of neural blockade.[1-2] Other studies have reported no effect.[3] Adjustment of pH to increase the nonionized fraction of local anesthetic which can more easily cross the nerve cell membrane would be expected to shorten the onset of the block. This study was designed to evaluate the effect of the pH adjustment of mepivacaine on onset for axillary brachial plexus blockade for patients having hand surgery.

METHODS: This study was approved by the Institutional Review Board. Written informed consent was obtained. Patients scheduled for hand surgery were randomized into a control group and a study group. Twenty patients in the control group received an axillary block with 40 ml of 1.4% mepivacaine with 1:200,000 epinephrine and patients in the study group received an axillary block with 40 ml of 1.4% mepivacaine with 1:200,000 epinephrine with 4 ml of sodium bicarbonate (1 mEq/ml).

In both groups, the block was performed using a 25 gauge blunt bevel needle in a transarterial fashion. Onset of sensory blockade was assessed using pin-prick at the anticipated site of surgery. Motor blockade was assessed by detecting forearm paresis. Measurements were taken at 30 second intervals by an examiner unaware of the patient group. Data was evaluated with Wilcoxon's Rank sum test and considered significant at $p<0.05$.

RESULTS: The pH of the mepivacaine was 5.5 plain and 7.30-7.35 after alkalinization. The two groups were similar demographically. All patients had anesthesia adequate for completion of surgery. Table 1 shows onset times for both groups. Onset of both sensory and motor blockade was statistically more rapid in the study group using the Wilcoxon's Rank sum test ($p<0.001$). No complications were noted.

DISCUSSION: Alkalinization of mepivacaine appears to shorten the onset of both sensory and motor blockade in axillary brachial plexus anesthesia, confirming previous studies which show decreases in onset times for brachial plexus anesthesia.[1-2] Mepivacaine may be an ideal agent for alkalinization since a large change in nonionized fraction is possible without precipitation, unlike bupivacaine.

REFERENCES:

1. Regional Anesthesia 15:242-244, 1990.
2. Regional Anesthesia 14:121-123, 1989.
3. Anesthesia Analgesia 67:48-52, 1988.

TABLE 1

	ONSET TIMES	(MEAN / SD)
	Sensory (Min)	Motor (Min)
Study Group	1.5 / 0.6	2.2 / 0.8
Control Group	6.3 / 1.3	8.4 / 1.7
p value < 0.001		

IMPROVED SAFETY IN BIER BLOCK ANESTHESIA BY TOURNIQUET CUFF PRESSURE OPTIMIZATION.

Brian Warriner, M.D., Peter Fancourt-Smith, M.D., Jim McEwen, PhD, Judy Crane, BScN.
Departments of Anesthesia and Biomedical Engineering, St. Paul's Hospital and Vancouver General Hospital, Vancouver, B.C.

INTRODUCTION: Intravenous regional anesthesia (IVRA) is commonly used for anesthesia of the upper limb and less commonly used for anesthesia of the lower limb. Failures of IVRA are often attributed to tourniquet failure, particularly when dual bladder cuffs are used. Tourniquet pressures are chosen according to systolic pressure (twice systolic[1], 100 torr above systolic[2], 50 torr above systolic[3]) or at a pressure of 250 torr for upper limbs and 300 torr for lower limbs[1]. Dual bladder cuffs are often set at 300 torr for upper limb IVRA. These recommendations do not take into account the other factors that affect arterial occlusion such as patient anatomy, variations in cuff design and variations in cuff application. Nor do they take into account that the maintenance of lowest possible effective pressure reduces muscle injury.[4] We have reported the accuracy of a simple limb arterial occlusion pressure (LOP) module, the Safe Tourniquet Occlusion Pressure Sensor (STOP sensor, Western Clinical Engineering)[5]. In this study we used the STOP sensor to set tourniquet cuff pressure for patients undergoing upper limb surgery with IVRA using either single bladder or dual bladder tourniquet cuffs.

METHODS: Ethical approval was obtained from the U.B.C., St. Paul's, and Vancouver General Ethics Reviews Committees. All patients in the various studies had IVRA carried out by injection of 0.5% lidocaine, 3mg/Kg (maximum: 200mg) into the surgical limb through an IV cannula inserted in the dorsum of the hand after exsanguination by esmarch bandage and application and inflation of the tourniquet cuff. **Study 1:** 18 patients received IVRA after application of a single bladder tourniquet cuff (Western Clinical Engineering) previously described.[5] Tourniquet cuff pressure was determined from recommendations given by the STOP sensor after measurement of LOP. Tourniquet cuff pressure was compared to the pressures that would have been needed if literature advice were followed (100 torr above systolic, twice systolic, or 250 torr). **Study 2:** 19 patients received IVRA after application of a dual bladder tourniquet cuff (Western Clinical Engineering). Tourniquet cuff pressure was determined from recommendations given by the STOP sensor after measurement of LOP. Tourniquet cuff pressure was compared to the pressures described in the literature. **Study 3:** Tourniquet pressures were compared between single bladder and dual bladder groups.

RESULTS: Surgical conditions were described as "good" or "excellent" in all patients by the surgeons. There were no anesthetic side effects in any patient and IVRA was successful in all patients. **Study 1:** Mean cuff pressure in the single bladder group was 203 torr +/- 28. This was significantly (paired Student's t-test) lower than "systolic plus 100 torr": 241 torr +/- 20 ($p<.001$), "cuff pressure at 250 torr" ($p<.001$), or "twice systolic": 282 +/- 40 ($p<.001$). It was not significantly different from "systolic plus 50 torr": 191 +/- 20 but 2 patients would have had tourniquet pressure set below measured LOP. **Study 2:** Mean cuff pressure in the dual group was 254 torr +/- 39. This was significantly lower that "cuff set at 300 torr" ($p<.001$) and "twice systolic": 295 torr +/- 44 ($p<.001$). It was not significantly different from "systolic plus 100 torr": 247 torr +/- 22 but 2 patients would have pressures set below LOP. It was significantly greater than "systolic plus 50 torr": 197 torr +/- 22 ($p<.001$) but 9 of these patients would have had tourniquet pressures set below LOP. **Study 3:** Single bladder tourniquet pressure was significantly (unpaired Student's t-test) lower than dual bladder tourniquet pressures ($p<.001$).

DISCUSSION: This study shows that current recommendations for tourniquet cuff pressure in IVRA are either too high (300 torr above systolic, twice systolic) or too unreliable (systolic plus 50 torr) to be accepted for safe application in practice. High pressure has been shown to be associated with an increased incidence of muscle damage[4]. Unreliable pressure settings increase the risk of "cuff failure" causing poor surgical conditions or systemic toxicity of local anesthetics. Measurement of LOP prior to tourniquet cuff inflation allows pressures to be set a the lowest pressure that will produce adequate surgical anesthesia, adequate surgical conditions, and minimal risk of drug toxicity.

This study was supported by B.C. Health Development Fund Joint Grant 5-90.

REFERENCES: 1. Canadian Journal of Anesthesia, 36:3, 1989, 2. Canadian Journal of Anesthesia, 36:5, 1989, 3. Orthopedic Transactions, 6, (Abstract), 1982, 4. Journal of Hand Surgery, 16A:4, 610, 1991, 5. American Society of Regional Anesthesia - Abstract, Mar. 1992.

0.125% BUPIVACAINE-THE OPTIMUM CONCENTRATION FOR POSTOPERATIVE EPIDURAL FENTANYL: RESPIRATORY EFFECTS

Authors: NH Badner MD, R Bhandari MD, WE Komar RN, S Ganapathy MD
Affiliation: Department of Anesthesia, University of Western Ontario, London, Ontario, Canada

Introduction:

Epidural infusions of fentanyl combined with bupivacaine are claimed to be superior to fentanyl alone for postoperative analgesia.[1] We have recently shown that this is not true for the concentration of 0.1% bupivacaine following either total knee joint replacement,[2] or abdominal and thoracic surgery.[3] To determine if there is an optimum effective concentration, we repeated the study using 0.125%, and 0.25% bupivacaine.

Methods:

Following institutional approval and written informed consent, 30 patients scheduled for abdominal or thoracic surgery received in random, double-blind fashion, continuous epidural infusions of a mixture of fentanyl and either 0, 0.125% or 0.25% bupivacaine postoperatively. Patients with contraindications to epidural catheter insertion, age greater than 75, or the presence of neurologic, psychiatric, or significant cardiovascular disease were excluded.

The epidural catheter was inserted prior to surgery and its position verified with 2% CO_2 lidocaine. Patients received general anaesthesia for the operative procedure. At wound closure patients received an epidural bolus of 0.1 ml/kg of the study solution, and on arrival in the recovery room an infusion was started at 6 ml/hr. Solution concentrations were fentanyl 10 ug/ml with either 0, 0.125%, or 0.25% bupivacaine. Following arrival in the recovery room, patients were continuously monitored for oxygen saturation (SpO_2) using a cardiorespiratory oximeter (Nonin Medical Inc., Associated Respiratory Services, Mississauga, Ont.). Oxygen therapy was not conrolled and was ordered by the attending physicians. Measurements of blood gases were made at the times shown (N.B. recovery room departure = RRD). Inadequate analgesia was treated with a 3 ml bolus and an increase in the infusion rate of 2 ml/hr. Excessive drowsiness and/or sedation, or a respiratory < 10 was treated with a decrease in the infusion rate of 2 ml/hr.

Parametric data was analyzed using analysis of variance, and nonparametric data with chi-square and Mann-Whitney U analyses.

Results:

One patient in the 0.125% group, who in retrospect was a narcotic addict, could not be made comfortable in RR, in spite of an infusion of 14 ml/hr and was removed from the study. In the remainder of patients there were no significant differences in demographic data or type of surgical procedure between the three groups. The incidences of desaturation are shown in tables 1 and 2, while the pCO_2 values are shown in figure 1. There were no significant differences in any of these variables between the three groups.

SpO_2 < 90 %

Time Period	Fentanyl	Fent-0.125%	Fent-0.25%
RRD-POD1AM	2.5 ± 1.2	6.0 ± 5.8	1.9 ± 1.2
POD1AM-PM	3.8 ± 2.6	4.5 ± 2.2	6.3 ± 3.8
POD1PM-2AM	3.7 ± 1.8	2.7 ± 0.8	7.9 ± 4.5

Table 1. Values are % of time monitored (means ± SEM)

SpO_2 < 85 %

Time Period	Fentanyl	Fent-0.125%	Fent-0.25%
RRD-POD1AM	1.2 ± 1.0	1.6 ± 1.4	0.9 ± 0.4
POD1AM-PM	4.2 ± 4.2	1.8 ± 0.8	1.2 ± 0.6
POD1PM-2AM	0.6 ± 0.4	3.3 ± 2.6	4.1 ± 3.7

Table 2. Values are % of time monitored (means ± SEM)

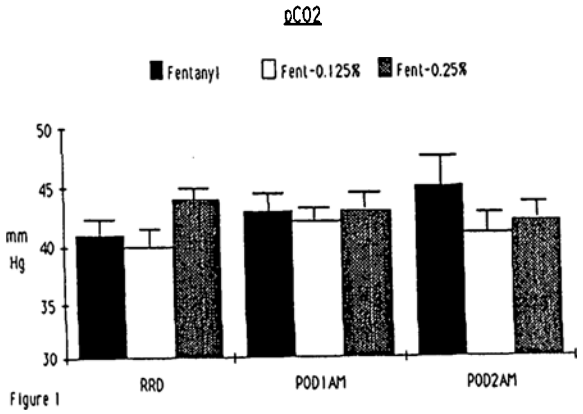


Figure 1

Values are means ± SEM. NS differences.

Discussion:

As there were no significant differences in the incidence of desaturation, or pCO_2 we conclude that the addition of 0.125% or 0.25% bupivacaine does not improve respiratory function during epidural fentanyl infusion analgesia.

References:

1. Reg Anesth 14:25:32, 1989
2. Anesth Analg 72:337-41, 1991
3. Can J Anaesth 38:A117, 1991

0.125% BUPIVACAINE-THE OPTIMUM CONCENTRATION FOR POSTOPERATIVE EPIDURAL FENTANYL: ANALGESIC EFFECTS

Authors: NH Badner MD, R Bhandari MD, WE Komar RN, S Ganapathy MD
Affiliation: Department of Anesthesia, University of Western Ontario, London, Ontario, Canada

Introduction:

Epidural infusions of fentanyl combined with bupivacaine are claimed to be superior to fentanyl alone for postoperative analgesia.[1] We have recently shown that this is not true for the concentration of 0.1% bupivacaine following either total knee joint replacement,[2] or abdominal and thoracic surgery.[3] To determine if there is an optimum effective concentration, we repeated the study using 0.125%, and 0.25% bupivacaine.

Methods:

Following institutional approval and written informed consent, 30 patients scheduled for abdominal or thoracic surgery received in random, double-blind fashion, continuous epidural infusions of a mixture of fentanyl and either 0, 0.125% or 0.25% bupivacaine postoperatively. Patients with contraindications to epidural catheter insertion, age greater than 75, or the presence of neurologic, psychiatric, or significant cardiovascular disease were excluded.

The epidural catheter was inserted prior to surgery and its position verified with 2% CO_2 lidocaine. Patients received general anaesthesia for the operative procedure. At wound closure patients received an epidural bolus of 0.1 ml/kg of the study solution, and on arrival in the recovery room an infusion was started at 6 ml/hr. Solution concentrations were fentanyl 10 ug/ml with either 0, 0.125%, or 0.25% bupivacaine. Patients were assessed for analgesia using a visual analogue scale (VAS, 0 = no pain, 100 = worst pain ever), side effects, sensory loss to pinprick or ice, motor blockade using the Bromage scale, and postural hypotension at the four times shown (N.B. recovery room departure = RRD). Inadequate analgesia was treated with a 3 ml bolus and an increase in the infusion rate of 2 ml/hr. Excessive drowsiness and/or sedation was treated with a decrease in the infusion rate of 2 ml/hr.

Parametric data was analyzed using analysis of variance, and nonparametric data with chi-square and Mann-Whitney U analyses.

Results:

One patient in the 0.125% group, a narcotic addict, could not be made comfortable in RR, in spite of an infusion of 14 ml/hr and was removed from the study. In the remainder of patients there were no significant differences in demographic data or type of surgical procedure between the three groups. The infusion rates and pain scores at the measurement times are shown in figures 1 & 2. There was a trend towards lower infusion rates in the groups receiving both 0.125% and 0.25% bupivacaine that achieved signifance by POD2AM, while the VAS scores were not statistically different. There was no difference in the incidence of side effects between the three groups. Two patients in the 0.125% group, and eight patients in the 0.25% group had sensory loss to pinprick and ice ($p < 0.05$).

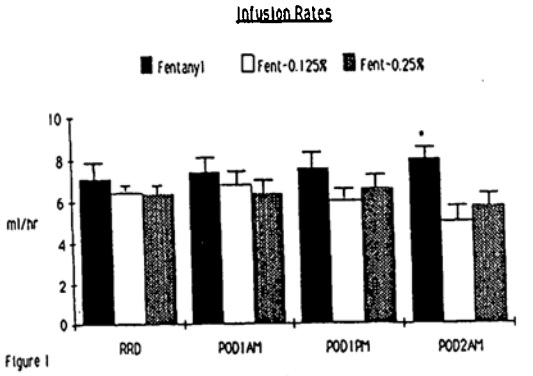


Figure 1

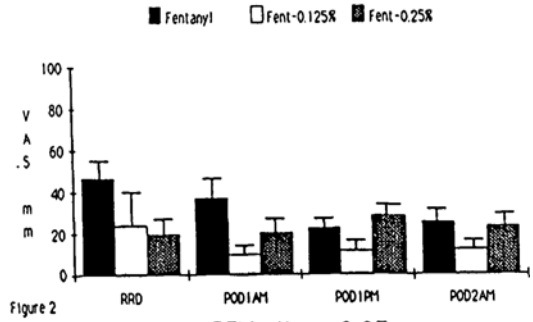


Figure 2

Values are means ± SEM. * $p < 0.05$.

Discussion:

Since the addition of 0.125% bupivacaine allowed lower infusion rates while producing equal analgesia with a lower incidence of sensory deficits, we conclude that it is the optimum effective concentration for postoperative epidural fentanyl infusion analgesia.

References:

1. Reg Anesth 14:2S:32, 1989
2. Anesth Analg 72:337-41, 1991
3. Can J Anaesth 38:A117, 1991

A DOUBLE-BLIND COMPARISON OF REGULARLY DOSED ORAL MORPHINE AND INTERMITTENT INTRAMUSCULAR MORPHINE IN THE TREATMENT OF POST SURGICAL PAIN SECONDARY TO TOTAL HIP ARTHROPLASTY

C.B. Warriner, M.D., J.P. McCormack, Pharm.D., M. Levine, Ph.D., N. Glick, Ph.D.
Faculties of Pharmaceutical Sciences, Medicine, Department of Statistics, U.B.C.; Departments of Pharmacy, Anesthesia, and Clinical Pharmacology, St.Paul's Hospital, Vancouver, B.C. V6Z 1Y6

INTRODUCTION. Post surgical pain (PSP) is common, and effective treatment of PSP is important for recovery from surgical procedures. Many reports have shown that treatment of PSP is often inadequate despite the availability of effective narcotic analgesic. Ineffective treatment is often due to the use of intermittent or on demand intramuscular (IM) narcotic administration. We have previously shown that regularly dosed oral morphine is effective in the treatment of PSP secondary to total hip arthroplasty(1). This double-blind study was designed to compare the effectiveness of regularly dosed oral morphine to intermittent IM morphine use in the treatment of PSP. Adverse effects were also compared.

METHODS. With ethics committee approval, patients who were scheduled to undergo total hip arthroplasty were enrolled in the study after informed consent was obtained. All patients had their PSP controlled initially with 1-4mg of morphine I.V. as needed every 10-15 minutes while in the post-anaesthetic room. Upon arrival on the ward, patients were randomnly assigned to one of the regimens below.

Regularly dosed Oral Morphine Solution (5 mg/ml)	Intermittent (PRN) Intramuscular Morphine
Oral morphine 20 mg PO Q4H	Matching Oral placebo PO Q4H
Patient Requests Pain Medication for Breakthrough pain	
Matching IM placebo plus 10 mg oral morphine	5-10 mg IM morphine plus matching oral placebo

When breakthrough pain medication was requested, the next regularly dosed oral solution was increased by 5 mg. The oral solution was administered until 0200 on post op day(POD) 3. Pain intensity was evaluated prior to each oral dose using a 10 cm visual analog scale (VAS). Average pain scores in the two groups were compared during POD 1 and 2. Level of sedation was assessed before each dose using a 4 point scale on which a score of 1 indicates awake, 2 - easily arousable, 3 - difficult to arouse, and 4 - unarousable. Respiratory rate (RR) was also recorded prior to each dose. If the patient scored either a 3 or 4 on the sedation scale, or the respiratory rate was less than 10, the dose was omitted. The incidence of nausea and vomiting was also recorded during the study period. Antinauseants were used at the discretion of the investigators.

RESULTS. A total of 47 patients were enrolled in the study. Twenty three patients were enrolled in the regularly dosed oral morphine group and 24 patients were enrolled in the PRN IM morphine group. Patient demographics were similar. Average pain scores for POD 1 and POD2 were lower in the regularly dosed morphine group (see fig 1). The number of patients requesting medication for breakthrough pain was also significantly less on both POD 1 and POD 2 in the oral morphine group(see fig 2). The incidence of adverse effects was similar in each group (see table).

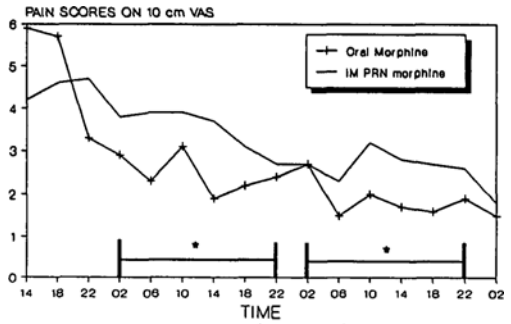
There were 6 dropouts (2 N/V, 3 sedation, 1 poor pain control) in the regularly dosed oral morphine group and 7 dropouts (4 N/V, 3 poor pain control) in the PRN IM morphine group. These patients pain scores were included up until time of withdrawal.

DISCUSSION The use of regularly dosed oral morphine every four hours was more effective than intermittent IM morphine and equally well tolerated when used for the treatment of PSP secondary to total hip arthroplasty. Regularly dosed oral morphine has many potential advantages over the use of intermittent intramuscular morphine injections as it is easier to administer, titrate, has high patient acceptability and is inexpensive. However, clinicians must be aware of the potential for sedation(especially in the elderly), and doses must be titrated accordingly.A pharmacokinetic evaluation of the absorption of narcotics in the perioperative period is presently underway.

Supported by grants from the Vancouver Foundation and PMAC/MRC.

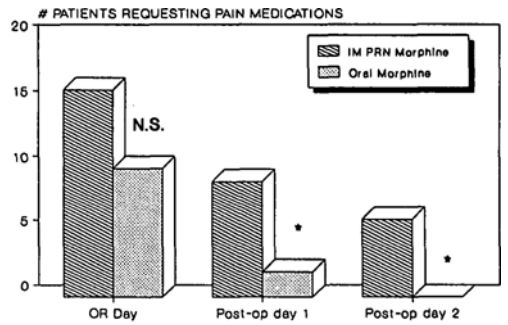
1)Can J Anes 1990;37:S57

Figure 1



* Average pain scores over interval (POD 1 and 2) p<0.05

Figure 2



* Requests for pain medications less for oral morphine group p<0.05

Table

Number of patients with at least one episode	Regularly dosed oral morphine	PRN IM morphine
Nausea	13	16
Vomiting	9	9
Sedation	5	1
Decreased resp rate	0	2

PATIENT CONTROLLED ANALGESIA (PCA) THERAPY: COST SAVING IN NURSING TIME AND EARLY HOSPITAL DISCHARGE?

V.W.S. Chan MD, F. Chung MD, M. McQuestion RN, M. Gomez MD, C. Cruise MD, D. Evans MD, D. Shumka MD
Department of Anaesthesia, Toronto Western Division, The Toronto Hospital, Toronto, Ontario, Canada

INTRODUCTION

While outcome studies have demonstrated positive impacts of PCA on postoperative morbidity and recovery, none has evaluated the potential saving of nursing time during PCA therapy.1,2 This study compared the cost effectiveness of PCA therapy with intramuscular (IM) therapy in: (1) pain relief and patient satisfaction, (2) the demand of nursing time, (3) the rate of postoperative recovery and (4) the cost of treatment.

METHODS

With institutional approval and informed consent, 20 patients (ASA 1-2, 22-67 yo, 47-100 kg, 137-183 cm) undergoing elective cholecystectomy with a subcostal incision were randomly assigned to receive postoperatively: (1) PCA morphine (n=10) at 1.5-2 mg i.v. q 8-10 min on demand, or (2) IM morphine (n=10) at 5-10 mg q 3-4 h as required from ward nurses. In each group, no restriction was set on the dose of narcotic given intraoperatively or morphine administration in the PACU. Both PCA and IM treatments were terminated and substituted by acetaminophen/codeine when p.o. intake became satisfactory.

Serial assessments of pain score by visual analogue scale (VAS) and satisfaction level by a similar linear analogue scale (0=no, 10=complete) were done q 4 h. As per hospital policy, nursing assessment to monitor levels of somnolence and respiration were done and recorded on a flow sheet q 2 h in the PCA group. In the IM group, routine assessment was done q 4-6 h. Continuous time-and-motion recording of every nursing activity for patient care during the course of PCA or IM treatment was performed by independent trained personnel, aided by a bedside FM voice monitor. Postoperative recovery parameters were checked daily and the time to achieve each functional level was documented. From the cumulative doses, the cost of PCA therapy per patient was calculated (based on cost per item of Abbott morphine 30 ml vial at 2 mg/ml, PCA tubing set and infuser) and compared to IM therapy (based on cost per item of morphine 1 ml ampoule at 10 mg/ml and accessory equipment per injection). Data were mean ± SEM and analyzed using Student's t-test where appropriate. $P<0.05$ was considered significant.

RESULTS

There were no significant differences in demographic data, surgical time and the doses of intraoperative and PACU narcotics between the 2 groups. The 36 h pain and satisfaction scores in both groups were also similar (fig.1). During the study period, the total nursing time per patient in checking, selecting, obtaining and recording, and preparing morphine for IM injections was significantly longer while charting time (PCA monitoring flow sheet) was significantly longer in the PCA group (table 1). Time for other nursing activities unrelated to analgesic administration (e.g. vital sign check, hygiene care, assistance in elimination, positioning, ambulation, and administration of concomitant medications) was similar in both groups. The mean nurse response time to IM analgesic request was 37.8 ± 23.4 min. Postoperative recovery data, as shown in table 2, suggested that hospital discharge time was shorter in the PCA group (94.6 ± 6.6 h vs 134.6 ± 23.6 h). However, the cost of PCA morphine and equipment was significantly higher (table 3).

DISCUSSION

This study demonstrates that a small, but significant, amount of nursing time for analgesic administration can be saved during PCA therapy. However, this time saving was offset by the time lost in frequent monitoring and charting. A more substantial amount of cost saving may result from earlier hospital discharge in the PCA group, but confirmation of this benefit will require further study on a larger group of patients.

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2. Ross et al. Anesthesiology 1988;69:A710

Figure 1

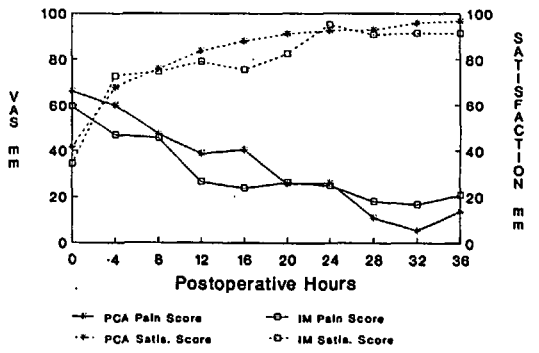

Table 1.

Total Nursing Time per Patient (min) for:	PCA (n=10)	IM (n=10)
Analgesic Administration:		
Checking of Medication	0.20±0.15	3.35± 0.54*
Selecting the Drug	0.35±0.17	2.98± 0.41*
Obtaining and Recording	0.95±0.40	8.85± 1.43*
Preparing the Drug	0.20±0.15	3.90± 0.49*
Changing the Syringe	1.10±0.48	0.0
Administering the Drug	0.0	5.65± 1.27
Programming the PCA Machine	1.00±0.42	0.0
Checking the PCA Machine	6.25±1.78	0.0
Subtotal	10.05±9.63	24.73±10.87*
Checking Patient/IV line	17.90±3.91	11.29± 3.00
Charting	13.08±1.44*	2.85± 0.70
Others (see text)	80.85±7.77	78.33±18.95
Total	121.89±7.11	117.21±17.52

*p<.05

Table 2.

Time (hours) to...	PCA	IM
Reach Satisfactory Oral Analgesia	46.6±4.9	43.3± 3.7
Resume Oral Feeding	51.9±7.5	49.9± 5.5
Ambulate without support	35.5±4.2	44.8± 5.3
Resume Activities of Daily Living	51.4±5.0	57.4± 7.1
Return of Normal Bowel Function	54.2±6.8	49.9± 5.7
Hospital Discharge	94.6±6.6	134.6±23.6

Table 3.

	PCA	IM
Treatment Duration (h)	39.0±2.7	36.0±3.8
Total Morphine Dose (mg)	71.0±7.8	56.2±7.6
Cost of Treatment (CDN$)	19.2±0.1	1.1±0.1*

*p<.05

A SURVEY OF ANAESTHETIC CHOICE FOR MINOR SURGERY

RJ Smyth MSc, MD, M Graham MD, F Chung FRCPC

Western Division, The Toronto Hospital, University of Toronto, 399 Bathurst Street, Toronto, Ontario. M5T 2S8

INTRODUCTION:

Despite the proven efficacy of regional techniques, regional anaesthesia (RA) remains an underutilized specialty. Studies have shown that practicing anaesthetists prefer to have their own surgery performed under RA[1,2], however general anaesthesia (GA) is still the technique of choice for most procedures. We conducted this survey of practicing anaesthetists to assess the percentage of minor surgery performed under RA and to examine the demographic and educational factors which may influence their choice of anaesthetic technique.

METHODS:

A total of 989 questionnaires were mailed to all physicians registered with the Anaesthesia Section of the Ontario Medical Association. Demographic data included university/community practice, years of practice, self-rated ability in administering RA and the location of their residency program. Respondants were asked which anaesthetic technique they would prefer if they were a i) a patient and, ii) the attending anaesthetist for five minor surgical procedures: knee arthroscopy, carpal tunnel release, bunionectomy, cataract excision and hemorrhoidectomy. Each respondant chose their techniques from the following list: GA- mask, laryngeal mask, tracheal intubation; RA- spinal/epidural, IV block, nerve block, infiltration with/without sedation. If the two choices for any procedure differed, they were asked to select a reason for the discrepancy from the following list:

1) time constraints
2) patient refusal
3) staff expertise
4) unacceptable to surgeon
5) side effects
6) medico-legal
7) other

All replies were anonymous and confidential.

RESULTS:

Four hundred forty five questionnaires (45.0%) were returned. The group was comprised of 57.5% community and 42.5% university practitioners. Sixty one percent had < 10 yrs experience. Table 1 shows that although respondants preferred to receive RA for all procedures, GA was administered more frequently for knee scopes, bunion and hemorrhoid surgery. Figure 1 shows that the most common deterrants to the use of RA for these procedures are time constraints and patient refusal. Table 2 shows that respondants with < 10 yrs experience, university practice or adequate ability in RA are more likely to give RA for all procedures ($p<0.05$). Quality of training in RA was not a significant factor in the use of RA. Residency training in RA was felt to be poor by 60.3% of those trained in Toronto and 46.2% from the rest of Canada, outside of Ontario. Most foreign graduates (71.9%) describe poor RA training however only 20% of those who trained in > 1 centre rated their RA training as poor.

DISCUSSION:

Our results agree with earlier reports[1,2] indicating that anaesthetists would prefer RA for their own surgery. Factors such as location and duration of their practice and confidence in administering RA were related to frequency of use of RA for minor procedures. The majority of respondants described their training in RA to be poor despite the fact that ability in RA was rated as adequate by most of the respondants. This suggests that skills in administering RA are being acquired after the residency programs.

REFERENCES:

1) Broadman LM et al. Anesth Analg 1987; 66: S20.
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TABLE 1
PREFERENCE OF ANAESTHETIC TECHNIQUE AS A PATIENT (receive) AND AS AN ATTENDING ANAESTHETIST (give)

	KNEE SCOPE	BUN.	HEMOR.	CARPAL TUNNEL	CATARACT
REGIONAL ANAESTHESIA					
To Give	12.4%	22.1%	18.5%	83.5%	95.7%
To Receive	39.4%*	44.5%*	38.1%*	90.2%*	97.1%
GENERAL ANAESTHESIA					
To Give	87.6%	77.9%	81.5%	16.5%	4.3%
To Receive	60.6%*	55.5%*	61.9%*	9.8%*	2.9%

*$p<0.01$

Figure 1

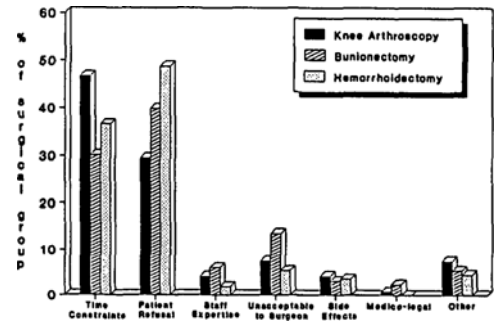

TABLE 2
USE OF REGIONAL ANAESTHESIA

	KNEE SCOPE	BUN.	HEMOR.	CARPAL TUNNEL	CATARACT
EXPERIENCE (YRS)					
0 - 10	15.5%	30.8%	20.0%	84.1%	97.6%
10 +	10.0%	16.6%*	17.3%	83.5%	94.5%
PRACTICE					
Community	9.1%	16.7%	14.3%	83.3%	94.4%
University	16.0%*	29.6%*	23.8%*	84.2%	97.3%
TRAINING					
Good	12.7%	22.9%	19.0%	82.2%	95.3%
Poor	12.1%	21.7%	18.3%	84.4%	96.0%
ABILITY					
Adequate	13.4%	24.9%	21.4%	85.7%	95.8%
Inadequate	7.5%	13.3%*	8.2%*	76.5%*	95.5%

*$p<0.05$

QUANTIFICATION OF FENTANYL, BUPIVACAINE AND EPINEPHRINE BINDING BY AN EPIDURAL CATHETER INFUSION SYSTEM

David Halpenny, M.D., Gerald V. Goresky, FRCPC, J. Eldon Zaretski, BSP
Departments of Anaesthesia and Pharmacy, Alberta Children's Hospital at the University of Calgary, Calgary, Alberta T2T 5C7

INTRODUCTION:
While administering continuous epidural analgesia, we have encountered patients who seem to be resistant to our treatment, and asked whether the medication was being delivered to the epidural space, as dispensed from pharmacy. This question arose, because there have been reports of fentanyl adherance to polyvinyl chloride tubing, reservoirs, filters and the Scimed® cardiopulmonary bypass oxygenator.
Yu-sing et al analyzed the stability of fentanyl and bupivacaine in Pharmacia® Deltec Medication Cassette Reservoirs, demonstrating that fentanyl citrate and bupivacaine hydrochloride can be stored for up to 30 days. The authors conceded that each solution, drug, and reservoir should be confirmed as being compatible. We have been using Bard® Ambulatory PCA pumps and reservoirs. Our objective was therefore to determine the stability of bupivacaine, fentanyl, and epinephrine in Bard reservior bags, before and after infusion through an epidural catheter.

METHODS:
Using a Bard Ambulatory PCA infusion pump with a 250cc reservoir and the supplied connecting tubing (101 inches), the reservoir was filled to capacity with bupivacaine 0.125% with epinephrine 1 in 400,000 in saline diluent and fentanyl 2 ug/ml. The system was primed and the pump was set to run at a rate of 5 cc/hr. After infusion through a 24 gauge Preferred Medical® epidural catheter samples were collected in silanized glass tubes at 0,8,24,32 and 48 hours. The samples were stored at room temperature until the end of the completion of collection, after which they were extracted and evaporated. One week later, each sample was reconstituted and analyzed in triplicate for bupivacaine and fentanyl and in duplicate for epinephrine.
Analysis of fentanyl, bupivacaine and epinephrine was by HPLC using a Nova Pak Phenyl(Waters) column . For fentanyl, the internal standard was sufentanil citrate. For bupivacaine the internal standard used was xylocaine.

RESULTS:
Results are shown in the accompanying charts.The coefficient of variation for analysis of all three constituents was reported as less than 5%.

CONCLUSION:
As reported with other reservoir bags, there is no cumulative sequestration of fentanyl (mixed in a saline solution) by Bard reservoir bags over a 48 hour period using a delivery system which incorporated a 24-gauge Preferred Medical epidural catheter. Inadequate pain relief from epidural analgesia is unlikely to be related to inadquate delivery of medication by the aforementioned infusion system.

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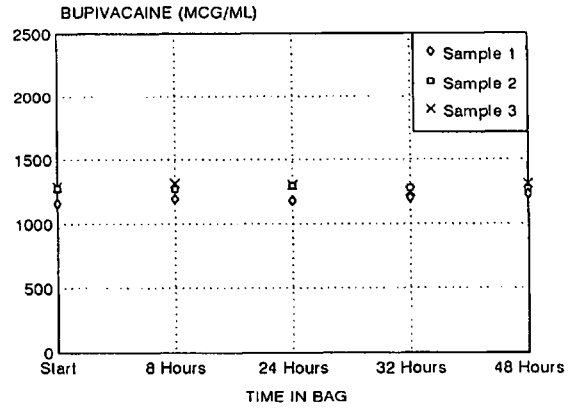
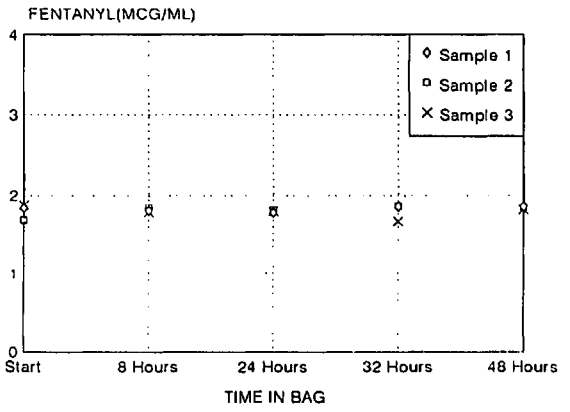
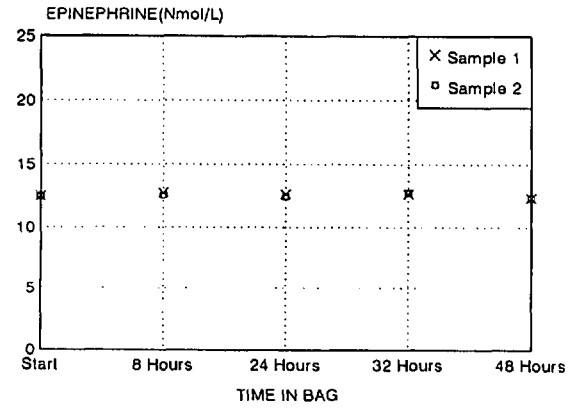
2. Koren G. et al. Sequestration of fentanyl by the cardiopulmonary bypass. Eur J Clin Pharmacol 1984;27:51-6.
3. Yu-Hsing Tu Stability of fentanyl and bupivacaine in portable pump reservoirs. Am J of Hosp Pharm 1990;47:2037-9.

FIGURES 1, 2, AND 3: Bupivacaine, fentanyl, and epinephrine levels in each of 5 samples from epidural infusion system







IS POSTOPERATIVE PAIN REDUCED BY PREOPERATIVE MULTI-MODAL NOCICEPTIVE BLOCKADE? : A RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED STUDY.

B Kavanagh MB, J Katz PhD, A Sandler MB, H Nierenberg BScN, S Roger BSc, J Boylan MB, A Davies MB, M Friedlander MB.
The Acute Pain Research Unit, Department of Anaesthesia, and The Department of Psychology, The Toronto Hospital (General Division), Toronto, Ontario.

INTRODUCTION: Evidence is accumulating from the basic science[1,2] and clinical[3,4] literature, which suggests that surgical incision may induce a process of central nervous system sensitization that contributes to and enhances the postoperative pain experience. This theory of neuronal plasticity has received support by a recent study which reported a reduction in postoperative pain and narcotic consumption when a preemptive epidural narcotic was administered before rather than after surgical incision.[5] Under double-blind placebo controlled conditions, we are investigating the hypothesis that preoperative administration of a combined nociceptive blockade consisting of morphine and indomethacin, followed by preincisional intercostal local anaesthetic blockade, would reduce postoperative pain and narcotic consumption.

METHODOLOGY: Following institutional ethics committee approval and completion of written consent 7 patients scheduled for elective lateral thoracotomy incision were randomly assigned to one of two groups. Patients in group 1 received morphine (0.1-0.2mg.kg^{-1} im) and indomethacin (100mg pr) 30 minutes before surgery, and following induction of anaesthesia received intercostal blocks (bupivicaine 0.5% with epinephrine 1:200,000 1.0mg.kg^{-1} in 5 divided doses), in the interspace of the surgical incision plus 2 spaces above and 2 below. Patients in group 2 received midazolam (0.05 mg.kg^{-1} im) and a placebo suppository 30 mins before surgery, and following induction of anaesthesia, received placebo intercostal saline injections as above. All patients received general anaesthesia with thiopentone, N_2O/O_2, isoflurane, muscle relaxants, and fentanyl (1μg.kg^{-1}.hr^{-1}). No other analgesics were administered before or during surgery. Post-operative analgesia was administered as PCA iv morphine for the first 48-72 hrs following surgery. PCA usage (mg morphine) was assessed at 2, 4, 6, 12, 24, and 48 hrs after completion of surgery. VAS pain scores at rest (VAS-R) were measured at 6, 12, 24, 48, 72, and 96 hrs following surgery, and after standardized mobilization (VAS-M) were measured at 24, 48, 72, and 96 hrs. Parametric data were analyzed by unpaired t-tests (one-tailed) comparing the two groups at each time point. Non-parametric data were analyzed by Fisher's exact test. Data are presented as means ± SEM. $P < 0.05$ was considered statistically significant.

RESULTS: There were no significant demographic differences between the two groups. There was a strong trend towards a reduction in VAS(R) between 6 and 48 hours following surgery in group 1 vs group 2 (Fig. 1), although these differences did not reach statistical significance. The VAS(M) scores at day 1 were significantly less in group 1 than in group 2 ($P<0.05$) (Fig. 2), and there was a trend in the same direction on days 2 and 3 although these later differences did not reach statistical significance. The cumulative PCA morphine consumption (mg) was significantly less at 6 hours in group 1 vs group 2 (Fig. 3); again there was a trend towards less self-administration of morphine in group 1 vs group 2 at later time points.

CONCLUSIONS: These results represent preliminary data only from this ongoing clinical study. Nevertheless, the trends towards reduced postoperative pain and morphine use are striking, and at times statistically significant, despite the small number of patients. Corroboration of these results requires study of larger patient numbers as is currently being undertaken. Of particular interest is the suggestion that the effects of the preoperative analgesia regimen extend long after the expected clinical duration of action of the drugs administered preoperatively.

Fig. 1

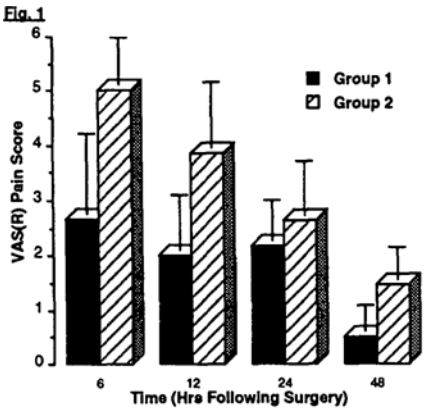


Fig. 2

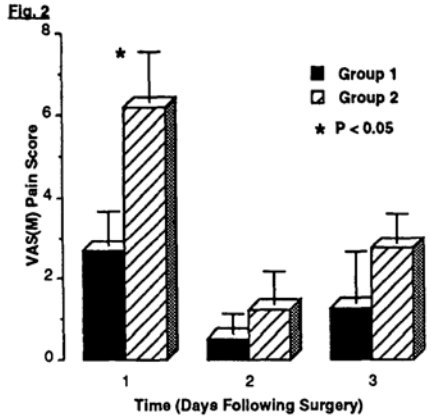
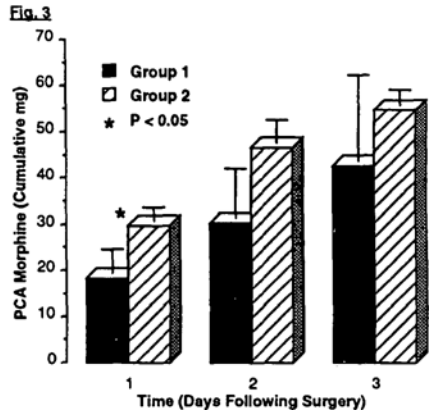


Fig. 3



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WHAT DO WE KNOW ABOUT PATIENT COMFORT AFTER ANAESTHESIA?

Cohen MM, Duncan PG, Pope WDB, Biehl D, Merchant R, WA Tweed
Universities of Manitoba, Saskatchewan and Western Ontario

INTRODUCTION: Quality care in anaesthesia has traditionally focused on major adverse outcomes or mortality (1). However, recent studies have shown that anaesthesia per se contributes little to such events (2,3,4). Therefore future quality improvement in the specialty will be concerned with patient comfort and satisfaction. As part of a large Canadian study of anaesthetic outcomes, we interviewed adult surgical patients in four Canadian hospitals to determine the rates of patient discomfort.

METHODS: After receiving institutional ethics approval, we studied each adult inpatient attended by an anaesthetist at four teaching hospitals. Anaesthetists completed preoperative patient assessments and recorded intraoperative events and following the operation, PACU nurses recorded adverse events. Within 72 hours of the operation, trained research nurses visited all inpatients, attempted an interview and reviewed the hospital chart. Patients were not interviewed if they were non English speaking, were too ill or could not be found (2 attempts). Patients were asked (closed question format) if they had experienced any of a list of symptoms. If affirmative, the patient was asked to rate the severity of the symptom on a visual analogue scale where 1=mild and 5=excrutiating. Finally, patients were asked to rate their anaesthetic experience on a 1-5 scale where 1=very satisfied and 5=very dissatisfied. The rate of each symptom was determined by hospital.

RESULTS: The proportion of the 27,195 inpatients interviewed ranged between hospitals from 40.3% to 73.7%. Interviewed patients (as contrasted to those not interviewed) tended to be younger, healthier and undergoing elective procedures.

The proportion reporting each symptom (Table) varied considerably across the four centres. Nausea, vomiting and sore throat were the most frequently reported at all hospitals, followed by backache and headache. A high proportion of patients who reported a symptom had received some treatment. Patient satisfaction was high; only 0.2 to 1.8% of patients reported dissatisfaction (rating 3-5) with their anaesthetic experience.

DISCUSSION: While the vast majority of the patients were "satisfied" with their anaesthetic, a significant number had experienced postoperative discomfort. Although the majority of those interviewed were younger and healthier and might be expected to be more bothered by minor discomforts, the degree of symptom reporting was higher than expected. The differences in rates of symptoms between hospitals requires further exploration, but may be related to types of surgical procedures, anaesthetic technique used, postoperative analgesia or unknown factors. This survey suggests that patient discomfort after anaesthesia and surgery is frequent and that there is much room for further study and improvement.

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Table: Patient reporting of Symptoms by Hospital

	Hospital			
	A	B	C	D
% Interviewed	63	40	74	63
% of Elective Patients Interviewed	85	89	84	91
% of Females Interviewed	48	47	52	52
% of Males Interviewed	52	53	48	48
% Nausea	25	39	21	37
% Requiring tx	26	46	30	13
% Vomiting	17	25	12	26
% Requiring tx	20	31	18	7
% Sore throat	13	30	20	28
% Requiring tx	79	86	92	94
% Headache	9	24	6	11
% Requiring tx	45	48	53	66
% Backache	8	13	2	8
% Requiring tx	53	37	52	57
% Muscle Pain	3	13	3	4
% Requiring tx	60	43	90	82
% Dissatisfied	1	1	0	2

IS PHANTOM LIMB PAIN INDUCED BY SPINAL ANAESTHESIA IN LOWER LIMB AMPUTEES?

Michael J. Tessler MD FRCPC; Mark Angle MD FRCPC; Simcha Kleiman MD FRCPC
Department of Anaesthesia, Sir Mortimer B. Davis - Jewish General Hospital and McGill University, Montreal, Canada.

INTRODUCTION: Spinal anaesthesia has recently been reported to precipitate intense phantom limb pain in amputees. Because of this possibility, some have recommended that prior lower limb amputation be considered a contraindication to performing a spinal anaesthetic. [1-3] This recommendation is based on anecdotal experiences. We designed a study to attempt to determine the incidence of phantom limb pain in amputees undergoing spinal anaesthesia.

METHOD: Institutional approval was obtained for the study. All patients with prior lower limb amputations who could reliably give a history of phantom limb pain were included in the study. Patients with isolated single toe amputations were excluded. Prior to induction of spinal anaesthesia we recorded the date and indication for the prior amputation as well as the onset and frequency of the phantom limb sensations. Once the block was completed, the presence of phantom limb sensations and a description of these sensations was noted. If a patient complained of pain in his amputated limb a McGill pain score assessment was performed. A score of three or greater was considered as significant pain. (see figure)

Statistical analysis of the incidence of phantom limb pain was performed using confidence interval analysis.

RESULTS: Twenty patients with previous lower limb amputations who had spinal anaesthesia for various procedures were studied. Only one patient complained of a phantom limb pain that he scored at a pain level of three (incidence=5%) while another felt a mild discomfort. No other patient complained of phantom limb pain at any time from induction to offset of their block.

DISCUSSION: If spinal anaesthesia induced severe phantom limb pain in a large percentage of patients, it would be reasonable to avoid this procedure where possible in these patients. However, we found an incidence of only 5% of significant phantom limb pain following spinal anaesthesia (95% confidence interval -4.95 to 14.55%). Consequently, given the low incidence of this phenomenon, and the fact that spinal anaesthesia is often an excellent anaesthetic technique for many types of lower limb and lower abdominal surgery, we do not consider previous amputation to be a contraindication to spinal anaesthesia. Nevertheless, our two cases of spinal anaesthesia induced phantom limb pain in lower limb amputees and the isolated case reports in the literature suggest that further study of this phenomenon is warranted, and that perhaps a susceptible subgroup can be defined.

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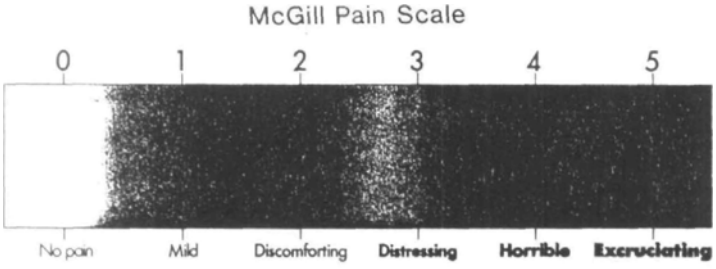


The McGill pain scale is a linear visual analogue scale that uses both words and colours to determine the degree of pain experienced.

PAIN AND NARCOTIC USE FOLLOWING THORACIC SURGERY ARE REDUCED BY PREEMPTIVE LUMBAR EPIDURAL FENTANYL : A RANDOMIZED PROSPECTIVE DOUBLE-BLIND CROSSOVER STUDY.

BP Kavanagh MB, J Katz PhD, AN Sandler MB, H Nierenberg BSc, JF Boylan MB, M Friedlander MB, A Davies MB.
The Acute Pain Research Unit, Department of Anaesthesia and The Department of Psychology, The Toronto Hospital (General Division), Toronto, Ontario M5G 2C4.

INTRODUCTION: There is a growing body of evidence suggesting that surgical incision may sensitize CNS cells and induce lasting changes which influence responses to subsequent somatosensory inputs, and contribute to enhanced post-operative pain.[1,2] The data strongly suggest that this injury-induced "neuroplasticity" may contribute to the experience of pain long after the offending stimulus has been removed.[3,4] The aim of the present study was to test the hypothesis that nociceptive pathway blockade before surgical incision would result in less post-operative pain and narcotic consumption when compared with nociceptive pathway blockade after incision.

METHODOLOGY: Following institutional ethics committee approval and completion of written informed consent, 30 patients (ASA I or II) scheduled for elective thoracic surgery through a lateral thoracotomy incision, were randomized to one of two groups, and prospectively studied in a double-blinded manner. Exclusion criteria were contraindications to regional anaesthesia, ASA status > II, age > 76, and incision other than lateral thoracotomy. Epidural catheters were placed in the L2-3 or L3-4 interspaces pre-operatively, and the position confirmed with lidocaine. Group 1 (n = 15) received epidural fentanyl (4μg/kg, in 20 cc normal saline) prior to surgical incision, followed by epidural normal saline (20 cc) infused 15 min after incision. Group 2 (n = 15) received epidural normal saline (20 cc) prior to surgical incision, followed by epidural fentanyl (4μg/kg, in 20 cc normal saline) infused 15 min after incision. Narcotic analgesics were not used for pre-medication or intra-operatively. All patients were anaesthetized with thiopentone, N_2O/O_2, isoflurane, and vecuronium or pancuronium. Post-operative analgesia consisted of PCA iv morphine. PCA usage (mg morphine) was assessed at 2, 4, 6, 12, 24, and 48 hrs after completion of surgery; VAS pain scores were measured at 6, 12, 24, 48, 72, and 96 hrs; and plasma fentanyl levels were analyzed at 2, 4, and 6 hrs. Parametric data were analyzed by unpaired t-tests (one-tailed) comparing the two groups at each time point using Bonferonni's Type I error rate correction. Non-parametric data were analyzed by Fisher's exact test. Data are presented as means ± SEM. $P < 0.05$ (uncorrected) was considered statistically significant.

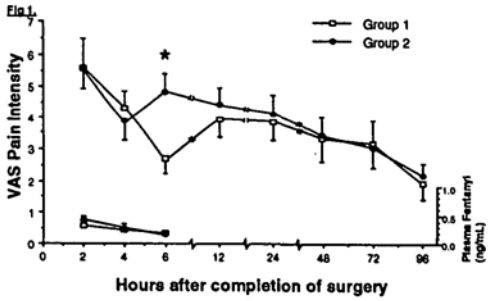
RESULTS: Demographic data are presented in Table 1. VAS pain scores were significantly lower in Group 1 than Group 2 six hours after completion of surgery (Fig. 1) but not at other time points. Plasma fentanyl levels were equal and far below therapeutic levels for both groups at 2, 4, and 6 hrs (Fig. 1). PCA morphine consumption was similar for the two groups (Fig. 1), except between 12 and 24 hrs when group 2 self-administered more than twice the amount of morphine as Group 1 (Fig. 2).

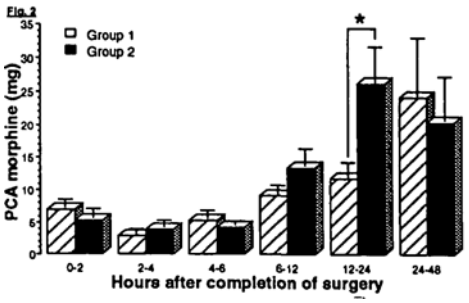
CONCLUSIONS: These results suggest that pre-incisional administration of analgesic agents may result in a significant reduction in post-operative pain. This is clearly not a pharmacokinetic phenomenon, and may be due to attenuation of central pain sensitization processes. Further research is required to evaluate the potential benefits of pre-emptive analgesia using other analgesics and routes of administration.

Table 1.

Variable	GROUP 1	GROUP 2	*P*-value
Age (yr)	61.9(2.8)	49.5(4.7)	0.03*
Weight (kg)	70.9(3.7)	71.1(3.3)	ns
Males (n)	6	12	ns
Syr 2-Syr 1 (min)	100(10.9)	80(7.7)	ns
Dur Surgery (min)	180(18.0)	188(9.0)	ns
Fentanyl (μg)	283.5(14.8)	284.5(13.2)	ns

*Significant age difference is due to two patients in Group 2 who were more than 2 standard deviations below the mean age. Removing these two patients from the statistical analyses had no effect on the results of the VAS pain score or the morphine requirement analysis.





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Objective Measures of Anxiety and Depression Before Thoracic Surgery

H Nierenberg BScN, S Roger BSc, B Kavanagh MB, J Katz PhD, A Sandler MB.
The Acute Pain Research Unit, Department of Anaesthesia, The Department of Psychology, The Toronto Hospital (General Division), and the Departments of Anaesthesia and Behavioural Science, University of Toronto, Toronto, Ontario, Canada.

INTRODUCTION: Health care professionals often encounter patients with high levels of anxiety and depression prior to major surgical procedures (1). In addition, high levels of pre-operative anxiety are associated with increased postoperative pain intensity (2). Although it has been suspected that patients undergoing surgery for malignant disease may be more anxious or depressed than patients with non-malignant disease, this has not been formally assessed. The aims of this study were to prospectively quantify anxiety and depression using objective, validated scoring instruments, in patients undergoing surgery for malignant or non-malignant disease.

METHODS: Following institutional ethics committee approval and completion of written informed consent, 14 patients have been recruited into this ongoing study. Spielberger State-Trait Anxiety Inventory - Trait (STAI-T) and State (STAI-S) questionnaires were used to evaluate state and trait anxiety respectively (3). The Beck Depression Inventory (BDI) was used to evaluate depression (4) All questionnaires were administered the evening before surgery following the routine nursing preoperative teaching session and pre-anaesthetic consultation. Data are presented as means ± SEM for group 1 (cancer) and group 2 (non-cancer). Comparisons were made using unpaired t-tests and Fisher's exact test. Statistical significance was inferred if $P < 0.05$

RESULTS: There were no significant demographic differences between the 2 groups. There were no significant between group differences in anxiety or depression scores as shown in Fig. 1 (BDI: group 1 = 8.5 ± 3.6; group 2 = 5.3 ± 3.4. STAI-T: group 1 = 37.8 ± 4.3; group 2 = 32.5 ± 6.8. STAI-S: group 1 = 43.8 ± 5.9; group 2 = 40.2 ± 5.1. The incidence of mild depression (BDI ≥ 10) in group 1 and 2 was 33% and 17%, respectively. The incidence of higher-than-normal levels of state anxiety (STAI-S ≥ 37) was 17% and 50%, respectively.

DISCUSSION: Patients with cancer who are scheduled for thoracic surgical procedures do not necessarily experience higher levels of preoperative anxiety or depression compared with non-cancer patients scheduled for comparable surgical procedures. Nevertheless, mild to moderate levels of anxiety or depression may be present in some patients before surgery. Pre-anaesthetic consultation, teaching, assessment and perhaps premedication of all thoracic surgical patients may be effective in reducing preoperative emotional distress.

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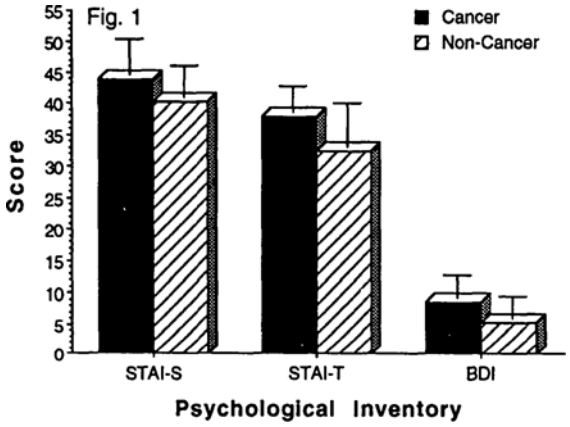

EFFECT OF HYPOTHERMIA OR HYPERVENTILATION ON ENFLURANE MAC REDUCTION FOLLOWING PARTIAL CPB IN DOGS.

GJ Doak,MD,FRCPC, G Li,MD,MSc, RI Hall,MD,FRCPC and JA Sullivan,MD,FRCSC.

Departments of Anaesthesia, Pharmacology and Cardiovascular Surgery, Dalhousie University, the Victoria General Hospital, and the Maritime Heart Centre, Halifax, Nova Scotia.
Supported by the New Brunswick Heart and Stroke Foundation.

INTRODUCTION: Recent work has shown that requirements for enflurane anesthesia (MAC) are altered following cardiopulmonary bypass (CPB)[1]. This study on dogs determined the influence of systemic cooling and hypocarbia during partial (femoral artery-vein) CPB, on enflurane MAC reduction.

METHODS: With the approval of the institutional Animal Care and Use Committee, 12 fasting, mongrel dogs were each anesthetized with enflurane in oxygen, on two separate occasions. Tracheal intubation was performed, monitors placed, and end-tidal enflurane concentration measured via a Puritan-Bennett® Anesthesia Agent Monitor. MAC, according to the tail-clamp method, was determined twice with a 1 h interval (MAC 1 and MAC 2). Partial CPB was then initiated using femoral artery-vein cannulation and maintained for 1 h using a bubble oxygenator, a crystalloid prime, and flows of 30-40 $ml \cdot kg^{-1} \cdot min^{-1}$ with mean systemic pressure maintained between 50-70 mmHg. Following separation from CPB, MAC was again determined, twice with a 1 h interval (MAC 3 and MAC 4). Dogs were randomly assigned according to PaCO2 management during CPB (LOW vs NORMAL). The first experiment on each dog was undertaken using normothermia during CPB (WARM) while the second experiment (at least 2 weeks later) was conducted using hypothermia (28- 30 °C) during CPB (COLD). Differences between groups were determined with a repeated measures ANOVA ($p < 0.05$) and post hoc analysis ($p < 0.01$ for multiple comparisons).

RESULTS: Analysis of the 23 complete data sets obtained, revealed MAC 3 (1.95 ± .33%, post-CPB) to be reduced when compared to MAC 1 (2.18 ± .28%, $p < 0.01$) or MAC 2 (2.10 ± .22%, $p < 0.01$), determined pre-CPB. Taking the entire group, multivariate repeated measures analysis revealed no independent effects of hypothermia or arterial hypocarbia during CPB, on MAC reduction. However analysis of the four groups (CPB temperature X PaCO2 management, Fig. 1a-d) showed a statistically significant change in MAC post-CPB only in the WARM*NORMAL group ($p = 0.034$, Fig. 1a). There were small decreases in temperature, hematocrit, mean arterial pressure, and acid-base status but not of sufficient clinical magnitude to account for the changes observed.

DISCUSSION: We found enflurane MAC in dogs to be reduced following partial CPB, largely as a result of changes in the WARM*NORMAL group. This may be secondary to cerebral injury produced by microemboli associated with CPB. Cerebroprotective maneuvers such as hypothermia and hyperventilation might be expected to reduce this effect. The authors conclude that partial CPB alters enflurane MAC in the dog and hypothermia or hyperventilation during CPB may affect the magnitude of this alteration.

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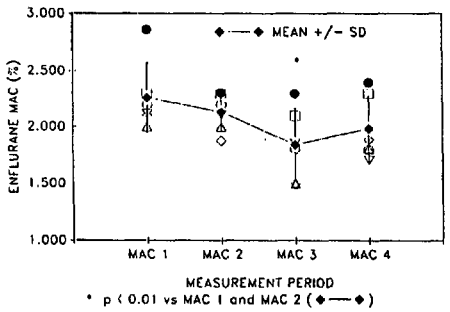
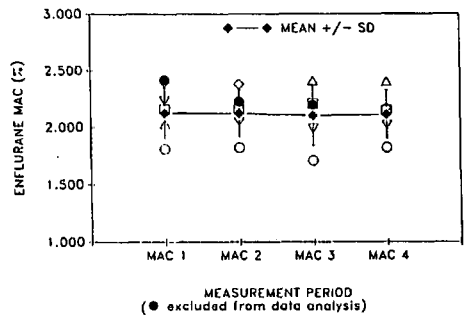
Figure 1(a-d) Enflurane MAC pre- (MAC 1 and 2) and post-CPB (MAC 3 and 4).

a) GROUP I WARM * NORMAL



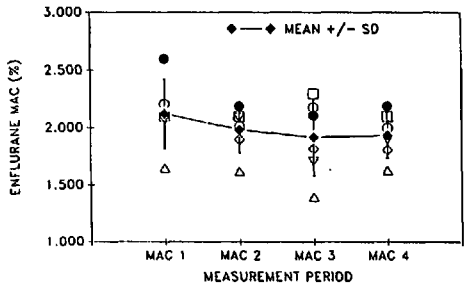
* $p < 0.01$ vs MAC 1 and MAC 2 (◆—◆)

b) GROUP II WARM * LOW

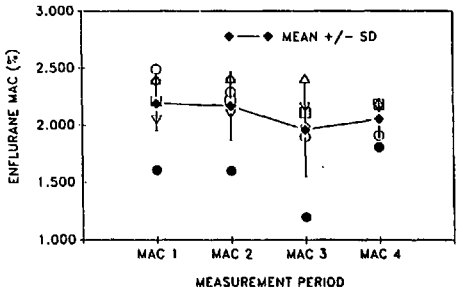


(● excluded from data analysis)

c) GROUP III COLD * NORMAL



d) GROUP IV COLD * LOW



A COMPARISON OF TWO DOSES OF EPIDURAL FENTANYL FOR CAESAREAN SECTION USING CARBONATED LIDOCAINE

I. Yee MD FRCPC, S. Halpern MD FRCPC, R. Pittini, C. Huh

Department of Anaesthesia, Women's College Hospital and University of Toronto, Toronto, Ontario

INTRODUCTION Epidural fentanyl (EF), 50 to 100 μg, has been shown to improve the quality of anaesthesia for Caesarean section (CS) when added to local anaesthetic[1,2,3]. Side effects such as drowsiness and nausea are common with these doses. In this study, we compared the effectiveness and incidence of side effects of 25 μg vs 50 μg of EF in a randomized double blind prospective manner.

METHODS After Ethics Committee approval and informed consent, 50 patients having elective CS under epidural anaesthesia were randomized into two groups. After a standard test dose patients in Group I (N=24) received 25 μg of EF in a 1 ml volume and Group II (N=26) received 50 μg in the same fashion. Continuous epidural anaesthesia was induced using 2% carbonated lidocaine with 1:200,000 epinephrine, titrated to a T_4 sensory level. The quality of analgesia was measured by visual analogue scores (VAS) and the need for intravenous fentanyl intraoperatively, and by the Short Form McGill Pain Questionnaire (SF-MPQ)[4] immediately postoperatively. The incidence of side effects such as hypotension, drowsiness, nausea, pruritus, and respiratory depression was also recorded. Neonates were assessed using 1 and 5 minute Apgar scores and umbilical cord gases. All recordings were made by a blinded observer. Demographic data were analyzed using unpaired T tests. Analgesia and side effects were compared using the Fisher's Exact test and unpaired T tests where appropriate. A p value < 0.05 was considered significant.

RESULTS The study groups did not differ in age, height, or weight. Surgical characteristics, anaesthetic requirements, and side effects were similar in both groups (Table). Mean VAS pain scores (Figure 1) and SF-MPQ scores (Figure 2) did not differ significantly. There were no differences in birth weights, Apgar scores, and cord blood gases between neonates in the two groups.

DISCUSSION The results of this study show no significant differences between the two groups in the quality of analgesia, as measured by each of the three methods described. Group I tended to have higher pain scores, greater need for supplemental IV fentanyl, and less nausea than Group II, but these differences were not statistically significant. Use of the lower dose of epidural fentanyl did not significantly reduce the incidence of side effects. Although 25 μg of epidural fentanyl offers similar analgesia to 50 μg for Caesarean section, it has no other advantages to recommend its routine use. This study supports the use of 50 μg of epidural fentanyl for Caesarean section as a safe and effective dose.

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TABLE

	Group I N=24 fentanyl 25μg (mean ± S.D.)	Group II N=26 fentanyl 50μg (mean ± S.D.)	P
SURGERY			
Ind-del time (min)	33.5 ± 7.8	38.7 ± 11.5	ns
Ut incis-del time (sec)	144 ± 53	133 ± 55	ns
Total operative time (min)	66.6 ± 21.3	72.1 ± 13.0	ns
Uterus exteriorized (%)	21	31	ns
ANAESTHESIA			
Local anaesthetic (ml)	22.3 ± 4.6	23.0 ± 5.6	n
IV fentanyl required (%)	20	7.7	0.17
SIDE EFFECTS			
Hypotension (%)	67	46	ns
Drowsiness (%)	54	54	ns
Nausea (%)	25	46	0.10
Pruritus (%)	0	0	ns
Respiratory depression (%)	0	0	ns

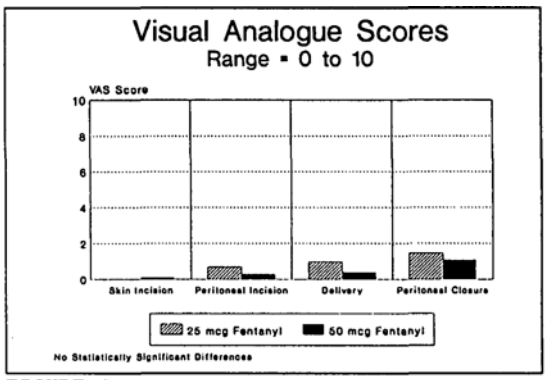

FIGURE 1

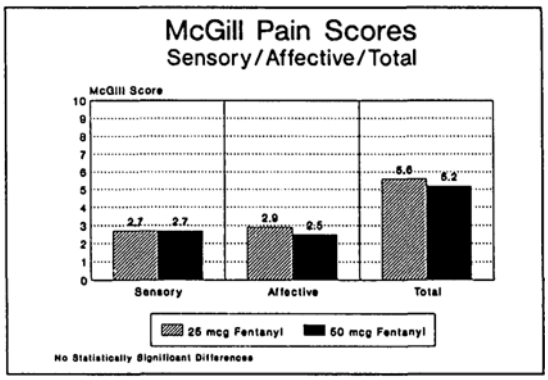

FIGURE 2

EPIDURAL SUFENTANIL DOES NOT ALTER MATERNAL HAEMODYNAMICS DURING CAESAREAN SECTION

G.L. Bryson MD, E.T. Crosby MD, R.D. Elliott MD, R. Gverzdys MD
Ottawa General Hospital, University of Ottawa, Ottawa, Ontario, Canada, K1H 8L6.

Introduction: The addition of opiates to lumbar epidural anaesthesia (LEA) has been shown to reduce intraoperative pain and nausea during Caesarean section (CS)[1]. Thoracic Electric Bioimpedance (TEB) allows non-invasive assessment of central haemodynamics which has been shown to correlate well with invasive techniques in both pregnant and non-pregnant subjects. The purpose of this study was to compare haemodynamic measurements as assessed by TEB in patients undergoing CS under LEA with and without epidural sufentanil.

Methods: Following approval by the hospital ethics committee and informed consent, ASA I/II patients were randomized to control (GC) and study (GS) groups. Following standardized intravenous prehydration, an epidural catheter was placed at the L_{2-3} or L_{3-4} interspace. After negative test dose, in a double-blinded protocol, patients in GS received sufentanil 30 μg in 4.4 ml of 2% lidocaine carbonate with 5 $\mu g\text{-}ml^{-1}$ epinephrine (total volume 5 ml) while those in GC received 5 ml of 2% lidocaine carbonate with epinephrine. Lidocaine carbonate with 5 $\mu g\text{-}ml^{-1}$ epinephrine was titrated to establish a anaesthetic level of T_{4-6}. Heart rate (HR), mean arterial pressure (MAP), cardiac index (CI), ejection fraction (EF), and end diastolic index (EDI) were measured non-invasively at the following times: (1) before insertion of the epidural catheter (Base); (2) after catheter insertion (Epid); (3) after the test dose (Test); (4) after establishment of the epidural block (Block); (5) at skin incision (Skin); (6) at cord clamping (Cord); (7) one minute after exteriorization of the uterus (Ut Out); (8) after uterine replacement (Ut In); and (9) after skin closure (Close). Maternal hypotension, defined as a decrease of > 20% from baseline or a systolic blood pressure of less than 100 mm Hg, was treated with intravenous ephedrine 5-10 mg. The incidence and severity of intraoperative pain was assessed using a visual analogue pain scale. Intraoperative pain was treated with intravenous sufentanil 10 μg. The occurrence of nausea and vomiting was also noted. Hemodynamic variables were compared within and between groups using ANOVA while the incidences of pain, nausea and vomiting were compared using the Fisher exact test. $P < 0.05$ was significant.

Results: 20 patients have been randomized, 12 to GS and 8 to GC. The mean volume of local anaesthetic used was GC=21.6 ml and GS=20.3 ml. Intraoperative pain occurred in 1 patient (GS) and nausea/vomiting related to visceral stimulus occurred in 1 patient in each group. There were no significant differences noted in haemodynamic measurements between the groups at any event. However significant differences occurred within the groups when compared with baseline values with respect to both HR and CI (Tukey's HSD Test). (Figures 1,2)

Discussion: Maternal hemodynamic measurements as assessed by TEB, during CS, were not altered by the addition of sufentanil to carbonated lidocaine for LEA. Epidural sufentanil has been shown to provide analgesia of rapid onset and relatively short duration with little respiratory depression.[2,3] These attributes make sufentanil an appealing choice as a supplement to LEA for CS.

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Figure 1. Heart Rate

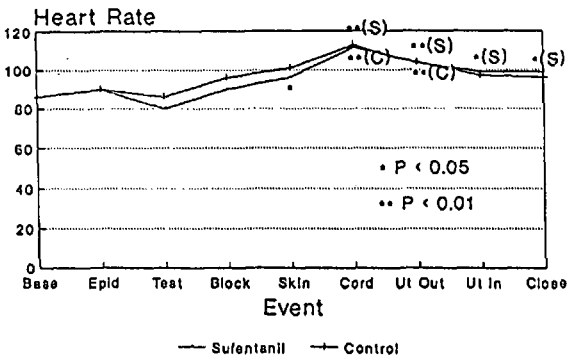
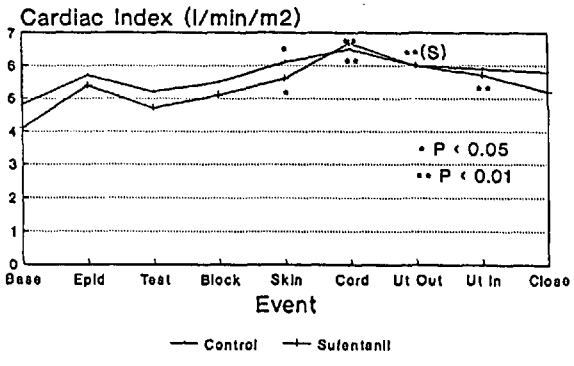


Figure 2. Cardiac Index



THE DIFFICULT AIRWAY: A TEACHING HOSPITAL'S EXPERIENCE

DK Rose, Dept. of Anaesthesia, St. Michael's Hospital, MM Cohen, Clinical Epidemiology Unit, Sunnybrook Health Science Centre, Toronto Ontario

INTRODUCTION Disastrous outcomes have been described when a difficult laryngoscopy or failed intubation follows the induction of general anaesthesia.[1,2] To determine if there were problems of management and assessment of airways at our hospital, we prospectively examined all intubations in the operating room over a nine month period.

METHODS After obtaining ethics approval, information was obtained prospectively from carbonless copies of the OR (operating room) and PACU (post anaesthetic care unit) records. All anaesthetists (30), residents (10) and PACU nurses (24) were instructed on completion of these records. The intubation techniques (asleep/direct, asleep/indirect, asleep/fibreoptic, awake/direct, awake/indirect, awake/fibreoptic or awake/tracheostomy) and failures (abandoned or alternate approach required) were recorded.

Laryngoscopy following asleep/direct approach was recorded on the chart as easy or difficult (>2 laryngoscopy attempts) as well as the total number of laryngoscopy attempts. Further management of these difficult laryngoscopies was also noted.

To determine if these difficult laryngoscopies could be identified preoperatively we compared characteristics of two groups, the easy and the difficult, using relative risk ratios and 95% CI[3] (the % difficult who have the characteristic divided by the % easy who have the same characteristic). These characteristics included preoperative factors (eg age, ASA status, weight, surgical urgency, illnesses etc.). We also noted if physical examination and overall assessment of the airway were documented by the anaesthetists. Documentation was by check boxes on the OR record to record the physical examination of the airway (mouth opening <2 fingers, neck flexion limited, thyromental distance < 3 fingers, and failure to visualize the hypopharnyx). The overall assessment, (normal, equivocal, or abnormal) was made dependent on these 4 physical characteristics or any other features (eg. dentition or past history) which were relevant. Assessments and examinations which were missing were also noted.

RESULTS Over the 9 months intubation was attempted in 6785 patients. Fig. 1 outlines the different techniques and their rates of failure.

For the most common method of intubation (asleep/direct), 114 patients (1.7%) had a difficult laryngoscopy. Ninety-four of these patients who were difficult, were successfully intubated with multiple laryngoscopies (18.5% required ≥ 4 laryngoscopies). The 20 failures were managed by cancelling the case (4), and/or using an alternate technique (16). The successful alternate techniques were divided into two categories - those that were continued under general anaesthesia (6 mask GA's and 4 asleep/fibreoptic intubations) and those patients who were awakened from anaesthesia (1 neurolept, 4 fibreoptic/awake intubations and 1 awake/retrograde technique).

Characteristics which have a significantly higher relative risk difficult laryngoscopy include male sex (1.3), spine surgery (2.0), mouth opening <2 fingers (5.4), thyromental distance <3 fingers (4.9), inability to visualize the hypopharynx (3.7) and a difficult or equivocal assessment (4.7).

Adverse events following attempts at asleep/direct intubation in the difficult groups occurred at induction (desaturation, dysrhythmias and dental damage were 6.3, 4.7, and 10.9 times more common than easy) and in the PACU (room air desaturation and unanticipated ICU admission 2.6, 6.4 times more frequent).

Anaesthetists documented in advance that 25 of the 114 patients had an abnormal or equivocal preoperative airway assessment (21.4% sensitivity). However, in these patients who had a difficult laryngoscopy, anaesthetists or residents failed to access the airway preoperatively in 20.2% of cases. Physical examinations were also missing; mouth opening (21.4%), neck movement (22.3%), thyromental distance (36.9%) and visualization of the hypopharynx (42.7%).

Conversely in all patients who were intubated by the asleep/direct approach, 325 (4.9% of those with a preop assessment) were assessed as abnormal or equivocal preoperatively. Only 20 of these actually had a difficult laryngoscopy. Therefore the predictive value of our assessment system was 20/325 or 6.1%.

CONCLUSION Alternate techniques for airway management are used infrequently and are not without failures. The majority of the difficult asleep/direct laryngoscopies were eventually successful but 2 patients required an unanticipated ICU admission for postoperative respiratory complications and 4 other cases were cancelled. Our present methods for predicting difficult laryngoscopy have low sensitivity and predictability scores. Increase emphasis on preoperative documentation, validity of the examination, and increase familiarity with alternate techniques may be beneficial.

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FIGURE 1 Methods and failures of intubation

TECHNIQUE	# Pts Intubated	# of Failures
asleep/direct	6644	20 (.3%)
asleep/indirect	9	1
asleep/F.O.	3	1
awake/direct	17	2 (11.8%)
awake/indirect	5	1
awake/F.O.	100	3 (3%)
awake/trach.	7	0

POST-SPINAL HEADACHE AFTER CAESAREAN SECTION: HISTORY OF AN ABORTED STUDY

Authors: C. Perreault M.D., L. Ferland M.D., F. Gobeil M.D., D. Girard M.D.
Notre-Dame Hospital, University of Montreal, Montreal.

Introduction: The incidence of post-spinal headache after Caesarean section varies widely from one study to the other. The use of 25G or 26G Quincke needles for spinal anaesthesia during Caesarean sections has been associated with an incidence ranging from 0.4 to 28%.[1-3] Our own experience with 25G Quincke needles yielded an incidence of 16% (unpublished data). The prevention of post-spinal headache is difficult, but some authors suggested that epidural or intrathecal narcotics might help. The present study was designed to evaluate if the addition of fentanyl to bupivacaine during spinal anaesthesia would decrease the incidence or prevent the development of post-spinal headache using 27G Quincke needles. We expected the incidence of post-spinal headache with 27G Quincke needles to be somewhat similar to 25G and 26G needles, that is as high as 28%.

Methods: This double blind study was approved by the Research and Ethics Committees of our institution, and involved 40 pregnant patients at term undergoing elective Caesarean section. Each patient gave her written consent and was assigned to one of two groups: the fentanyl or the placebo group. The anaesthesia technique was the same for both groups: with the patient sitting, spinal anaesthesia was performed with a 27G Quincke needle in the low lumbar region. The lumbar puncture was done with the bevel of the needle parallel to the cephalo-caudad axis, and a 12 mg dose of bupivacaine 0.75% was injected to each patient. The patients in the fentanyl group also received 10µg (2 ml) of fentanyl mixed to the local anaesthetic; the patients in the placebo group received 2 ml of NaCl 0.9% mixed with the local anaesthetic. All patients received at least 2 litres of Ringers lactate IV before the local anaesthetic was injected. Patients were then placed in the supine position with a wedge under their right hip. Parameters noted during the Caesarean section were the vital signs, the sensory levels and the side effects such as nausea, vomiting and paresthesias. Neonates were evaluated using the Apgar scores at one, five and ten minutes and the umbilical cord arterial pH. Parameters noted in the post-operative period were the time when intramuscular analgesia was first needed (starting from the injection of the spinal bupivacaine), and the development of typical headaches in the first five post-operative days. Statistical analysis was done with the Student "t" test or the Mann Whitney U test when appropriate. A value of $p < 0.05$ was considered significant.

Results: Preliminary results were analysed for the first 29 patients (14 in the placebo group and 15 in the fentanyl group). The demographic data, data relating to the anaesthesia technique (ponction site, number of ponctions needed, paresthesias), heart rate and systolic blood pressure taken at 0, 5 and 10 minutes after injection of the local anaesthetic and at arrival in the recovery room were all similar in both groups. Sensory levels were significantly higher in the fentanyl group ten minutes after injection both groups and no patient in either group reported pruritus. The time at which intramuscular analgesia was needed in the post-operative period was significantly longer in the fentanyl group [197.7 ± 40.2 min vs 155.8 ± 57.1 min (mean ± SD)]. One patient in the fentanyl group presented a post-spinal headache on the second post-operative day, which lasted for one day and had an intensity of 0.6 on a visual analogue scale of 10. No patient in the placebo group presented a post-spinal headache. The evaluation of the neonates was similar in both groups, and all had adequate Apgar scores and umbilical cord arterial pH.

Discussion: Epidural morphine has been used for the prevention of post-spinal ponction headache (17G Tuohy needles) in non-obstetrical patients.[4,5] A retrospective study by Johnson et al. suggested that intrathecal fentanyl may reduce the incidence of post-spinal headache.[6] Our preliminary results revealed an incidence of post-spinal headache of only 3% (1 in 29 patients), which was much less than the incidence we expected. To our knowledge, no study reported on the incidence of post-spinal headache with the use of 27G Quincke needles during Caesarean sections. Those results drastically changed the number of patients needed to validate our study. Assuming an alpha error of 5% and a beta error of 10%, and assuming that the addition of fentanyl would reduce the incidence of post-spinal headache by 50%, it would take 4,368 patients to concluded our study! Unfortunatly, it would take more than 20 years to conduct such a study in our institution...
In conclusion, although we have not been able to demonstrate that the addition of intrathecal fentanyl reduced the incidence of post-spinal headache after Caesarean sections, we suggest that the incidence of post-spinal headache using 27G Quincke needles is around 3%.

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TABLE: SENSORY LEVELS

	Placebo	Fentanyl
Level at 5 min	T_{10} (T_3 - T_{10})	T_8 (T_2 - T_{12})
Level at 10 min	T_4 (T_2 - T_6)	T_2 (T_1 - T_6)*
Level at skin closure	T_2 (T_2 - T_4)	T_3 (T_2 - T_8)
Level at discharge	T_{10} (T_3 - T_{12})	T_4, T_{10} (T_4 - L_1)

Mode (range)
* $p < 0.05$

A NEW DEVICE FOR ORAL AND NASOTRACHEAL LIGHT-GUIDED INTUBATION

Sarah C. Stevens, MD, Orlando R. Hung, FRCPC

Department of Anaesthesia, Victoria General Hospital, Dalhousie University, Halifax, NS B3H2Y9

INTRODUCTION: Transillumination of the soft tissues of the neck to place tracheal (ET) tubes has been practised for the last two decades. The first intubating stylet, a laryngoscope bulb attached to a copper wire[1], was developed by the Japanese for nasotracheal intubation. A small portable surgical flashlight (Flexilum® Surgical Light, Concept Corp., Clearwater, FL) was used in the 70s as a rigid lightwand to perform light-guided intubation.[2-3] This device consisted of a proximal battery housing unit from which extended a 25 cm copper wire and a laryngoscope bulb. Minor refinements of the design of the Flexilum® device were made in the early 80s (Tube-stat®, Concept Corp., Clearwater. FL) and further studies of lightwand intubation were reported in both elective and emergency situations.[4-5] Nasotracheal intubation was also reported using this device.[6] Despite these improvements, difficulties persisted with regard to the ease of use and other aspects of lightwand technology. Placement of a rotational switch at the proximal end of the battery casing was awkward and unreliable. The bulb of the device directed light down into the airway and was not readily seen from the side. The light intensity of the bulb did not easily transilluminate the tissues of some patients, particularly in bright ambient lighting. The length of the lightwand also limited its use to ET tubes 25 cm or shorter in length.

DESIGN IMPROVEMENTS: The development of a "lightwand" designed specifically for tracheal intubation and tube positioning was based on the desire to broaden the use of transillumination and to improve on previous limitations. A need was recognized for both rigid and flexible versions of the lightwand; the rigid for use in oral intubation and the flexible for nasal intubation. The Stewart Tracheal Lightwand® (STL), a new design, incorporates the following changes: (1) a brighter light bulb with the light beam pointing both anteriorly and downward into the airway; (2) a retractable inner rigid trocar which can be removed to convert the lightwand to a flexible instrument suitable for nasal intubation; (3) a longer stylet portion enabling the use of the lightwand with ET tubes of standard length; (4) a side clip to secure the tube firmly to the stylet; (5) a conveniently-placed, and easily activated on/off switch.

EVALUATION: Studies of transilluminated light from lightwands placed in both the oesophagus and trachea were used to determine the intensity of the light source necessary to produce an easily seen glow through the tracheal wall and soft tissues of the neck. These studies were carried out under varied levels of ambient lighting. Initial prototypes were evaluated to determine the tolerance of the human oral mucosa to heat given off by the bulb. Direct application of the bulb to the oral mucosa of volunteers was tolerated in most subjects for more than 30 seconds. Results from preliminary patient studies permitted further improvements in light intensity, the on/off switch, and the special clip designed to secure the tube to the stylet. Videotapes of the lightwand procedure were used for time/motion studies allowing further refinement of the STL design.

TECHNIQUE: Ambient lighting levels were usually reduced during lightwand intubation. With the production of a more intense light source for the stylet, higher ambient light levels are now used without compromising the ability of the intubator to see the transilluminated glow. The stylet of the STL can be introduced into the ET tube and adjusted so that the bulb is just within the distal end of the tube. The clip holds the tube firmly to the battery housing of the STL so that the stylet does not migrate proximally or distally. The ET tube/STL unit may be bent to less than 90 degrees at the level of the proximal attachment of the tube cuff. Following the induction of anaesthesia, the ET tube/STL unit is introduced into the oropharynx. The intensity of the transilluminated glow, likely to be seen through the trachea in ambient light levels, may be easily determined by placing the end of the ET tube/STL unit against the buccal mucosa of the patient's cheek. The ET tube/STL unit is advanced to transilluminate the left pyriform fossa, the tip then manipulated to "hook up" the epiglottis and enter the glottic opening. An easily seen, circumscribed transilluminated glow in the midline at the level of the thyroid prominence indicates laryngeal placement. The trocar of the stylet is pulled back several centimetres and the stylet/STL unit advanced so the glow rests at the level of the sternal notch. The STL is then withdrawn from the ET tube.

FURTHER APPLICATIONS: The sternal notch, consistently demonstrated in previous studies, is half-way between cords and carina[7]. Using the STL device, an accurate placement of the tip of the ET tube can be confirmed by observing the circumscribed glow of light at the sternal notch. The problem of misplaced ET tubes (right mainstem, etc.) has been estimated in intensive care units to approach 12%, and following cardiac arrest in emergency medicine to be as high as 28%.[8]. The STL device would be a significant advantage in emergency medicine, intensive care units, and in the operating rooms. It would allow a simple method to accurately place ET tubes or rapidly detect those that are misplaced.

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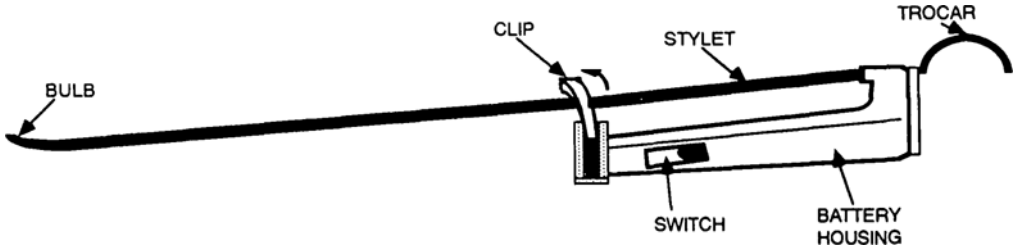
FIGURE: Diagram of the STL lightwand showing design changes.



COAGULOPATHIES IN TRANSURETHRAL PROSTATIC RESECTION: SPINAL VS GENERAL ANAESTHESIA

R SMYTH MSc, MD, D CHENG FRCPC, F CHUNG FRCPC, B ASOKUMAR MD, M GLYNN FRCPC

Western Division, The Toronto Hospital, University of Toronto, 399 Bathurst Street, Toronto, Ontario, M5T 2S8

INTRODUCTION:

Significant postop bleeding frequently occurs following transurethral prostatic resection (TURP). Retrospective studies[1] have attempted to correlate changes in coagulation factors with the development of postop coagulopathies. The effects of spinal vs general (GA) anaesthesia to intraop blood loss remains controversial. This prospective study compares the influence of spinal and GA anaesthesia on periop blood loss and postop bleeding diatheses following TURP.

METHODS:

Following Institutional Ethical Committee approval, patients undergoing TURP were randomly assigned to receive either GA or spinal anaesthesia. Preop, the patients were attached to a continuous EKG monitor for periop rhythm and ST segment analysis. Coagulation parameters (PT,PTT,Bleeding Time,Factor V, Plasminogen, Fibrinogen, FDP, Antithrombin III), hemoglobin (Hb) and platelets (PLT) were measured preop and at 1,6, 24 hours postop. Blood loss was calculated[2] for the intraop and postop periods (1,6,24 hours). For each periop interval, the rate of blood loss (ml/hr) was calculated using spectrophotometric analysis. All results are expressed as mean standard deviation.

RESULTS:

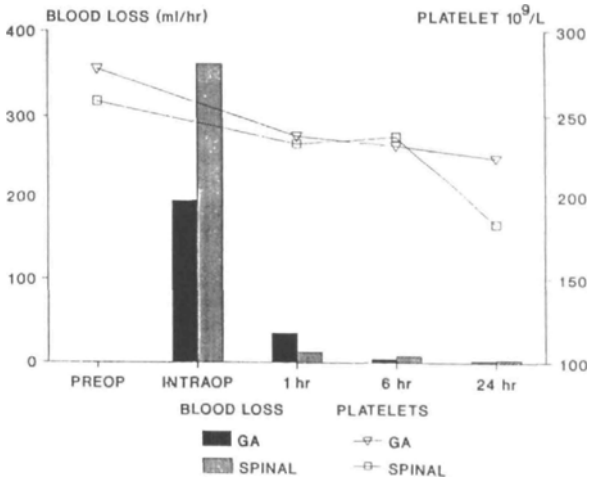
There were no significant differences in age, surgical duration or excised prostatic tissue weight between the two groups (Table 1). In addition, no significant ST segmental changes or arrhythmias were recorded in either group however, 2/7 (28%) of the GA group showed postop bradycardia (< 50/min.).Intraop blood loss was 249.3 ± 109.5 and 367.7 ± 100.2 ml in GA and spinal respectively. The rate of blood loss showed a steady decline in both groups over the postop period. Although not statistically significant, periop blood loss was higher in the spinal group. The platelet count was lower in the spinal group at 24 hours postop (Figure 1). The 24 hour postop PTT was prolonged by 16.8% in the spinal group as compared to 7.2% in the GA group. The postop PT and Bleeding Time did not show any changes. There were no statistical differences in Hb level, volume of fluid administration or serum sodium between the two groups. The resected tissue weight and duration of surgery were significantly correlated ($r > 0.75$) with intraop and 1 hour blood postop blood loss in both groups.

DISCUSSION:

This preliminary data suggests that spinal anaesthesia is associated with higher blood loss in TURP patients. Specific coagulation factors will be analyzed to define the underlying coagulation defects contributing to periop blood loss.

Table 1: DEMOGRAPHIC DATA

	GENERAL (n=7)	SPINAL (n=7)
Age (yr)	74.7 ± 3.3	79.0 ± 8.8
Surgical Duration (min)	56.3 ± 32.3	53.9 ± 21.3
Tissue Weight (gm)	25.1 ± 23.9	25.9 ± 2.7



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Ergonomic Display Methods for Patient Controlled Analgesia

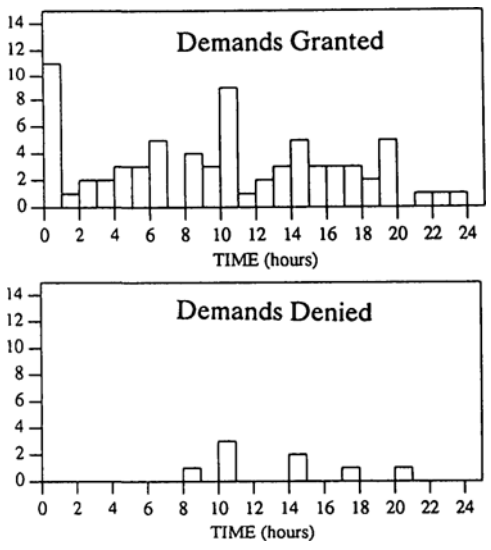
D. John Doyle[1], Sandra Silveira[2], Jeff Clark[2], Paul Milgram[2]
[1]Department of Anaesthesia, Toronto General Division, The Toronto Hospital
[2]Department of Industrial Engineering, University of Toronto

Introduction While Patient Controlled Analgesia (PCA) has become very popular for postoperative pain relief, the means by which PCA data are usually presented to the clinician are primitive. Despite being based on the latest microcomputer technology, PCA pumps have focused on reliability and safety, and not on display ergonomics. Most of the time, the simple sequential display of programming parameters and the time of each delivered dose is all the information needed to assess the suitability of a particular PCA prescription to a suitable patient. However, with some patients a particular set of PCA programming parameters may fail to provide patient satisfaction. For situations such as these, the clinician must review and modify the PCA parameters. Here we discuss some advanced ways of PCA data processing which may help clinicians deal with PCA problems. Specifically, we present some preliminary work on methods of computer-based PCA data analysis:

1. Analgesic Demand Histograms
2. Graphical Event Displays (Event Frequency Diagram)
3. PCA Time Series Analysis

Methods Printouts of PCA event timing provided from an Abbott PCA machine were obtained from five postoperative patients using PCA. This data was then manually reentered onto floppy disk for analysis. [Although automatic transfer of this data is possible, the development effort needed far exceeds the ease of simple manual data transfer.] Graphics software written for Sun Computer Workstations was then used for display the data in a variety of ways.

Results Figure 1 illustrates a histogram of analgesic request frequency over a 24 hour span. Compare the ease of interpretation of the graph to the raw data provided by the PCA machine (Figure 2, showing a portion of a sample printout from the PCA pump). Figure 3 shows a sample graphical "PCA Event Frequency Diagram" generated from this kind of raw data. Such a chart provides a quick overview of all the pertinent events recorded by the PCA pump.




```
--------------------        EVENT LOG:
    PATIENT ID:
                          AM 11:52 PRINTOUT
                          AM 11:34 PAT. DEMAND
--------------------      AM 11:29 PAT. DELIVR   1.5 MG
 DRUG ADMINISTERED:       AM 10:29 PAT. DELIVR   1.5 MG
                          AM 10:24 PRINTOUT
                          AM 10:22 PAT. DEMAND
--------------------      AM 10:19 PAT. DELIVR   1.5 MG
                          AM 09:54 PAT. DEMAND
AM 11:52 NOV 29 91        AM 09:54 PAT. DEMAND
                          AM 09:49 PAT. DELIVR   1.5 MG
MODE: PCA                 AM 09:39 PAT. DELIVR   1.5 MG
                          AM 09:16 PAT. DELIVR   1.5 MG
      SETTINGS:           AM 08:56 PAT. DELIVR   1.5 MG
                          AM 08:28 PAT. DELIVR   1.5 MG
CONC.      2.0 MG/ML      AM 07:58 PAT. DELIVR   1.5 MG
PCA DOSE     1.5 MG       AM 07:28 PAT. DELIVR   1.5 MG
LOCKOUT TIME   6 MIN      AM 07:09 PAT. DELIVR   1.5 MG
4 HR LIMIT   30.0 MG      AM 07:08 PAT. DEMAND
                          AM 07:02 PAT. DELIVR   1.5 MG
      DELIVERED:          AM 06:43 PAT. DELIVR   1.5 MG
                          AM 06:38 PAT. DEMAND
LOADING       0.0 MG      AM 06:36 PAT. DEMAND
G. TOTAL     33.0 MG      AM 06:36 PAT. DEMAND
                          AM 06:35 PAT. DELIVR   1.5 MG
  24 HOURS HISTORY:       AM 06:35 PAT. DEMAND
                          AM 04:42 PAT. DEMAND
PCA INJECTED       22     AM 04:42 PAT. DELIVR   1.5 MG
PCA PARTIAL         0     AM 02:39 PAT. DELIVR   1.5 MG
PCA DEMANDS        10     AM 01:57 PAT. DELIVR   1.5 MG
                          AM 01:50 PAT. DELIVR   1.5 MG
                          NOV 29 91 NEW DATE *
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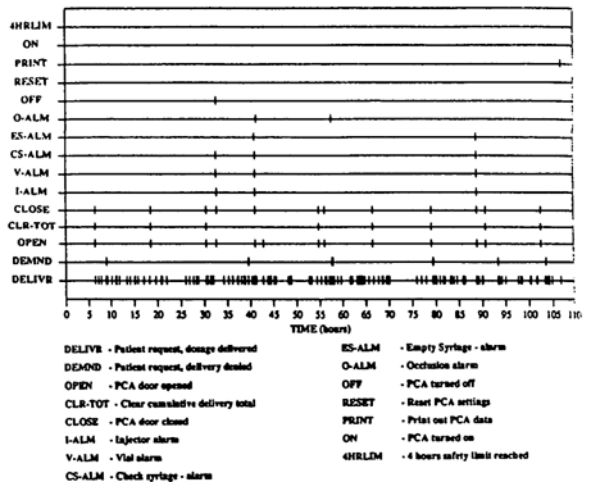

Figure 1 *(bottom left)*. Sample analgesic demand histograms for a 24 hour period) [*top:* analgesic demands granted; *bottom:* analgesic demands denied] Figure 2 *(top right)*. Sample output of "raw data" from the PCA machine. Figure 3 *(bottom right)* An "event frequency diagram" illustrating graphically the timing of all the principal events of interest in studying PCA usage patterns.

P_{50} Effects with Altitude Hypoxemia: Why a Left-Shift is Beneficial

D. John Doyle
Department of Anaesthesia, Toronto General Division, The Toronto Hospital
Institute of Biomedical Engineering, University of Toronto

INTRODUCTION

It is well known that the oxyhemoglobin dissociation curve may shift in response to physiological changes. For example, acidosis, hypercarbia, increased temperature and increased levels of 2,3-DPG all shift the curve to the right, reducing hemoglobin affinity for oxygen and thereby facilitating its release into tissues. Similarly, with chronic anemia, intraerythrocyte 2,3-DPG levels increase, yielding a right-shifted oxyhemoglobin curve [1]. Since such a shift apparently increases oxygen release into tissues, teleologically it would also appear to be an appropriate response to high altitude hypoxemia. In fact, however, the opposite appears to be true. Animals which have successfully adapted to high altitude hypoxemia have left-shifted curves [2,3] as do the Sherpas [4,5]. In this report, we propose a possible explanation for this finding.

ANALYSIS

It is proposed here that the reason that a left-shifted curve is beneficial in high-altitude hypoxemia is that it increases arterial oxygen content by virtue of increasing end-pulmonary capillary oxygen content. To demonstrate this, first suppose that a person has a pulmonary shunt fraction Qs/Qt. Then from the shunt equation [6] we have

$$CaO_2 = CcO_2 - \frac{Qs/Qt}{1-Qs/Qt} \cdot CavO_2$$

so that, at constant pulmonary shunt and arterio-venous oxygen content difference, increases in end-pulmonary capillary oxygen content will increase arterial oxygen content. However, the end-pulmonary capillary oxygen content, CcO_2, consists of two terms, the first being the oxygen bound to hemoglobin and the second being the oxygen dissolved in plasma: $CcO_2 = 1.34\ Hb\ ScO_2 + 0.0031\ PAO_2$. PAO_2 is determined only by the alveolar gas equation [6] and is independent of the oxy-hemoglobin curve position. Thus the dissolved oxygen portion of CcO_2 is also independent of the curve position. However, the ScO_2 term does vary with curve position and increases with a left-shifted curve. Thus CcO_2 also increases with a left shift, and takes on a maximum value of $[CcO_2]_{max} = 1.34\ Hb + 0.0031\ PAO_2$

This analysis demonstrates that a left-shifted curve increases arterial oxygen content by increasing end-pulmonary capillary oxygen content.

Example 1

Consider a patient with high altitude hypoxemia as a result of an alveolar oxygen tension (PAO_2) of 50 mmHg. With a cardiac output of 5 liters/min, hemoglobin concentration (Hb) of 15 g/dl, oxygen consumption (VO_2) of 250 ml/min and shunt fraction (Qs/Qt) of 0.1, it can be shown (see Appendix and Table 1) that CaO_2 goes from 16.41 vol% with a P_{50} of 27 mmHg to 18.44 vol% with a P_{50} of 18 mmHg, a significant increase.

Example 2

Consider a patient with a large pulmonary shunt (Qs/Qt = 0.4), a normal alveolar oxygen tension (PAO_2 = 100 mmHg), and other parameters as in Example 1. Here CaO_2 goes from 16.47 vol% with a P_{50} of 27 mmHg to 16.87 vol% with a P_{50} of 18 mmHg, an insignificant change.

Figure 1 illustrates this concept in more detail, where the two examples are studied for P_{50} values from 10 to 50.

DISCUSSION

These two examples demonstrate that a left-shift to the oxyhemoglobin dissociation curve significantly improves arterial oxygen content in the case of high-altitude hypoxemia but not in the case of large shunts. This observation is consistent with the fact that with right-to-left shunts, such as those in cyanotic heart disease, a rightshifted curve is the general finding [7]. The reason that in this latter case a left-shifted curve is not beneficial, is that only a trivial improvement in end-pulmonary capillary oxygen content (and thus arterial oxygen content) is obtained. Teleologically, it may be argued that in the presence of hypoxemia, at approximately equal arterial contents the body prefers higher oxygen tensions (right-shift preferred), but if arterial oxygen content can be significantly improved, despite a decrease in oxygen tension, a left-shift is preferred.

APPENDIX

The numbers provided in Examples 1 and 2 and in Figure 1 were obtained using a computer model of the oxy-hemoglobin dissociation curve. Hill's equation relating saturation, tension and P50 [8] was used in conjunction with Doyle's equation for arterial oxygen tension [9] and solved using TK! Solver, an equation solving package [10].

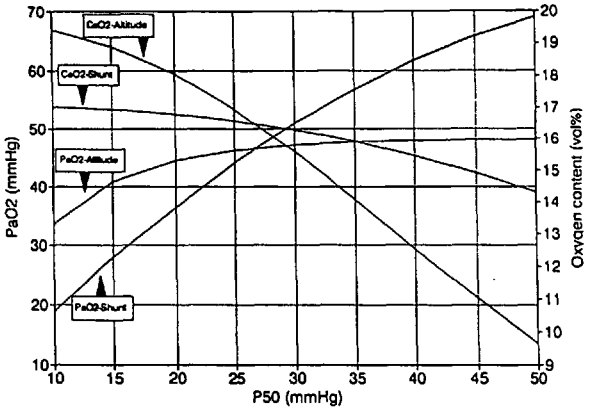

Figure 1 Arterial oxygen tension (PaO2) and arterial oxygen content (CaO2) as a function of P_{50} for the situations depicted in Examples 1 and 2. Notice that in the altitude hypoxemia case a decrease in P_{50} (left-shifted curve) significantly increases oxygen content, but not in the shunt hypoxemia case.

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MIDAZOLAM REDUCES VOMITING AFTER TONSILLECTOMY IN CHILDREN

WM Splinter MD, HB MacNeill MD, EA Ménard MD, EJ Rhine MD, DJ Roberts MD, GM Gould MD, GG Johnson MD.
Department of Anaesthesia, Children's Hospital of Eastern Ontario, Ottawa.

INTRODUCTION

Vomiting after tonsillectomy is a common and significant problem among children.[1] Recently, the administration of lorazepam, diazepam or midazolam has been associated with decreased vomiting among oncology patients.[2] In a perioperative investigation of the effect of benzodiazepines as antiemetics, Khalil et al[3] observed decreased vomiting among adult ophthalmic-surgery patients treated with lorazepam. We hypothesized that midazolam would decrease vomiting after tonsillectomy in children.

METHODS

With parental consent and Hospital Ethics Committee approval we studied 215 healthy children of ages 1.5-14 yr undergoing adenotonsillectomy or tonsillectomy. Subjects were excluded if they had an allergy to a study drug or a non-study anaesthetic was deemed more appropriate. Monitoring included ECG, blood pressure, oximetry, and end-tidal gases. After sedation with N_2O, anaesthesia was induced either by inhalation with halothane or IV with 6 $mg.kg^{-1}$ sodium thiopentone. After induction of anaesthesia, subjects were given 80 $\mu g.kg^{-1}$ vecuronium, 1.5 $\mu g.kg^{-1}$ fentanyl, and a study drug (75 $\mu g.kg^{-1}$ midazolam or placebo in a random, blocked, double-blind fashion). Anaesthesia was maintained with 70% N_2O/30% O_2/0.75-1.5% halothane and titrated to maintain HR and SBP within normal limits. After surgery, patients received: fentanyl (in the PAR), acetaminophen elixir, and/or codeine prn for pain. Also, the patients were given dimenhydrinate prn for vomiting greater than 3 times prior to discharge. Parents were contacted the day after surgery to ascertain the incidence of vomiting after discharge. Data was compared with paired and unpaired t tests, Chi-square analysis or Fisher Exact test, where appropriate.

RESULTS

The groups were very similar with respect to age, weight, gender, mode of induction and length of anaesthesia and surgical procedure. The 108 midazolam-treated children had a lower incidence (42% vs 57%) of vomiting when compared to the placebo group, $P<0.02$. The groups were similar with respect to narcotic administration and length of stay in the recovery room and the Day Care Surgical Unit. However, the placebo group had a higher incidence (9% vs 2%) of unscheduled admissions due to nausea and vomiting, $P<0.05$.

DISCUSSION

Midazolam administered intravenously to children during surgery significantly reduces vomiting after tonsil surgery. The mechanism of action of midazolam needs to be determined.

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CSF OR LOCAL ANAESTHETIC: WHICH IDENTIFICATION TEST IS MOST RECOGNIZABLE?

Michael J. Tessler MD FRCPC; Daniel Quance MD FRCPC; Saul Wiesel MD FRCPC

Department of Anaesthesia, Sir Mortimer B. Davis - Jewish General Hospital and McGill University, Montreal.

INTRODUCTION : Local anaesthetic (LA) is commonly used to enlarge the epidural space in preparation for passage of a catheter. The subsequent aspiration of fluid from the newly placed epidural catheter may represent either the LA that has been used or cerebrospinal fluid (CSF). Four methods of differentiating CSF from LA have been described and each is based on a different physicochemical property. These are 1) temperature, 2) glucose concentration, 3) pH and 4) formation of a precipitate when mixed with thiopental. This study compares the reliability of each method to distinguish between the two fluids for a small volume of aspirate.

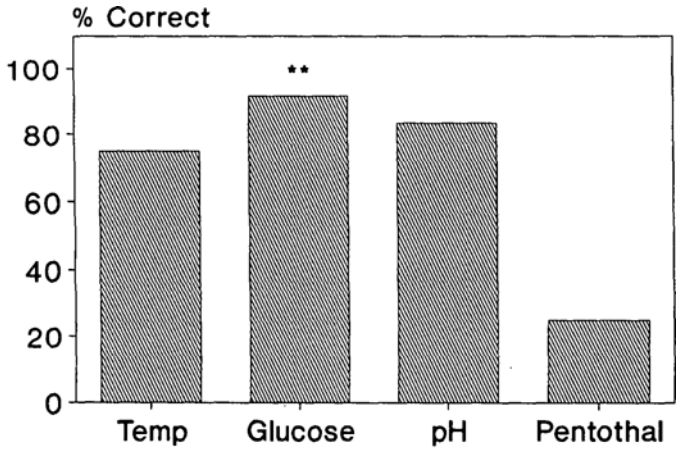
METHODS : Twelve attending anaesthesiologists who frequently perform regional anaesthesia at this institution participated in this study. All had received their anaesthesia training in either Canada or the United States and had been in practice from 3-30 years. Each of the 12 participating anaesthesiologists was shown the results of the four physicochemical tests performed with blinded samples of freshly prepared mock CSF and LA and asked to identify each. The tests were performed in an identical manner as follows: Temperature: Two 0.1 ml samples of mock CSF, the first one warmed to 37°C and the second at room temperature, were dropped onto the volar aspect of the forearm. Each subject was then asked to identify, based on temperature, the identity of each sample. Glucose Concentration: 0.1 ml of mock CSF (glucose content 50 mg/100 mL) and 0.1 ml of non-dextrose containing LA were tested on Rapignost total-screen urine test strips (Behring). Each subject was shown these two strips and asked to identify which strip represented mock CSF. pH: samples of the two solutions (CSF pH 7.4 and LA pH 5.4) were tested for hydrogen ion concentration using the Rapignost system as outlined above. Precipitation with Thiopental: 0.1 ml samples of mock CSF and LA (bupivacaine 0.25%)were mixed with an equal volume of thiopental on a glass slide and assessed for turbidity. Each subject was asked to identify the CSF based on the results seen.

Statistical analysis used Chi square with $p<0.05$ considered significant.

RESULTS : None of the methods used to verify LA led to consistently correct identification of CSF and LA. However, the method using glucose as the marker for CSF was the single most recognized, while the one using precipitation with pentothal was the least (Figure; $p< 0.05$).

CONCLUSIONS : The anaesthesiologist should familiarize himself with the results of the physicochemical tests to help differentiate CSF from LA before these situations are encountered clinically. This study suggests that no single test result is completely reliable in distinguishing between CSF and LA. However, testing for glucose in the aspirated fluid appears to be the single most recognizable method.

Figure



**p<0.05 compared to pentothal

POSTDURAL PUNCTURE HEADACHE: 27 GAUGE QUINCKE VERSUS 24 GAUGE SPROTTE IN YOUNG PATIENTS

Saul Wiesel MD FRCPC; Jane Easdown MD FRCPC; Michael Tessler MD FRCPC
Departments of Anaesthesia, Sir Mortimer B. Davis - Jewish General Hospital
and McGill University, Montreal, Canada.

INTRODUCTION: The postdural puncture headache (PDPH) may complicate recovery after spinal anaesthesia. A PDPH may lead to patient distress, prolong hospitalization and may necessitate the use of an epidural blood patch.

A recent study originating in this institution using the 27 gauge Quincke needle in an unselected group of patients found an incidence of PDPH of 10.3% overall which increased to 19.6% in a subset of patients less than 40 years of age[1] (Cote et al, 1991). Others have found a PDPH rate of 2.5% in outpatients under the age of 40 years[2].

Two series using the 24 gauge Sprotte needle have found no PDPHs in their patients having Caesarian section[3,4].

The purpose of this study is to examine the use of these two needles, the 27 gauge Quincke needle and the 24 gauge Sprotte needle in a population of young patients at increased risk for PDPH. This study is designed to answer the following questions: 1. Is there a difference in the incidence and severity of PDPHs? 2. Is the Sprotte needle more difficult to use than the Quincke needle?

METHODS: Institutional approval and written, informed consent were obtained from patients less than 45 years of age scheduled to have surgery where spinal anaesthesia was appropriate. Obstetrical patients were excluded. Patients were randomized to receive spinal anaesthesia with either the 27 gauge Quincke (BD) or the 24 gauge Sprotte (Pajunk). Clinical decisions concerning type and baricity of the local anaesthetic used, the addition of epinephrine or narcotics, and position of the patient for induction of the block were left to the attending anaesthetist. The Quincke needle was inserted with the bevel parallel in order to minimize the incidence of PDPH. The ease of use of the needle was described by the anaesthetist as "easy, mildly difficult or difficult". Patients were followed up by an observer blinded to the type of needle used for three postoperative days. The criteria of Driessen were used to identify a patient with a PDPH. Severity of a PDPH was judged by the patient as either "mild, moderate or severe". Furthermore, patients were asked the following two questions on the third postoperative day: 1. Were you satisfied with the conduct of the anaesthetic? 2. Would you accept the same anaesthetic for a similar operation in the future?

STATISTICAL ANALYSIS: Chi squared analysis and Student's t-test for nonparametric data and parametric data, respectively. A level of $p<0.05$ was considered statistically significant.

RESULTS: Preliminary results are presented: The Sprotte needle was used in 29 patients and the Quincke in 28. Group demographics are presented in the table. There were no differences in terms of patient sex, elective nature of surgery or ASA status. Patients receiving the Sprotte were approximately four years younger, but this did not reach statistical significance (p=0.076). There were no differences in the position used during induction of spinal anaesthesia or in the type or baricity of local anaesthetic used. More patients in the Sprotte group received spinal narcotics, however (55.2% vs 28.6%, p=0.043). Use of the Sprotte was rated as "easy" in 82.8% of cases, compared to 96.4% of cases using the Quincke (p=0.093).

Two patients in the Sprotte group (6.9%) and four patients in the Quincke group (14.3%) had PDPHs (p=.36). Both of the PDPHs in the Sprotte group were judged by the patients to be mild, while three of four headaches in the Quincke group were moderate or severe (p=0.084). All six patients with PDPHs were satisfied with their anaesthetic and would accept the same anaesthetic for a similar procedure. By comparison, of the 51 patients who did not experience a PDPH, 92.2% were satisfied and 88.2% would want the same anaesthetic in the future (p=0.47 and 0.33, respectively).

CONCLUSIONS: There appears to be a trend towards lower PDPH rates and milder headaches with the use of the Sprotte needle in young patients. The definitive result requires completion of this study.

1. CJA 1991;38:A32.
2. Anesthesiology 1990;73:A22.
3. Anaesthesia 1990;45:656-8.
4. Anesthesiology 1990;73:A1003.

Table1

	Sprotte (n=29)	Quincke (n=28)
Age	31.8 +/- 7.5	35.5 +/- 8.3
Sex	16 male, 13 female	15 male, 13 female
Elective surgery (%)	86.2	92.9
ASA 1 (%)	93.1	89.3
Single attempt (%)	69	67.9
Use "EASY" (%)	82.8	96.4
Sitting (%)	96.6	92.9
Lidocaine (%)	82.8	71.4
Bupivacaine (%)	17.2	28.6
Hyperbaric (%)	93.1	85.7
Narcotic (%)	55.2**	28.6**
PDPH (%)	6.9	14.3

**0.05

AXILLOFEMORAL AND AXILLOBIFEMORAL BYPASS: FACTORS PREDICTING A HIGH MORTALITY RATE

Saul Wiesel MD; N. Tien Truong MD; Normand Miller MD; Nathan Sheiner MD
Departments of Anaesthesia and Surgery, Sir Mortimer B. Davis - Jewish General Hospital and McGill University, Montreal, Canada.

INTRODUCTION: Axillofemoral (AxF) and axillo-bifemoral (AxBF) bypass procedures are extra-anatomical, vascular bypasses performed to restore blood flow to the leg(s). They are indicated for the patient who is considered at an unacceptably high risk to tolerate aortobifemoral bypass. Other indications include revascularization of the lower extremities after removal of an infected AAA or ABF graft. The patient presenting for AxF or AxBF is a challenge for the anaesthesiologist, because associated with peripheral vascular disease is coronary artery disease, cerebrovascular disease, chronic obstructive pulmonary disease and diabetes. Furthermore, the operative site extends from the clavicle to the groins and surgery may require distal vascular runoff procedures, both of which make regional anaesthesia difficult.

In order to characterize this population of patients and identify risk factors for mortality, we retrospectively reviewed our anaesthetic and surgical experience with patients having AxF and AxBF.

METHODS: Institutional approval was obtained. Hospital charts were reviewed for patients having either an AxF or AxBF in the previous 15 years. Charts were examined for preoperative medical and surgical factors, intraoperative and postoperative events. Univariant analysis was performed with Chi square analysis, with $p<0.05$ considered significant.

RESULTS: The charts of 37 patients were obtained (25 male, 12 female) with an in-hospital mortality of 19% (7/37). The mean age of patients was 71.9 +/- 9.7 years (range 49-85 years). Eight patients were ASA status 1 or 2, 27 ASA 3 and 2 ASA 4 patients. All patients were operated under general anaesthesia. In terms of cardiac history, 43% had a history of MI, 35% had CHF and 29% had angina. The mean duration of surgery was 134 min (range 50-320). The mean duration of hospital stay was 23.4 days (range 7-159). Intraoperative and postoperative complications are presented in the figures.

Preoperative medical factors associated with in-hospital mortality (Table 1)included a history of angina or renal insufficiency and chronic use of lasix, nitroglycerin or anticoagulants; on the resting preoperative ECG, LVH and nonspecific ischemic changes were associated with mortality, while Q-wave infarction was not. Only intra-operative ischemia was associated with postoperative mortality, while transient hemodynamic abberations were not.

DISCUSSION: This study has identified various markers as associated with mortality in the high risk patient presenting for AxF and AxBF.

Figure 1
INTRAOPERATIVE COMPLICATIONS

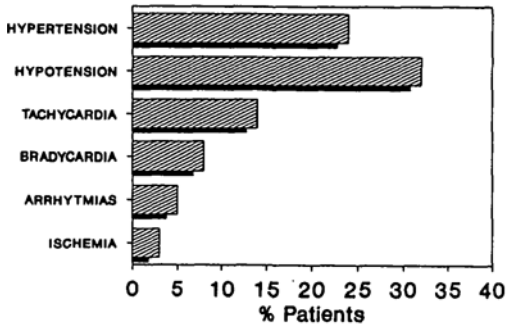


Figure 2
POSTOPERATIVE COMPLICATIONS

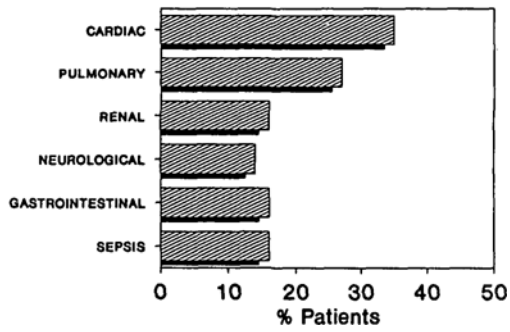


TABLE 1
PREDICTORS OF POSTOPERATIVE MORTALITY

PREOPERATIVE FACTORS			
Age >70	0.082	LVH on ECG	0.017**
Angina	0.005**	Nonsinus rhythm	0.066
History MI	0.405	Q wave MI	0.828
History CHF	0.405	NS-ischemic	0.014**
Hypertension	0.104	BUN elevated	0.002**
Diabetes	0.574	Anemia	0.053
Obesity	0.053		
ASA 3 and 4	0.160	INTRAOPERATIVE FACTORS	
Emergency	0.066	Hypertension	0.574
Infected AAA/ABF	0.034**	Hypotension	0.316
Lasix	0.009**	Tachycardia	0.807
Nitroglycerin	0.014**	Bradycardia	0.427
Beta Blockers	0.748	Ischemia	0.022**
Coumadin/ASA	0.039**	Arrythmia	0.163
		Transfusion	0.066

**Chi square, p<0.05

APPLE JUICE INGESTION TWO HOURS BEFORE SURGERY DOES NOT INCREASE BLOOD GLUCOSE CONCENTRATIONS IN PEDIATRIC PATIENTS

L. Welborn, M.D., J. Norden, MSN, R. Hannallah, M.D., L. Broadman, M.D., N. Seiden, M.D.
Children's National Medical Center and George Washington University, Washington, D.C. 20010

INTRODUCTION:

Although all anesthesiologists concur that a preoperative fast is a prerequisite for elective procedures, few agree on the duration of fasting, and whether a glucose containing infusion should be administered intraoperatively to prevent hypoglycemia. The purpose of this study was to: (1) compare blood glucose (BG) concentrations in two groups of patients, Group A: followed routine fasting guidelines, Group B: those whose fasting is modified by the ingestion of apple juice 2-3 hours prior to the induction of anesthesia, (2) determine the safety of a modified preoperative fasting policy.

METHODS:

Healthy, unpremedicated children, ages 1-10 years, scheduled for elective outpatient surgery were studied. Informed consent and institutional approval for the study were obtained. All patients had BG determinations preoperatively on admission, during induction of anesthesia, and at conclusion of surgery using Glucometer II which in previous studies has shown good correlation with the laboratory glucose-oxidase method. All patients did not ingest solids after midnight. On the day of surgery, they were randomly assigned to one of two groups. Group A: children were encouraged to drink clear liquids up to 6 h prior to surgery, and Group B: ingested up to 10 cc/kg of apple juice 2-3 hours prior to the induction of anesthesia. Following induction of anesthesia, gastric contents were aspirated and volume and pH were recorded. All patients received Lactated Ringer's solution intraoperatively, unless hypoglycemia (BG < 50 mg/dL) was identified, in which case D2.5LR was administered.

RESULTS:

See Tables 1 and 2

DISCUSSION:

This study confirms the findings in recent clinical studies, that gastric fluid pH and volume are independent of the duration of the fluid fast beyond two hours, provided that only clear liquids are consumed. Although clear liquids ingested 2-3 hours prior to induction of anesthesia provided a decrease in irritability of children and improved hydration, both groups of patients showed a similar incidence of a decrease or no change in BG concentrations perioperatively. This shows that a drink of apple juice 2-3 hours prior to surgery does not modify perioperative glucose homeostasis in children.

Table 1: Age distribution, duration of fasting, BG concentrations and gastric fluid volume and pH in Groups A and B

	Age (m)	NPO duration (h)	Preop.BG (mg/dL)	Ind.BG (mg/dL)	Postop.BG (mg/dL)	Gastric fluid Vol(ml)	pH
Group A (n=113)							
mean	49.3	13.1	79.7	79.7	110.9	1.43	1.38
± SD	26.4	3.0	14.0	16.8	30.5	2.87	0.2
Group B (n=87)							
mean	44.3	2.93	78.2	81.6	111.2	1.28	1.48
± SD	23.0	0.71	14.5	17.2	24.7	2.82	0.1

Table 2: Incidence of perioperative decrease or no change in Blood Glucose concentration in Groups A and B

	Age (m)	NPO Duration (h)	Preop. BG (mg/dL)	Ind. BG (mg/dL)	Postop. BG (mg/dL)
Group A (n=59)					
mean	48.9	13.2	83.5	73.1	105.7
range	15-127	4.3-18.3	58-113	41-101	59-181
Group B (n=37)					
mean	44.2	2.93	84.3	72.2	104.9
range	13-109	1.83-4.17	62-126	51-92	67-156

HALOTHANE ANAESTHESIA SLIGHTLY PROLONGS SINUS NODE RECOVERY TIME IN CHILDREN .

M. Iwai,M.D., R.Iwai,M.D., H.Horigome,M.D., M.Yamashita,M.D.
Department of Anaesthesiology and Paediatrics ,
Ibaraki Children's Hospital, Mito, 311-41, Japan

INTRODUCTION:
Negative chronotropic action of halothane is well documented in children. And in vitro study[1] also has documented depression of sinus node function by halothane. However, effects of halothane on sinus node recovery time in children are not fully elucidated.
The present study was carried out to evaluate the influence of halothane on the sinus node recovery time in children.

METHODS:
Nine paediatric patients with congenital heart diseases <ASD (5), VSD(2), PS(1), PDA(1)> scheduled for cardiac catheterization were the subjects of the study. The institutional approval and informed consent from the parents were obtained. The patients were premedicated with diazepam 0.5mg/kg P.O. one hour prior to catheterization. The catheterizations were performed under local anaesthesia and intravenous sedation with pentazocine (1mg/kg) and midazolam (0.15-0.4mg/kg). No parasympatholytic agents were administered before or during the study period. After the scheduled diagnostic catheterization procedures , intracardiac pacing electrode was inserted via the catheter introducer being placed in the femoral vein. The tip of the electrode was placed at the right atrial-superior vena caval junction. After the basic heart rate recording, the sinus node was stimulated at the rate of 120,150, or 180 beats per minute for 30 sec twice for each rate. Same procedures were repeated under mask halothane-O_2 inhalation (age-adjusted end-tidal 1 MAC). The sinus node recovery time (SNRT) was obtained from the strip chart of EKG (chart speed of 100mm/ sec.) . The mean of the two measurements obtained from the stimulation rate that resulted in the longest SNRT . SNRT (in msec) was measured from the last pacing artifact to the onset of the first spontaneously occurring P wave of sinus origin . SNRT , expressed as a percentage of the basic PP interval[2] , and corrected SNRT (SNRT - basic PP interval) were also calculated . Student's paired t-test was used for statistical analysis and $p<0.05$ was considered to be significant.

RESULTS:
Age and weight of the patients were 8.1 ±2.8 yrs (M±SD), ranging 5-12 yrs , and 33.2 ± 16.1kg(M±SD), ranging 19-57kg, respectively . Mean control basic PP interval was 632±82 msec(M±SD). SNRT(%) in the control period and during halothane anaesthesia were 134±15 % and 143±14 % , respectively($P>0.05$, Paired t-test). Corrected SNRTs in the control period and during halothane anaesthesia were 214±91 msec and 283±76 msec (M ±SD), respectively ($P<0.05$, Paired t-test).

DISCUSSION:
The results showed the slight depressive effects of halothane on sinus node recovery time in children. Although the control corrected SNRTs in this study were obtained after pentazocine / midazolam sedation, these values were within normal range (normal value < 275 msec [2]). Our subjects ranged from 5 to 12 years , but when expressed as a percentage of the resting PP interval , it is documented that there are no significant differences in SNRT between children of the various age groups [3].
In conclusion, sinus node recovery time is slightly prolonged by halothane anaesthesia in children.

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COMPLICATIONS OF EPIDURAL ANALGESIA FOR PAIN RELIEF IN CHILDREN

Catherine E. Wood, MB ChB FCAnaes, Gerald V. Goresky, FRCPC, Kim Klassen, ORT
Department of Anaesthesia, Alberta Children's Hospital at the University of Calgary, 1820 Richmond Road, SE, Calgary, Alberta T2T 5C7

INTRODUCTION: Continuous epidural analgesia is now being used in a number of centres for the management of post-operative pain. In July 1990, we initiated a postoperative pain service incorporating the use of epidural analgesia. We report the incidences of complications arising from the use of continuous epidural infusions in a paediatric population.

METHOD: From the initiation of the postoperative pain service, a database was established. For each epidural administered a record has been kept of patients' age and weight, the duration of the epidural infusion and any problems encountered. Using this database, we have identified the occurrence and frequency of complications. The records of all children who had received continuous epidural infusions over a 15 month period were examined retrospectively.

RESULTS: 169 records were examined. The mean age of the children was 70 months (Range 1-222 months) and the mean weight was 22 kilograms (Range 4-88 kilograms). The mean duration of the epidural infusions was 4.5 days (Range 1-15 days).
All except one of the epidurals had been sited in the operating theatre, under general anaesthesia, immediately prior to the start of urological, orthopaedic or general surgery. The intra-operative use of the epidural varied between patients and was not recorded. The epidural infusion was started in the recovery room. The initial infusion regime for most patients was 0.1% bupivacaine with 1:500,000 adrenaline and 1 mcg/ml fentanyl at a rate of 0.5 ml/kg/hr. Children who had epidural infusions in progress had been nursed on designated wards. They had been seen regularly by members of the pain management team who had noted any problems and treated them appropriately. One epidural had been used as part of the management of a patient with reflex sympathetic dystrophy.
171 complications were recorded in 115 out of the 169 patients (68%). Complications led to the early discontinuation of the epidural infusion for 24 patients (14% of catheters). Additionally, 12 epidurals were removed early for other reasons eg. inadequate analgesia, unrelated medical problems, parental request.
Table 1. shows the frequencies of the different complications and whether they necessitated a change to an alternative form of analgesia.

DISCUSSION: Although 68% of the patients with epidurals experienced at least one complication, many of these were comparatively minor and easily managed. The commonest reasons for switching to a different form of analgesia involved technical problems with the epidural catheter eg. leakage around the catheter site or catheter occlusion. We are now using end hole catheters instead of multiple side hole catheters to try to reduce the frequency of leakage around the catheter site. Complications that could be considered serious occurred in 3 children (1 seizure, 1 case respiratory depression, 1 significant insertion site infection).
Our incidence of nausea and vomiting is comparable to that of previous series in children receiving epidural local anaesthetics and/or morphine (22-31%)(1,2).
Our incidence of pruritis is much lower than reported previously (87-89%). This may reflect our use of fentanyl which causes less histamine release than morphine. Many of the patients in our series had undergone urological surgery, and had suprapubic catheters in situ. Our reported incidence of urinary retention is probably therefore lower than the true value.
Epidural analgesia now has an established role in adult practice. It has also been shown to provide good post operative analgesia in children with a minimum of haemodynamic complications(1-5).
Continuous epidural analgesia can be used successfully in children of all ages and in a variety of surgical and medical situations. The initiation of a postoperative pain service using epidural analgesia should take into account the frequencies of complications that we have identified and the ability to monitor the occurrence of these complications.

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Table 1. Complications including those requiring change from epidural analgesia

	N	%	Epidural Stopped
Total Epidurals	169		
Nausea+Vomiting	37	21.8	0
Local Redness	27	15.9	2
Motor Block	26	15.3	1
Leak at Catheter	21	12.4	13
Urinary Retention	12	7.1	0
Catheter Occlusion	11	6.5	3
Oversedation	11	6.5	1
Pruritis	8	4.7	0
Jitteriness	5	2.9	1
Tachyphylaxis	4	2.4	1
Skin Lesions	2	1.2	0
Local Infection	1	0.6	1
Seizure	1	0.6	1
Resp Depression	1	0.6	1
Pump Failure	1	0.6	0
Dural Tap	1	0.6	0
Horner's Syndrome	1	0.6	0
Patient Anxiety	1	0.6	0

INDUCTION AND EMERGENCE CHARACTERISTICS OF AND HEMODYNAMIC RESPONSES TO SEVOFLURANE IN CHILDREN

S. Kleinman MD, J. Lerman MD, FRCPC, S.Yentis MB FCAnaes, N.Sikich RN
Department of Anaesthesia and Research Institute, Hospital for Sick Children, U. of T., Toronto, Ontario

INTRODUCTION: Sevoflurane is a potent new inhalational ether anaesthetic under investigation. It has physicochemical characteristics that would lead one to predict that it may have a role as an induction agent in children. Therefore, we evaluated sevoflurane for induction of anaesthesia in paediatric patients.

METHODS: With institutional approval and parental consent, 39 unpremedicated and fasted ASA PS I or II children scheduled for elective surgery were enrolled. The children were assigned to one of three groups according to age: (1-3 yr n=13, 3-5 yr n=12 and 5-12 yr n=14). Patients were anaesthetized with increasing inspired concentrations of sevoflurane (up to a maximum of 7% in 1.5% increments) in air/oxygen. The times from application of the face mask to loss of the eyelash reflex, and to intubation were recorded. The incidence of breathholding, coughing, laryngospasm, excitement and an arterial oxygen saturation (SaO_2) <90% during induction were noted. Heart rate and systolic arterial pressure were recorded pre-induction, and at ≈1MAC(steady-state) both before and after skin incision. Following conclusion of surgery, anaesthesia was discontinued from ≈1 MAC sevoflurane plus nitrous oxide/oxygen. Times to extubation, eye opening, first response to commands, and post-anaesthesia recovery room discharge(PAR) were recorded. Data were analyzed using one-way and repeated measures ANOVA and the Newman-Keuls test. $P<0.05$ was accepted.

RESULTS: During induction of anaesthesia, breathholding occurred in 3% of children, coughing in 9%, and mild excitement in 21%. There were no episodes of laryngospasm or SaO_2 <90%. The time to loss of the eyelash reflex (mean ± sd) was 1.2 ±0.2 minutes and to intubation, 4.2 ± 1.5 minutes. Heart rate increased after skin incision in the 3-5 and 5-12 yr groups compared to their baseline values (figure 1). Systolic pressure decreased at ≈1 MAC before incision in the 3-5 and 5-12 yr groups but did not change in the 1-3 yr group (figure 2). Emergence data is presented in Table 1. There were no significant differences among the three groups for time to extubation, eye opening, and response to commands. There was a statistically significant difference between the 1-3yr and 5-12yr groups for time to PAR discharge($p<0.05$).

TABLE 1 EMERGENCE DATA (minutes)†

AGE(yrs)	EXTUBATION	EYE OPENING	RESPONSE TO COMMANDS	PAR D/C
1 TO 3	6.01±1.34	10.31±3.50	15.95±4.52	44.34±10.27
3 TO 5	7.14±1.87	11.62±4.84	16.38±5.96	49.44±13.14
5 TO12	7.16±1.26	11.61±3.26	15.51±4.73	*67.04±10.93

† Data expressed as mean±sd *(p<0.05)

FIGURE 1

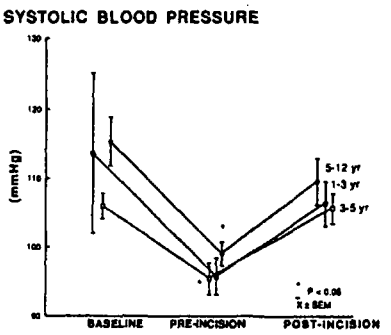
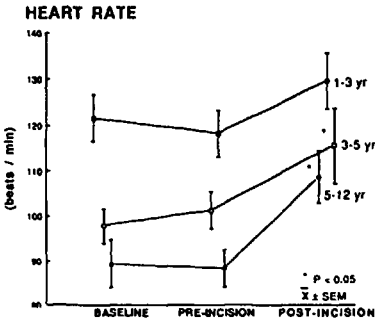


FIGURE 2



DISCUSSION: Induction of and emergence from anaesthesia with sevoflurane are smooth and rapid. Unlike isoflurane[1] and desflurane,[2] sevoflurane is devoid of irritant effects on the airway, accounting for the low incidence of adverse events during induction. Furthermore, hemodynamic responses are maintained at ≈1 MAC sevoflurane in oxygen. The speedy emergence, characteristic of sevoflurane, can be predicted by its low blood solubility(blood/gas partition coefficient of ≈0.6). We conclude that sevoflurane is an effective, smooth and rapid induction agent in children.

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ACKNOWLEDGEMENTS: Supported in part, by a grant from Maruishi Pharmaceutical Inc, Japan.

BEHAVIORAL ANALYSIS OF CHILDREN DURING HALOTHANE ANESTHETIC INDUCTIONS WITH AND WITHOUT PARENTAL PRESENCE. DOES THE PRESENCE OF A PARENT MAKE A DIFFERENCE?

T.A. Yemen M.D., B. Mascik M.D., W. Nelson M.D. Department of Anesthesia, University of Virginia Health Sciences Center, Charlottesville Virginia, 22908, and the Department of Child Psychology, Boston Children's Hospital, 300 Longwood Avenue, Boston, Ma., 02115

INTRODUCTION

The use of parental presence during pediatric inductions remains controversial in anesthetic practices across North America. Earlier studies have suggested that the presence of parents helps calm the child and allows for a pleasant induction.[1,2] More recently Bevan et al. suggested that preoperative assessment of parental anxiety was useful in predicting the value of a parent to their child during induction.[3]

We proposed to re-examine the value of parental presence during pediatric induction in a day surgery setting.

DESIGN

With the approval of the Committee for Human Studies and patient consent, 62 children, ASA I or II, undergoing anesthesia for day surgical procedures were studied prospectively. Children were randomly assigned on a day basis to one of two groups; parent present or parent absent. Additionally two study groups were designated; preschool, children 4 and 5 years old, and school age, children 6 to 10 years of age. None of the children had received a prior anesthetic. No child received premedication. All children were induced in a operating room. All anesthetic inductions were by one anesthesiologist. All children were induced using halothane. Parents present in the operating room were dressed in surgical gowns, hats, and masks. All children were video taped prior to induction and during induction, using a 8mm portable video camera. Filming was stopped once children were unresponsive to command and their eyelids closed. Video tapes of the inductions were then reviewed by the Child Psychology department. A modified behavioral scoring system using seven markers of anxiety was used to assess the child's response to the induction. Scoring of the video tapes was by two observers for each study patient. All children were interviewed prior to discharge and asked whether they would choose parental present or parental absent for a future anesthetic.

RESULTS

Six children were dropped from further study due to problems in videotaping. The preschool group contained 24 children, the school age group contained 32 children. There were no significant differences between the four groups regarding sex or type of surgery. Inter-observer agreement in scoring of the video tapes was in excess of 95%. Two way variable chi-square analysis of the behavioral scoring revealed that children without their parents scored significantly better ($p \leq 0.05$) in both the pre-school and school age groups. 55 of the 56 children interviewed postoperatively stated that they preferred to have to parents present at induction for a future anesthetic.

DISCUSSION

Minimizing the anxiety of children during anesthetic inductions has always been a laudable goal. The presence of parents at induction has become common method for some institutes in an effort to provide a more pleasant experience for the child. Its' use is also in response to increasing demands by parents to be involved in the medical care and decision making for their children. Our initial experience with parental presence seemed favorable but it was unclear whether or not all children benefit from the presence of their parents. Our random prospective study suggests two conclusions. First, that children, as a whole, do not demonstrate less anxiety or fear during a halothane induction with a parent present. Secondly, the preference of the child bears no relationship to his or her behavior at induction. It is possible that children feel at ease to express their anxieties when their parents are present, and not in their absence. Whether expression of this anxiety helps or hinders the child's emotional development remains unstudied.

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PLASMA INORGANIC FLUORIDE ION CONCENTRATION IN CHILDREN ANAESTHETIZED WITH SEVOFLURANE

J. Lerman MD, FRCPC, S. Kleinman MD, S. Yentis MB FCAnaes, N. Sikich RN, H. Ghantous* PhD, J.Gandolfi* PhD
Dept. of Anaesthesia and Research Institute, The Hospital for Sick Children, Toronto, Ontario, and U. of Arizona, Tucson*

INTRODUCTION: Sevoflurane, a fluorinated methyl isopropyl ether, is a new inhalational anaesthetic undergoing investigation in children. Like its predecessors, sevoflurane is metabolized by microsomal defluorination via cytochrome P450IIE1 isozyme[1]. One of the important products of defluorination is inorganic fluoride [F^-] which has been implicated in renal toxicity after methoxyflurane anaesthesia. To investigate the serum profile of inorganic [F^-] after sevoflurane, the following study was undertaken in healthy children.

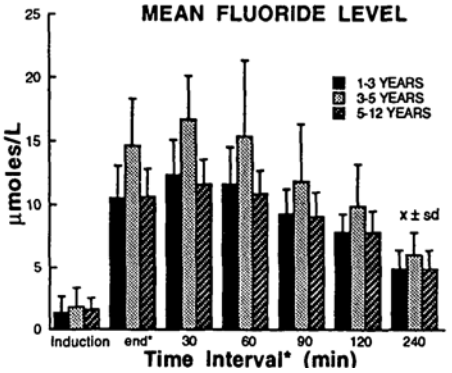
METHODS: After obtaining institutional approval and parental consent, 39 ASA I and II children [1-3yrs n=13, 3-5yrs n=12, and 5-12yrs n=14] with normal kidney and liver function were studied. None of the children had received drugs known to induce hepatic microsomal enzymes in the preceding year. All children were anaesthetized with sevoflurane in air/oxygen and maintained with sevoflurane in nitrous oxide (70%) and oxygen. Plasma was obtained via an indwelling IV cannula at induction, termination of the anaesthetic, and at 30, 60 90, 120, and 240 minutes after conclusion of anesthesia. Liver function tests, blood urea nitrogen (BUN), and creatinine levels were measured at induction and one hour postoperatively. Plasma [F^-] levels were determined using an Orion Ionanalyzer fitted with a fluoride specific electrode. Area under the fluoride concentration-time profile was determined using a three dimensional reconstruction technique (EM Lab, U of Colorado) with an inter-graph variation of <1%.

RESULTS: Mean values for duration of anaesthesia, MAC-hours, and peak plasma fluoride levels for the three groups are presented in Table 1. Mean peak [F^-] levels occurred at thirty minutes in all groups. No significant differences between age groups existed for duration of anaesthesia and MAC-hours. There was a significantly greater peak fluoride level in the 3-5 year old age group compared to the 1-3 and 5-12 year groups($p<0.05$), as well as a significantly larger area under the fluoride concentration-time profile for the same group ($p<0.05$).

TABLE 1

AGE (yrs)	SEVO EXPOSURE (min)	MAC HOURS	PEAK PLASMA [F-] (μM)
1 to 3	45.78 ± 10.59	0.79 ± 0.20	12.27 ± 2.75
3 to 5	55.40 ± 38.80	1.12 ± 0.72	16.65 ± 3.42
5 to12	42.50 ± 8.73	0.72 ± 0.19	11.66 ± 1.91

Data are means ± sd



DISCUSSION: In vivo sevoflurane metabolism in children yields peak plasma fluoride concentrations 30 minutes after anaesthesia that are similar to those found with enflurane anaesthesia[2]. These concentrations are below the levels previously reported for methoxyflurane in children.[3] The exposure of the kidney to inorganic fluoride may be better represented by the area under the [F^-]-time profile than by the peak fluoride concentration. The areas determined for sevoflurane are less than 10% of those reported previously with methoxyflurane for anaesthetics of similar duration in children. There was a tendency toward correlation between the areas under the fluoride concentration-time curve and MAC•h, which may become more apparent with anaesthetics greater than one hour. We conclude that plasma [F^-] levels in paediatric patients exposed to ≤1.12 MAC•h sevoflurane, does not pose a threat to renal function.

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THE EFFECT OF DONOR INOTROPE EXPOSURE ON GRAFT FUNCTION FOLLOWING LIVER TRANSPLANTATION

Gordon Wood MD, Mohamed Ali MD, Kevin Inman M.Sc.

Department of Critical Care Medicine, University Hospital, London, Ontario, N6A 5A5.

INTRODUCTION: Organ function following transplantation is influenced by the management of the brain dead organ donor prior to harvest (1). Hypotension in the organ donor (systolic blood pressure below 90 mmHg) is associated with subsequent impaired kidney allograft function (2,3). Initially fluids are used to maintain an adequate blood pressure in the donor. However this measure alone may not be sufficient and inotropes are frequently required. Because studies have demonstrated that high doses of inotropes increase the risk of postoperative acute tubular necrosis and reduced kidney allograft survival (4,5), donor organs exposed to high doses of inotropes are sometimes considered unsuitable for transplantation. The purpose of this study was to determine if donor inotrope exposure had a similar detrimental effect on transplanted liver function.

METHODS: A retrospective review was conducted on 50 consecutive liver transplants done at the University Hospital in London, Ontario between 1986 and 1991. To minimize the effect of cold ischemia time and to standardize donor management, only those patients who received livers from donors managed by the Department of Critical Care Medicine at the University of Western Ontario were included. Following adequate hydration with crystalloid and colloid solutions, dopamine was used if required to maintain a systolic blood pressure of greater than 90 mmHg. Epinephrine and/or norepinephrine infusions were added if 10 mcg/kg/min of dopamine was insufficient to maintain an adequate blood pressure. For analysis, donors were divided into two groups based on their mean inotrope exposure during the six hours prior to harvest; a low dose inotrope group (LDI 0-10 mcg/kg/min of dopamine) and a high dose inotrope group (HDI >10 mcg/kg/min of dopamine or the addition of epinephrine or norepinephrine). Assessment of transplanted liver function involved measurement of the peak postoperative aspartate aminotransferase (AST) and alanine aminotransferase (ALT) values, the mean prothrombin time (PT) over the first three postoperative days, and survival of the recipient at 30 days. Because the values for postoperative AST, ALT, and PT were not normally distributed the nonparametric Mann-Whitney Wilcoxon Rank Sum Test was used for statistical analysis and a p value less than 0.05 was considered significant.

RESULTS: Of the 50 donors, 21 were in the LDI group and 29 were in the HDI group. A comparison was made between the two donor inotrope groups to determine if they were similar regarding factors which could influence graft function other than donor inotrope exposure. The organ donor groups did not differ significantly with respect to donor age, sex, cause of death, pretransplant AST, time from original neurologic insult to organ harvest, time of brain death to harvest, or the cold and warm ischemia time of the transplanted organ. In addition, there was no significant difference in age, sex, cause of liver failure, or pretransplant patient functional status between organ recipients who received livers from the two different donor inotrope groups. Analysis of liver function (AST, ALT, and PT) following transplantation demonstrated no significant difference between patients who received organs from the two donor inotrope groups (Table 1). By 30 days, 5 of the recipients who received livers from donors in the LDI group had died while all of the recipients receiving livers from HDI donors were alive.

TABLE 1:

	LDI	HDI	p value
AST(U/L)	1737 (+/-661)	868 (+/-194)	0.41
ALT(U/L)	1186 (+/-382)	741 (+/-168)	0.17
PT(sec)	13.0 (+/-0.8)	11.8 (+/-0.3)	0.41

Donor inotrope exposure and recipient liver function. Data presented as Mean (+/- SEM) (P values were determined from the Mann-Whitney Wilcoxon Sum Rank Test).

DISCUSSION: This retrospective analysis demonstrates that graft function and recipient survival following liver transplantation are not adversely influenced by high doses of inotropes used to support the brain dead organ donor. The most significant factor limiting solid organ transplantation is the availability of donors. Livers should not be rejected for transplantation solely on the basis of the donor inotrope exposure.

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HEPARIN REQUIREMENTS BEFORE AND DURING CPB IN PATIENTS RECEIVING PREOPERATIVE INTRAVENOUS HEPARIN.

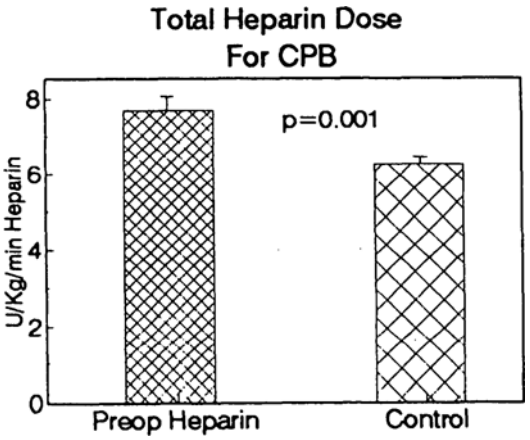
J.M. Karski M.D, S.J. Teasdale M.D, P. Norman M.D, J. Carroll R.N., M. Glynn M.D.
The Toronto Hospital, General Division, University of Toronto, 200 Elizabeth Street, Toronto, Ontario, M5G 2C4.

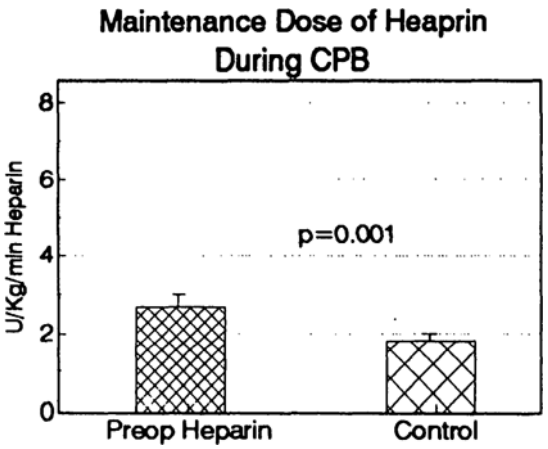
INTRODUCTION: Patients undergoing cardiopulmonary bypass (CPB) must be anticoagulated to prevent thromboemboli and clot generation. The dose of heparin, anticoagulant of choice, is 300 U/Kg body weight, to produce activated clotting time (ACT) exceeding 400 seconds. Often these heparin doses are inadequate if the patient has been given intravenous heparin therapy before surgery such that extra heparin must be given to achieve anticoagulation. The causes of this resistance to heparin are not established. Decreased levels of antithrombin III have not been uniformly documented nor have presence of antiheparins. We conducted a study to assess how much additional heparin is required post IV heparin therapy in our hospital to achieve full anticoagulation before CPB.

METHODS: We collected retrospective data on 179 patients undergoing CPB over the last 2 years. Seventy-two patients were being given IV heparin preoperatively for over 24 hours, partial prothrombin time (PTT) = 53±3.7 and 107 patients not on heparin were used as control (PTT=30.0±1.4). Heparin was stopped 3 hours before entering the operating room and baseline ACT did not differ between groups (145 vs 147 seconds). Routine high dose fentanyl anesthetic was used and patients were heparinized with IV heparin. No special protocol for dose of heparin was implemented apart from routine 300 U/kg initial dose and minimum of 400 sec ACT before commencing CPB. Pump was primed with 5000 U and if ACT approached 400 sec during pump run boluses of 5000 U were used.

STATISTICS: We used ANOVA analysis of variance to compare mean values. Fisher exact test and Chi-Square was used to compare frequencies.

RESULTS: The total dose of heparin (U) per kg body weight and time of CPB is presented in **Table I**. The dose needed during CPB (U/Kg/min) is presented in **Table II**.





Twenty-six percent of patients in the heparin group required a second dose of heparin before CPB vs 9% in the control group (p=0.057). A third dose of heparin before CPB was needed in 10% of heparin patients vs 0% in control (p=0.048).

Patients on heparin received mean 385+-120 vs 340 +-60 U (for control) of heparin to achieve ACT above 400 (p=0.001). 6% of patients on heparin required an initial dose > 600 U/kg vs 0% patients not on heparin. Apart from PTT, other hemostatic parameters did not differ before and during CPB in both groups and these patients did not bleed postoperatively more than control. Protamine requirement (1mg of protamine per 103 vs 94 U of heparin) and ACT after protamine (138 vs 142 control) did not differ statistically between groups.

CONCLUSIONS:

(1) The total heparin dose per kg/min needed for CPB anticoagulation in patients receiving IV heparin preoperatively was increased by 25% compared to control.

(2) Consumption of heparin during CPB for patients on preoperative heparin therapy was increased by 50% over control.

MASK VENTILATION : A Comparison of leak between ambulance personnel and anaesthetists.

Authors: J. H. Devitt, D. Brooks, P.A. Oakley, P. M. Webster.
From the departments of Anaesthesia and Emergency Medicine and the division of Respiratory Medicine, Sunnybrook Health Science Centre, University of Toronto, Toronto, Ontario.

INTRODUCTION: Paramedical personnel may be required to perform lung ventilation with a bag valve mask device. Most studies on these individuals looking at mask ventilation have used mannequins or other mechanical models rather than patients [1,2]. We undertook a comparison of the proficiency of basic life support ambulance officers and anaesthetists with the task of holding a mask on a patient's face during positive pressure ventilation.

METHODS: Patients of ASA status 1 or 2 undergoing elective surgical procedures which would normally require endotracheal intubation were studied. Basic life support ambulance officers with at least five years experience were contacted and brought to the operating room. All anaesthetists involved in the study had Royal College of Physicians and Surgeons of Canada certification. After induction of anaesthesia the patient was ventilated with a bag and mask using a standard anaesthesia circuit until the establishment of neuromuscular blockade. An oropharyngeal airway was then inserted and the anaesthetist or the ambulance officer was handed a Solco Adult Mask #5 (Laerdal) attached to the measuring equipment. Flow and pressure transducers were placed in the expiratory and inspiratory limbs of the breathing circuit of the ventilator. The output of these devices were sent to an electronic integrator to determine the inspiratory and expiratory volume. The inspiratory and expiratory volumes and airway pressure were recorded to computer disc for later analysis. Esophagogastric insufflation was qualitatively assessed by listening over the stomach with a stethoscope during the study period. The ambulance officer or anaesthetist then seated the mask on the patient's face and manipulated the patient's head and neck to achieve what was felt to be the best possible airway. At this point, the patient was ventilated with a Siemen's servo-C ventilator with a square wave form in the pressure control mode at 30 cm. of water. The order of hand grip (1 hand versus 2 hand) was randomized on each patient. Measurements were taken over 10 breaths at each mask hand grip. Data was collected from both mask hand grip techniques. Once data collection had occurred, calibration of the inspiratory and expiratory flow transducers was made against a spirometer while ventilating a test lung. The inspiratory and expiratory volumes were corrected with the calibration volume. Leak was then determined by subtracting the expiratory volume from the inspiratory volume. The leak was expressed as a fraction of the inspiratory volume. Leak with both hand grip techniques and utilizing anaesthetists or ambulance personnel was compared by analysis of variance. The frequency of esophagogastric insufflation was compared using a chi square analysis. A p value of less than 0.05 was considered significant.

RESULTS: 19 ambulance officers were studied on 24 patients while 21 anaesthetists were studied on 21 patients over a 16 month period. The results are presented in table I. There was no significant difference with regard to mask leak when ambulance officers were compared to anaesthetists and a 1 or 2 handed mask grip were used. However anaesthetists tended to have a smaller leak with a 2 handed grip when compared to a 1 handed grip or when compared to an ambulance officer performing a 2 handed grip. This difference was only 7% of the inspired volume. While ambulance officers tended to have a lower incidence of gastric insufflation this difference was not statistically significant.

Table I - Comparison of Hand Grip & Profession

	Anaesthetists		Ambulance	
	Leak	Insuff	Leak	Insuff
1 H	0.13±0.14	0.286	0.14±0.19	0.083
2 H	0.07±0.07	0.190	0.14±0.17	0.167

CONCLUSIONS: In healthy relaxed patients in the operating room setting there was little difference between the basic life support ambulance officers and fully qualified anaesthetists in mask holding ability. This study would suggest that the ambulance officers tested were adequately trained and further training would unlikely improve their performance of this particular skill. In an emergency situation, with or without ongoing external cardiac massage, mask ventilation may be inadequate or impossible. Only expertise in endotracheal intubation may improve airway management by, otherwise, well skilled ambulance officers.

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HAEMODYNAMIC AND MYOCARDIAL METABOLIC EFFECTS OF PEEP POST CABG.

S.J. Teasdale M.D., J.Karski M.D., T. Yao M.D., J. Ivanov R.N., P. Young R.N., S. Carson A.H.T., R.D. Weisel, M.D.
The Toronto Hospital, General Division, University of Toronto, 200 Elizabeth Street, Toronto, Ontario, M5G 2C4.

INTRODUCTION: PEEP is often used post coronary artery bypass grafting (CABG) to alleviate hypoxia and to tamponade intrathoracic bleeding vessels but its effect on myocardial contractility is still controversial. We attempted to assess indices of ventricular function coincident with evaluation of myocardial metabolism in response to increased levels of PEEP in post CABG patients.

METHODS: Ten patients with good ventricular function booked for primary elective CABG had radial arterial, pulmonary arterial and coronary sinus sampling catheters inserted at the time of operation. Postoperatively each patient was maintained with complete muscle paralysis on a volume ventilator with 10 ml/kg tidal volumes and rate adjusted to maintain normal blood gases. Haemodynamic measurements, arterial and coronary sinus blood lactates and serial nuclear angiograms using technetium red cell labelling and a portable gamma camera were obtained at 5 and 15 cm H2O PEEP before and after volume loading sufficient to raise the pulmonary capillary wedge pressure (PCWP) 2 mm Hg.

RESULTS: Load dependent indices such as CVP, PAPM and PCWP rose with increased PEEP. MAP increased over time but calculated indices, CI, R and LVEDVI and R and LVESVI, were not significantly different. Left ventricular systolic function as depicted by the slope of the linear regression was depressed (p=0.02) as was left ventricular function (Fig.I, p=0.025) with volume loading at 15 cm PEEP. Right ventricular systolic function slope and right ventricular stroke work index were not different with increased PEEP. Ventricular diastolic compliance was decreased bilaterally with 15 cm PEEP. Nine out of 10 patients had evidence of decreased lactate extraction (7 patients) or lactate production (2 patients) compatible with myocardial anaerobic metabolism after volume loading at 15 cm H_2O PEEP significantly different than lactate results at 5 cm PEEP (P=0.04).

STATISTICS: Measurements before and after volume loading were compared by paired t-tests and two way analysis of variance, (differences specified by Duncan's multiple range t-test when ANOVA was significant ($p<0.05$). Differences in myocardial performance and function were assessed by analysis of covariance, with the general linear model's procedure for simultaneous asessment of both slope and position. (SAS Institute Inc., Cary, NC)

DISCUSSION: We assessed right and left end systolic pressure-volume relationships which, within physiological limits, is independent of preload and incorporates afterload, and ventricular performance using ventricular volumes. The decrease in left ventricular systolic function and performance at 15 cm PEEP may reflect a higher incidence of myocardial ischaemia suggested by the lactate values. Right ventricular function changes are difficult to interpret because of the susceptibility of the right atrium, ventricle and pulmonary vasculature to the effects of raised intrathoracic pressure but the similar slopes suggest that the normal right ventricle can cope with volume loading at increased afterload (15 cm PEEP). The decrease in biventricular compliance could be attributable to increased intrathoracic pressure and, in fact, left chamber compliance was not different when the difference in CVP (3 mmHg) was equated with intrathoracic pressure increase and subtracted from the PCWP. Calculation of E_{ES} and Kp by means of pressure volume loops would provide results less influenced by changes in external pressures.

CONCLUSION: Increases in PEEP to 15 cm H_2O should be undertaken with caution in the post CABG patient with evidence of myocardial ischaemia.

Figure I

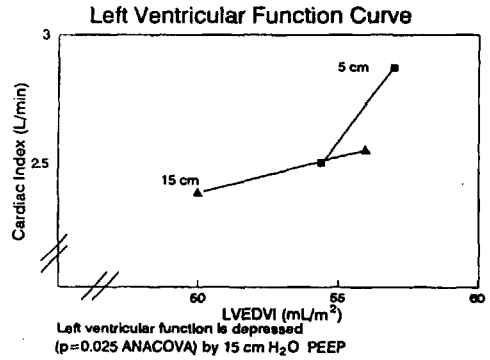
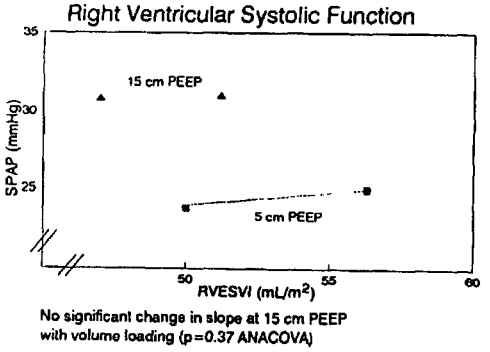


Figure II



Use of an Endotracheal Ventilation Catheter for Difficult Extubations

Richard M. Cooper B.Sc., M.Sc., M.D., FRCPC

Department of Anaesthesia, The Toronto Hospital, Toronto General Hospital.

Introduction:

A prototype catheter was developed after Bedger[1]. Over a two year period, experience has been acquired with this catheter involving over 35 patients, mostly on an emergency basis. These included patients who had been difficult intubations, most requiring awake fiberoptic intubation as well has eight patients who had undergone elective temporomandibular (TMJ) or maxillo-mandibular (MM) surgery. Such patients represent a particular challenge to the anaesthetist since the jaws are either wired shut or swelling severely restricts access to the airway following extubation, making the unanticipated reintubation potentially life-threatening or com-promising to the results of major surgical procedures.

Methods:

An endotracheal ventilation catheter (ETVC)* was developed, 65 cm long with an OD and ID of approximately 4 and 3 mm respectively. Proximally, it was fitted with a removable luer lock connection and distally, had both an end port and several side holes. The catheter had been tested in an artificial trachea with jet ventilation (50 psi) and demonstrated no significant catheter whip. Its ability to maintain satisfactory oxygenation and ventilation had been established in several life-threatening situations.

Patients who had been difficult intubations were extubated over the endotracheal catheter (ETVC), at the request of the attending or PACU anaesthetist. Institutional ethical review and written informed consent was obtained from patients undergoing elective TMJ or MM surgery in whom the oral surgeons planned to wire the jaws or when significant postoperative restriction of mouth opening was anticipated. The ETVC was passed through the existing nasal or oral endotracheal tube prior to extubation. The ETT was then removed while the ETVC remained in place until the patient was fit for discharge from the PACU. Generally, the ETVC was connected to either a capnograph for respiratory assessment (described elsewhere) or to humidified oxygen provided by insufflation at 2-4 LPM. A Sanders ventilator, with a driving pressure of 50 psi, remained at the bedside. When required, reintubation either blindly or under direct vision (insofar as possible) over the ETVC was attempted while oxygen insufflation or jet ventilation continued.

Observations:

Sufficient information was collected on thirty-one patients who were extubated over the ETVC, most either by the author or under his supervision. Only five patients were reintubated over the ETVC, three of these occurring in the ICU and two in the operating room. The latter involved a cuff rupture occurring following fiberoptic nasal intubation, but not recognized until the patient was anaesthetized and paralyzed. For technical reasons, this patient was reintubated twice over the ETVC.

In the ICU, two patients required reintubation. They were being ventilated on high FiO2 with 10 and 15 cm H_2O PEEP but poor pulmonary compliance and an uncorrectable cuff leak prevented adequate ventilation or the maintenance of PEEP. As well, tracheal suctioning caused significant and prolonged arterial desaturation. One of these patients had undergone a "difficult intubation" at another institution. A subsequent reintubation without the ETVC by the author and a colleague confirmed this and was accompanied by life-threatening hypoxemia.

Although experience with reintubation over the ETVC was limited, this was accomplished with the same degree of difficulty encountered in passing an ETT over a bronchoscope. With the ETVC, however access to airway was maintained and adequate ventilation and oxygenation were provided throughout the procedure.

All but two patients tolerated the ETVC following extubation. The first had the catheter resting on the carina and until this was recognized, was treated successfully with the instillation of lidocaine. The second had been intubated because of status asthmaticus and was extubated reluctantly after five days, with no leak around a deflated ETT. Since that time, other patients with reversible airways disease have tolerated the ETVC. One patient, with coronary artery disease and obesity, who had required three attempts to accomplish intubation, had marginal oxygenation in the PACU following a pulmonary resection. He had been extubated over the ETVC which remained in place for 48 hr and was very well tolerated.

Conclusions:

Although experience with the ETVC as a "stylet" is limited in our hands, Bedger has described use of a similar device for the intubation or reintubation of 59 patients. His catheter employed a removable 15 mm connector whereas ours has a removable luer lock connector. Ventilation through a long, narrow tube (65 cm, 3 mm ID) using conventional pressures is unlikely to provide adequate gas exchange[3]. Thus high pressures are likely required and a secure connection between the catheter and oxygen source must exist. Studies are currently underway to determine the pressure requirements with varying pulmonary compliance and the degree of air trapping with increased airway resistance.

While enthusiasm for jet ventilation has been expressed[2] our experience thusfar has supported the adequacy of oxygen insufflation for limited periods of time in all but those patients with very severe pulmonary disease. Further experience with jet ventilation, particularly in patients with upper airway obstruction will determine the safety of this approach.

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* The ETVC used was prepared by Murray Huntley RRT. A commercial product is to be manufactured by Cardiomed Supplies, Inc., Gormley, Ontario.

SEVERITY OF ILLNESS AND HOSPITAL OUTCOME FOR ICU PATIENTS: A COMPARISON OF A CANADIAN HOSPITAL TO UNITED STATES HOSPITALS.

David T. Wong MD*, Douglas P. Wagner PHD †, William A. Knaus.†
*Department of Anaesthesia, Toronto Western Hospital, 399 Bathurst St., Toronto, Ontario. M5T2S8.
†ICU Research, The George Washinton University Medical Center, Washington DC, USA.

INTRODUCTION

Jacobs et al found that ICU utilization in the United States (US) was two and a half times that in Canada in 1986 (1). Yet, little data exists that compares the severity of illness and outcome of ICU patients in the two countries. The APACHE II score has been shown to be an accurate measure of severity of illness and correlated strongly with patient outcome (2). The APACHE II mortality risk prediction equation has been used to accurately predict patient outcome in many countries worldwide (3). In our study, the APACHE II score and hospital mortality for ICU patients from a Canadian hospital will be compared to that from thirteen US hospitals. We will also attempt to validate the ability of the APACHE II mortality risk prediction equation to predict patient outcome in this Canadian ICU population.

METHODS

Our Canadian data was collected from a tertiary care University hospital *(TWH)*. From January to September 1991, consecutive patients admitted to a mixed medical-surgical ICU were studied. Cardiovascular surgery, neurosurgery and coronary care patients were admitted elsewhere and not included in the study. For each patient, demographic data, admitting diagnosis, day one APACHE II score, survival at ICU and hospital discharge were recorded. For the entire study group, the mean and frequency distribution of APACHE II scores, the overall hospital death rate (HDR) and HDR stratified by 10 point APACHE II ranges were derived.

The American ICU data was obtained from the APACHE II multi-center trial in 1982 involving 13 hospitals *(USH)*, 9 of which were tertiary care centers (2). To make the USH population comparable to our study population, cardiovascular surgery, neuro-surgery and CCU patients were excluded. The mean and distribution of APACHE II scores and the HDR stratified by APACHE II scores from the USH group were compared to the TWH counterparts. The mean APACHE II scores were compared using students' t-test while the HDRs were compared using chi-square analysis. Statistical significance ($p<0.05$) was accepted.

Finally, for each TWH study patient, the predicted mortality risk (PMR) was calculated by the formula below which was taken from the 1982 APACHE II trials (2).

$$\text{Ln}(\text{PMR} / 1\text{-PMR}) = -3.517 + (\text{APACHE II score} \times 0.146) + (\text{diagnostic category weight}) + (0.603, \text{if emergency surgery})$$

The predicted HDR for the whole TWH group was obtained by averaging the PMR for each individual patient. This predicted HDR was then compared to the actual observed HDR for the TWH group.

RESULTS

We collected data from 468 consecutive patients admitted to the TWH ICU. 230 were medical and 238 were surgical patients. The USH data base consisted of 4200 patients from the APACHE II trials. The mean APACHE II score were 14.5 and 14.7 (non-significant) for the TWH and USH patients while the hospital death rates (HDR) were 23.7% and 21.5% (non-significant) respectively. The frequency distribution of TWH and USH patients according to 10 point APACHE II ranges is shown in figure 1. The HDR in TWH and USH subgroups stratified by 10 point APACHE II ranges is shown in figure 2. The predicted HDR for the TWH patients was 23.1% which closely approximated the observed HDR of 23.7%.

DISCUSSION

Despite differences in ICU utilization and selection criteria for ICU admissions, we found the patients' severity of illness quantified by APACHE II scores and the hospital death rates (HDR) similar in our hospital and the American hospitals. The predicted HDR for the TWH group utilizing the APACHE II mortality risk prediction equation closely approximated the observed HDR. However, our institution is a tertiary care University hospital and is therefore not representative of Canadian hospitals. There is a need to establish a multi-center Canadian data base to allow comparison of ICU outcome with US data and to validate the ability of the APACHE II mortality risk equation in predicting outcome in Canadian patients.

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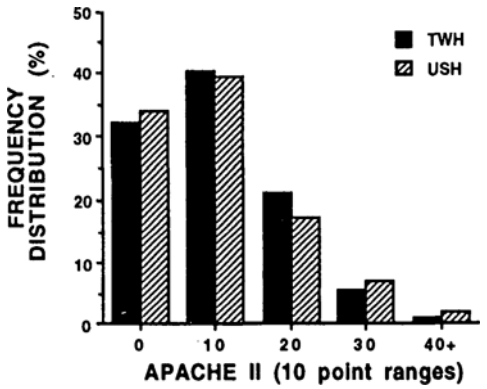

*FIGURE 1.

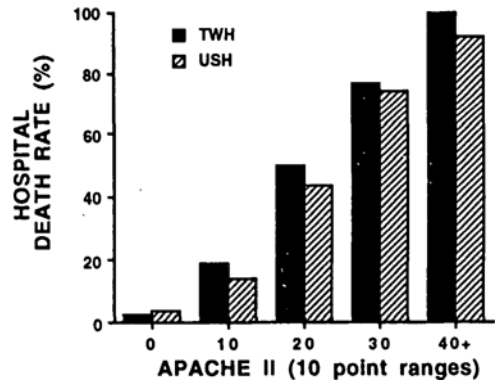

*FIGURE 2

INTRAVENOUS (I.V.) SEDATION AND MONITORING PRACTICES OUTSIDE THE OPERATING ROOM

Charul A. Munshi, MD, John P. Kampine, MD, PhD
Department of Anesthesiology, Medical College of Wisconsin, Milwaukee, WI 53226, USA

INTRODUCTION

Sedatives and narcotics are used during I.V. sedation ouside of the operating room for outpatient procedures. An earlier study at a gastroenterology (GI) clinic found significant O_2 desaturation when using I.V. midazolam and demerol.[1] This study examines the practice of I.V. sedation and monitoring in hospital-based GI clinics in the state of Wisconsin.

METHODS

The director of GI clinics in sixty hospitals was sent a questionnaire regarding drugs used in I.V. sedation, use of monitors, availability of resuscitative equipment, and use of anesthesia personnnel during outpatient GI procedures.

RESULTS

Forty-three out of sixty surveys (72%) were returned. All 43 respondents used some form of I.V. sedation (Figure 1). Multiple drug combinations were used in several hospitals. The most common drugs used were midazolam (96%) and demerol (80%). Pulse rate (96%) and pulse oximetry (91%) were the most common monitors used followed by respiratory rate and BP at 82% each (Figure 2). Seventy percent of the clinics monitored pulse rate, EKG, and respiratory rate during recovery.

All clinics had oxygen, suction, and emergency cart (airway equipment and resuscitation) available in the department. Anesthesiology was consulted for airway management and/or resuscitation 1-2 times/year by 65% of the respondents.

DISCUSSION

This survey shows that I.V. sedation with potent sedatives and narcotics is a common practice for outpatient GI procedures. Midazolam's popularity is probably due to absence of burning on injection and I.V. irritation, superior amnesic effect and potency compared to valium. Although fentanyl has largely replaced demerol and morphine in anesthesia practice, it is not commonly used by nonanesthesiologists because of lack of familiarity and high potency. Unlike an earlier survey of emergency departments where respiratory monitoring was infrequent while using anesthetic agents (I.V., muscle relaxants, N_2O),[2] our survey shows extensive use of respiratory and cardiac monitoring in the GI clinics.

It is important to provide uniform quality of patient care, and anesthesiologists can help by developing standards for monitoring and anesthetic care throughout the hospital.

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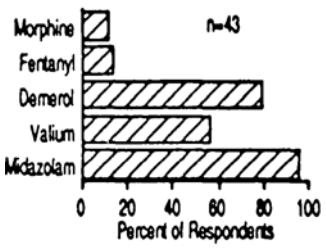

Figure 1. I.V. Sedation Drugs Used by GI Clinics

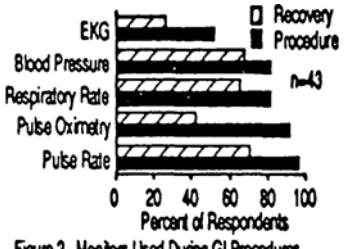

Figure 2. Monitors Used During GI Procedures and Recovery

LAPAROSCOPIC CHOLECYSTECTOMY -- IS IT BETTER?

DK Rose, Dept. of Anaesthesia, St. Michael's Hospital, MM Cohen, Clinical Epidemiology Unit, Sunnybrook Health Science Centre, ID Soutter, Dept. of Surgery, St. Michael's Hospital Toronto Ontario

INTRODUCTION: Laparoscopic cholecystectomy (LC) is gaining widespread acceptance. Reports are available from the surgical literature describing techniques, advantages, and complications.[1,2] However, the anaesthetic literature is limited to case reports or small series of patients undergoing LC with little comparative data.[3,4] Therefore this study was undertaken to determine the anaesthetic management and outcomes which were relevant to the anaesthetist in the operating room (OR) and recovery room (PACU) for all patients undergoing LC from its initiation at our institution. In order to put the rate of adverse events with LC into perspective, we compared LC to laparotomy cholecystectomy (C) and to gynecological laparoscopy (GL)

METHODS: Following ethics approval we prospectively collected data from copies of the OR and PACU records, and the medical records department database. Records contained information on preoperative case mix and OR and PACU management. As well, there was a list of events which were "less than ideal" defined directly on each record, which were circled by the anaesthetist or PACU nurse when they occurred. Over a ten-month period in 1991 we studied all cases of LC, C (we excluded 4 patients with acute cholecystitis who were ventilated preoperatively, and any case of bile duct exploration) and GL for gynecological examination (excluding those with a D&C or tubal ligation). Statistical analysis was performed using Chi square statistic or unpaired t test.

RESULTS: There were 78 consecutive LC over the ten-month period with increasing frequency during the later months. Casemix data included age (22% > 60 years), weight (19%, males > 100 kg or females > 80 kg), ASA status (5% ASA 3 or 4), sex (80% female), history of current illness (48% had one or more), and medication review (39% took one or more medications preoperatively). All were elective inpatients. Narcotic premedication was used in 40%of patients. Following an induction dose of pentothal all patients were mechanically ventilated and maintained with enflurane (68%) or isoflurane (32%), N_2O, and fentanyl (mean dose 1.1 µg ± .9 µg/kg/hr). Preoperative or intraoperative antiemetics were given to 68% of patients. Blood pressure was less than 80 for >5 min. or supported by ephedrine in 11.6% of patients. There was one case with airway pressures > 40 torr, but in no cases was end tidal CO_2 greater than 55 torr.

Total anaesthetic and OR time was 2.4 ± .7 hours and all patients were admitted to PACU postoperatively. In the PACU the rate of nausea and vomiting was 15.4%, excessive pain 2.6% (moaning and writhing with initial care dominated by pain control), and desaturation 8.0% (SpO_2 < 90 on room air prior to discharge). One patient required reintubation in the PACU for respiratory distress related to an anaphylactic reaction and was transferred to ICU for postoperative ventilation. The mean length of hospital stay was 2.8 ± 5.9 days (median 2 days) from the date of surgery. Abdominal re-exploration for bile leakage was required on a subsequent admission for two patients.

There were 84 patients undergoing C and another 388 undergoing GL. C patients were older (39% > 60 yrs.) and had a higher ASA (23% ASA ≥ 3) ($p<.05$). However patients undergoing GL had a significantly lower frequency of all parameters of documented casemix. Anaesthetic management with the exception of fewer premeds (2%) and increased use of propofol for induction (16%) in the GL group were similar.

Adverse events and length of stay are recorded in the Table. LC patients were more likely to have OR hypotension but less likely to have pain and desaturation in PACU. Due to pre-existing illness, four patients in the C group were discharged to ICU not PACU postoperatively, one was ventilated. No subsequent surgical procedures were reported for any patient in the C or GL group and there were no admissions reported for outpatients in the GL group.

CONCLUSIONS: Significant surgical and social advantages have been shown for patients undergoing LC. However, these results must be interpreted keeping in mind the differences in casemix in patients undergoing the different procedures. At this point in time LC patients were a selected healthy group as compared to the conventional C patients. The high incidence of intraoperative hypotension and of postoperative nausea and vomiting following LC, needs to be addressed in planning future anaesthetic management.

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TABLE Comparison of the 3 surgical procedures (* p<.05 different from LC)

EVENT/TIME	LC	C	GL
OR Hypotension %	11.6	3.6	.5*
PACU Nausea/vomit %	15.4	16.7	6.2*
PACU Excess pain %	2.6	13.1*	4.7
PACU Desaturation %	8.0	33.8*	1.6*
PACU Narcotics use %	73	94	30*
OR time (hr)	2.4±.7	1.9±.6*	.8±.2*
Hospital stay (inpatient days)	2.8±5.9	6.6±5.1*	1.6±1.3

PATIENT PROBLEMS DURING ANAESTHESIA - ARE THEY RELATED TO THE SURGICAL APPROACH ?

DK Rose, Dept. of Anaesthesia, St. Michael's Hospital, MM Cohen, Clinical Epidemiology Unit, Sunnybrook Health Science Centre, Toronto Ontario

INTRODUCTION: Studies have documented intraoperative morbidity and mortality for all surgical procedures and for single operations.[1,2] However the rate of adverse events for various surgical procedures has not been well defined. We wished to document the specific problems associated with different procedures and identify those procedures during which patients were at the highest or lowest risk of adverse events.

METHODS: Following Ethics approval, all OR patients attended by an anaesthetist from Oct.1990 to June 1991 were studied in a prospective manner (n=10574). The definitions of intraoperative patient problems (43 in total) during the induction, maintenance, and emergence periods were included directly on the OR anaesthetic record (eg. hypotension BP <80 for >5min, hypertension BP >200 for >5min, tachycardia HR >120 for >10 min, and excessive blood loss >6u pc). The problems chosen for the study were measured in all patients and reflect preoperative patient status, surgical interventions and anaesthetic management. They did not necessarily imply errors on the part of the anaesthetist. When these problems occurred they were noted by the anaesthetist. Copies of each record were reviewed daily before computer entry to ensure that any problems identified by handwritten notes or the vital signs graphs were included.

All surgical procedures were coded by the investigators using the ICD.9.CM system. These codes were further categorized into 15 different surgical approaches (SA) based on anatomical regions. Patients who had more than one SA during a single operative period (n=755) and patients who underwent open cardiac procedures or organ donations (n=554) were excluded from the analysis.

First, the rate of specific problems for each SA was determined. The Relative Risks (RR) and 99.9% Confidence Intervals (CI) for having each problem by SA were computed.[3] That is, the proportion of patients having a specific problem for one SA was compared to the proportion of patients having that same problem for all other SAs. Second, RR and CI for the occurrence of any problem (one or more) by SA was calculated to determine the overall relationship of patient problems and SA.

RESULTS: The commonest intraoperative problems (n=9265) were tachycardia 1.5%, hypotension 1.2%, desaturation 1.0%, difficult intubation 1.0%, and hypertension .8%. One or more problems were documented in 8.9% of cases.

Surgical approaches, where specific problems were more likely to occur compared to all other SA, were identified; ***intracranial*** (hypertension 7.8 times more likely), ***spine*** (excess blood loss 13.4), ***trunk*** (bronchospasm 3.1), ***endoscopy*** (desaturation 4.3, tachycardia 3.1), ***digestive/intrabdominal*** (excess blood loss 9.9, ischemia 9.2, hypovolemia 8.1, tachycardia 3.3, hypotension 2.7), ***thoracic*** (airway pressure greater than 40 torr 18.3, desaturation 12.9, dysrhythmia 8.0), ***major vascular*** (excess blood loss 17, hypovolemia 16.5, hypotension 14, tachycardia 5.9, dysrhythmia 5.2, desaturation 4.0). For all other SA no significant risks were identified.

The likelihood of one or more patient problems during an individual SA, was identified by the overall Relative Risk in Table 1. Major vascular and thoracic cases have the highest risk and perineal and gynaecological/abdominal the lowest.

DISCUSSION: Patient problems which are specific in nature have been identified during different surgical approaches. The SA is an important case mix factor and will be accounted for when comparing differences between anaesthetists and hospitals in future outcome studies. These results will help plan our future direction in teaching, allocating resources, and implementing effective anaesthetic interventions.

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FIG. 1 RELATIVE RISK (RR) OF ANY INTRAOPERATIVE PATIENT PROBLEM

SURGICAL APPROACH	n	RR
DIGESTIVE/ABDOMINAL	445	2.0*
ENDOSCOPY	317	1.4
EXTREMITIES	1,604	1.0
EYE,EAR,NOSE,THROAT	1,596	.8
GYNAECOLOGICAL/ABD	1,003	.6*
INTRACRANIAL	352	1.8*
MAJOR VASCULAR	133	4.2*
OTHER HEAD/NECK	318	1.2
OTHER SITES	739	1.2
PERINEAL	1,119	.4*
RENAL	556	1.2
SPINE	245	1.1
THERAPY/DIAGNOSTIC	207	.2
TRUNK	589	.9
THORACIC	42	3.0*

* CI Significantly different than 1.00 ($p < .001$)

ECONOMIC EVALUATION OF AN ANTIEMETIC PROGRAM FOR POSTOPERATIVE NAUSEA/VOMITING WITH DROPERIDOL

A. Mathieu, M.D., A. Gafni, Ph.D., A. Dauphin, M.D.
Depts of Epidemiology & Biostatistics and Center for Health Policy Analysis, McMaster Univ., Hamilton, ON L8N 3Z5, CA and Anesthesia Dept, Univ. of Cincinnati, Cincinnati, Ohio, USA

Introduction: As we face increasingly difficult decisions about the allocation of health resources, information about costs and consequences of therapeutic interventions may improve all decision-making process aimed at maximizing health benefits for the dollars spent. Thus, we are presenting a cost-effectiveness (CEA) and cost-benefit analysis (CBA) of a preventive program for postoperative nausea/vomiting (PONV) in women undergoing gynecological procedures, an ambulatory care patient population at high risk for PONV.[1]

Methods: Droperidol efficacy in decreasing the incidence of PONV from 65% (Program B) to 20% (Program A) was established from the results of randomized controlled trials [2,3] of preventive antiemetic therapy in that population. CEA: Program A consisted of PONV prevention with 20ug/kg^{-1} Droperidol administered preoperatively. Program B consisted of a "do nothing" approach with symptomatic treatment of persistent PONV in the recovery room if necessary. The steps for CEA are listed in Table 1. Following identification of all direct and indirect costs, an incremental cost comparison was performed, excluding the cost of resources common to both programs (Table 2). The cost differential between Program A and B (▲Cost) was calculated thereafter. The final number of PONV averted (▲ Health effect) was derived by applying to a hypothetical cohort of 1000 patients the selected rate of PONV for each program, and subtracting the number obtained for Program B from that of Program A. The cost/effectiveness (C/E) ratio was derived by dividing ▲Cost by ▲E.

The CBA was carried out through a questionnaire using the Willingness to Pay (WTP) approach as a method of valuing risk reduction for PONV. The total WTP amount reflects the monetary value attributed to Program A by a cohort of 20 patients (pilot study). To obtain the cost-benefit (C/B) ratio, the differential cost between Program A and B was calculated for 20 patients and divided thereafter by the total WTP.

Results: 1. CEA: A C/E ratio of less than zero Canadian dollar per case of PONV averted was obtained comparing Program A with B (Table 3). Sensitivity analyses were performed assuming: 1) a lower bound of effectiveness, i.e., a 30% PONV rate incidence with Droperidol (Program C), and 2) a higher, but not more effective, dose of Droperidol, 75ug/kg^{-1} (Program D) which yielded C/E ratios of $13.20 and $18.70 respectively. 2. CBA: Preliminary results from our pilot study (WTP on 20 women) revealed a total WTP of $1800.00. The cost-benefit ratio for Program A versus B was not calculated since the benefit was self-evident. Program C would still be beneficial if all 20 members of the cohort (100%) required surgery, a worst case scenario. Last, a C/B ratio of 1/9 was calculated if a higher, but not more effective dose of Droperidol (Program D) was used.

Discussion: The C/E ratio < 0 clearly establishes the effectiveness of Program A versus B. The CBA further connects cost-effectiveness with value. Both analyses constitute essential steps in facilitating the incorporation of cost into practice policies.[4] By evaluating the economic effects of clinical decisions, such analyses will help anesthesia practitioners make better informed decisions under probabilistic circumstances.

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TABLE 1 STEPS USED IN COST-EFFECTIVENESS ANALYSIS (CEA)

1. **DEFINE THE PROGRAMS**
   - Program A - Droperidol 20ug/kg^{-1}
   - Program B - Traditional "Do Nothing"
2. **COMPUTE NET COSTS**
   DIFFERENTIAL COSTS
   - Drug Cost Prevention
   - Drug Cost in RR
   - RR Stay (Extra)
   - Hospitalization
   - Physicians Fee (Charges)
   - Laboratory Cost
   - Wages Lost
3. **COMPUTE NET HEALTH EFFECT**
   ▲ Rates PONV
4. **APPLY DECISION RULES**
5. **SENSITIVITY ANALYSIS**
   - Higher Dose 75ug/kg
   - Lower Effectiveness 30%

TABLE 2A COSTS COMMON TO BOTH PROGRAMS

- Surgeons' fee
- Anesthesia provider's fee
- OR and RR hospital cost
- SSU patients' preparation costs
- Other support personnel & preoperative laboratory cost

TABLE 2B INCREMENTAL COST IN 1990 DOLLARS	PER PATIENT
1. Drug prophylaxis per patient including drug charge, syringe, needle, alcohol swab	15
2. Differential length of stay in RR (per hour)	105
3. Additional treatment of mod. or severe PONV in RR - drug cost for PONV includes drug & supplies	15-30 (1-2 doses)
4. Unanticipated hospitalization/day	371
5. Diagnostic laboratory test re hospitalization/tests	11
6. Lost wages for one day	120

TABLE 3 COST-EFFECTIVENESS ANALYSIS ($ VALUES)

Strategy	Data for 1000 Patients				
	Increm. cost	PONV	Diff. cost (▲C)	PONV Averted (▲E)	C/E RATIO
Program A	22,050	200	-6,570	450	< 0
Program B	28,620	650			
Program *C	33,240	300	+4,620	350	13.20
Program D	37,050	200	+8,430	450	18.70

A SURVEY OF ANAESTHETIC DRUG EXPENDITURES

L. Torsher, M.D., R.J. Martineau, M.D., M. Tierney, M.Sc., H.S. Hopkins, B.S.P., D.R. Miller, M.D.
Departments of Anaesthesia and Clincial Pharmacology, Ottawa General Hospital and The University of Ottawa, Ottawa, Ontario.

INTRODUCTION: Ongoing review of drug costs by clinicians is one method to heighten awareness of hospital operating expenses. To encourage and promote a more rational and parsimonious selection of drugs, we undertook a survey to review the current annual anaesthetic drug expenditures in a tertiary care, university-affiliated hospital. This was done as part of a departmental programme to inform anaesthesia staff and residents of drug costs.

METHODS: For the period April 1, 1990 to March 31, 1991, the costs and quantity of all anaesthetic drugs used in the Operating Room Department of the Ottawa General Hospital, a 539 bed tertiary care hospital, were surveyed. Information was obtained from the hospital pharmacy records for anaesthetic drugs, vasoactive and miscellaneous agents. In our institution, the Operating Room has been allocated an exclusive cost centre number, which is different from cost centre numbers of the ICU, Recovery Room, and the Obstetrical Suites. The costs of nitrous oxide, oxygen, and medical air are borne by the physical plant for the entire hospital, and were thus not included in this survey.

RESULTS: During the one year survey period, thirteen thousand procedures were performed in the operating room suite for all specialties excluding cardiac and paediatric surgery. The total hospital pharmacy budget for the period was $7,084,000, representing 4.8% of the total hospital budget. Anaesthesia-related drugs allocated to our cost centre amounted to a total of $407,000 or 5.7% of pharmaceutical costs, which represents 0.3% of the total hospital expenditures. Narcotics, muscle relaxants, volatile agents, and IV anaesthetic agents constituted the main costs, as shown in Figure 1. The eight anaesthetic agents constituting the major expenditures (greater than $5,000 per annum for each agent) are presented in Figure 2. In addition, naloxone expenses were 7% of the total.

DISCUSSION: With the introduction of newer anaesthetic agents, the cost of modern anaesthetic techniques has generated a great interest at many institutions. During our last hospital fiscal year, this expenditure represented less than 6% of the total pharmacy budget. As expected, the drugs which generated the greatest expenditures included the narcotics, muscle relaxants, inhalational and IV anaesthetic agents. Due to continuous end-tidal monitoring of the potent inhalational agents, there has been a reduction in fresh gas flow rates from our anaesthetic machines, which may explain the lower proportional expenditure related to isoflurane and enflurane. Naloxone expenditure was surprisingly high. On further analysis, this was explained by the high cost of each naloxone 2 mL ampoule ($37.05), and since this finding, we have changed to a lower concentration to reduce this cost. The expenditures related to local anaesthetic agents, vasoactive agents, anticholinesterease drugs and others such as droperidol were not insignificant (19%). As a cost-saving measure, it is important to utilize techniques which minimize drug wastage. Rational selection of anaesthetic drugs involves a number of important factors (Table), of which cost is only one. Our survey demonstrates that the cost of anaesthetic drugs constitutes a relatively small proportion of the hospital pharmacy budget. Ongoing review of these data should enable us to observe the effects, if any, of changes in practice patterns as they relate to drug expenditures.

PROPORTIONAL COST OF DRUGS

Figure 1

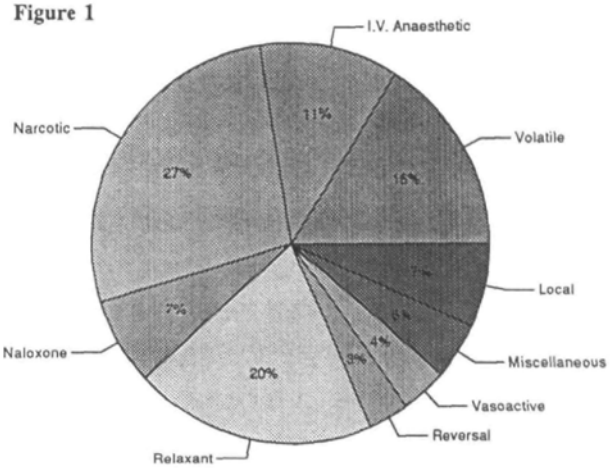
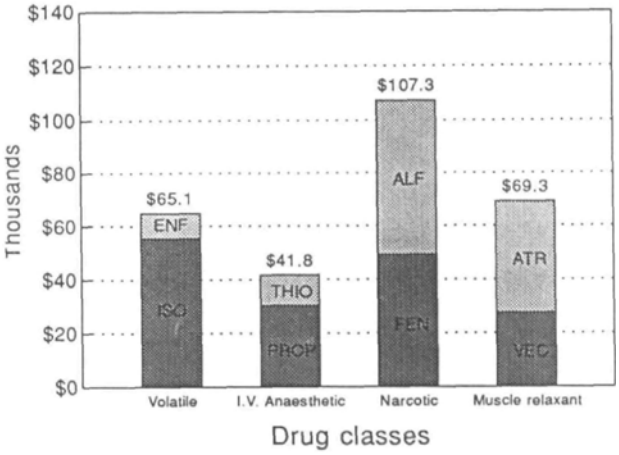


Figure 2

COST OF SPECIFIC AGENTS



Factors Influencing The Choice of Anaesthetic Drugs:

1. Familiarity with the agent
2. Pharmacokinetics and pharmacodynamics
3. Drug interactions
4. Medical condition of the patient
5. Type of surgical procedure
6. Plan for postoperative care
7. Local hospital practice patterns
8. Product information and promotion
9. Cost of drugs

CONTINUING MEDICAL EDUCATION: An Assessment of the Learning Needs and Interests of Anaesthetists.

G.J.Baylon MD, F.Chung FRCPC

Department of Anaesthesia, University of Toronto, Toronto Western Division, The Toronto Hospital., Toronto, ON, M5T 2S8

INTRODUCTION

Learning Needs Assessment is the term applied to the process of identifying or diagnosing a learner's educational needs. It is the foundation of a systematic Continuing Medical Education (CME) program. Needs assessment has been identified as the most pressing problem of Medical Education directors on North America[1]. Furthermore, the CME learning needs, interests or motivations of anaesthetists have never been studied. The amount of time and effort required for needs assessment is probably a major deterrent to this activity.

METHODS

The investigators adopted simple and straightforward means of assessing the "perceived learning needs" and topic interests of anaesthetists[2]. Questionnaires were sent by mail to anaesthetists practicing in teaching and non-teaching hospitals in the Toronto area. The questionnaire presented a list of CME content areas; the respondents were asked to indicate on scale of 1 to 10 their Current Expertise, Ideal-Desired Expertise, and Interest-Motivation levels for each content area. Need Score for each content area was defined and calculated by taking mean of the difference between Ideal and Current Expertise responses. The Interest-Motivation score for each area was simply the mean of all responses for that area.

RESULTS

A total of 101/305 anaesthetists (29%) responded to a survey by mail. Majority of the respondents were; in practice for less than 10 years, teaching hospital based, and had specialty certification (Table 1). Regional nerve block, Acute pain control and Medicolegal considerations received high overall ranks in both the Need (Table 2 and Figure 1) and Interest (Table 3) categories. Paediatric anaesthesia, Anaesthesia for trauma surgery and Thoracic anaesthesia got top ranks among the subspecialty fields. Regional anaesthesia techniques received higher need and interest ranks than intravenous and inhalational techniques.

DISCUSSION

This paper demonstrates a simple and quick way to assess the learning needs of potential CME program participants. The simplicity and adaptability of this method would allow providers of CME to conduct their own needs assessment. The development of programs based on needs assessment data would improve the quality of CME programs available to anaesthetists and also lead to a cost-effective utilization of CME resources.

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Table 1. Respondent Profile:

Years in Anaesthesia Practice:	<10 47%*	10-20 24%	>20 29%
Place of Practice			
Non-teaching Hospital(51.3)	19.7*	10.5	21.1
Teaching Hospital(44.7)	26.3	11.8	6.6
Both(4.0)	1.3	1.3	1.3
Type of Practice			
Full-Time(88.1)	40.8	21.1	26.3
Part-Time(11.8)	6.6	2.6	2.6
Specialty Certification			
w/ FRCPC(84.2)	42.1	18.4	23.7
w/o FRCPC(15.8)	5.3	5.3	5.3

*percentage of respondents

Table 2. Top 10 Content Areas in Terms of Perceived Need:

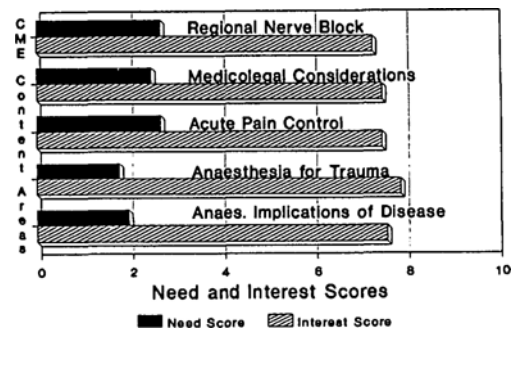
Rank	CONTENT AREA	Ideal Level	Current Level	Need* Score
1.5	Regional nerve block	8.2	5.5	2.7
1.5	Acute pain control (e.g. PCA service)	7.7	5.0	2.7
3	Medicolegal considerations	8.6	6.2	2.4
4	Chronic pain control	5.9	3.6	2.3
5	Critical care medicine	8.3	6.1	2.2
6	Statistical analysis	5.4	3.3	2.1
8	Anaesthetic implications of disease	9.2	7.2	2.0
8	Paediatric anaesthesia	7.3	5.3	2.0
8	Continuing medical education issues	7.0	5.0	2.0
10	Pharma. principles of Anaes. practice	8.7	6.8	1.9

*Need Score = (Ideal Level - Current Level)

Table 3. Top 10 Content Areas in Terms of Interest/Motivation:

Rank	CONTENT AREA	Motivation Level
1	Anaesthesia for trauma surgery	7.9
2.5	Anaesthetic implications of disease	7.6
2.5	Complications of anaesthesia	7.6
4	Medicolegal considerations	7.5
5.5	Regional nerve block	7.3
5.5	Acute pain control (e.g. PCA service)	7.3
7.5	Outpatient anaesthesia	7.2
7.5	Critical care medicine	7.2
9	Anaesthesia for the geriatric patient	7.0
10	Thoracic anaesthesia	6.9

Figure 1.



DOES A NEW NONINVASIVE TEST FOR MALIGNANT HYPERTHERMIA SUSCEPTIBILITY INFLUENCE TREATMENT DECISIONS?

Elizabeth A. Peter FRCPC MHSc, M. Joanne Douglas FRCPC
The Department of Health Care and Epidemiology and the Department of Anaesthesia, The University of British Columbia, 5804 Fairview Ave., Vancouver, B.C. V6T 1W5

INTRODUCTION: The clinical application of the new noninvasive test for Malignant Hyperthermia (MH); the Phosphorus Nuclear Magnetic Resonance Spectroscopy (P NMRS)[1] is examined with a medical decision analysis model[3]. Does this new test influence clinical management?

METHODS: Three anaesthetists with varying levels of expertise pertaining to MH (a tertiary care anaesthetist with an MH referral practice, a general hospital anaesthetist and a GP anaesthetist) were asked to assign numbers between 0 and 1.0 (Utilities) for constructed outcomes after diagnostic testing for MH susceptibility. The Utilities assigned were a quantitative measure of preference for the health states encountered after MH testing[3]. These values between 0 (least desirable) and 1.0 (most desirable) were estimated using an accepted technique for development of a "global" utility; the Standard Gamble[4]. These outcomes considered the clinical implications of test outcomes. In particular, treatment for patients with false positive results and consequences of missing the diagnosis in patients with false negative tests results were considered.

Three probabilities which characterize individual test performance in the clinical setting were calculated according to Sox (Figure 1)[2]. The "Treatment Threshold Probability" (P*) or the probability at which the physicians are indifferent to giving treatment or withholding treatment was derived using a clinical Cost and Benefit of the particular P NMRS test. This Cost and Benefit are based on the Utilities assigned to test outcomes by the anaesthetists. A pretest probability below which testing will not influence decision making is the "No Treatment-Test Threshold Probability" (P1). A pretest probability above which testing will not influence decision making is the "Test-Treatment Threshold Probability" (P2). These latter two probabilities incorporated the Cost, Benefit, and Utilities for test outcomes. The sensitivity and specificity of the P NMRS test were also entered into the equation. Sensitivity analyses were then performed utilizing the confidence interval limits of sensitivity and specificity in the reported test[1]. This sensitivity analysis tests the stability of the deduced probabilities in the most conservative manner.

RESULTS: The "Treatment Threshold Probability" (P*) was .04. The "No Treatment-Test Threshold Probability" (P1) was respectively, .002 and .01 with the best and worst quoted sensitivity and specificity of the test. The "Test-Treatment Threshold Probability" (P2) was respectively, .66 and .19 with the best and worst quoted sensitivity and specificity of the P NMRS test.

DISCUSSION: The pretest probability of disease at which the physician is indifferent to giving or withhold treatment (P*) is low (.04). This confirms the intuitive impression that the least hint of MH susceptibility in a patient will influence the practising anaesthetist to treat. Treatment in this instance, is the innocuous avoidance of triggering agents and the possible administration of Dantrolene. The extremely low P1 (.01) also confirms this clinical stance. The range of pretest probabilities at which testing would influence clinical decision making is very narrow (.01 to .19) when the worst sensitivity and specificity are used (Figure 2). The majority of worrisome clinical presentations (masseter spasm alone or with accompanying signs, unexplained cardiac arrest or death) have pretest probabilities above .19[5]. Therefore, testing in these situations will not influence clinical decision making. Testing in possible MH susceptible patients may be utilized for other reasons; to reassure patients, to prevent indiscriminant litigation, and to advance the understanding of disease.

Presentation of cases for MH testing are increasingly composed of those with less obvious signs as awareness of MH has increased, monitoring has improved, and the number of aborted cases has risen. Even in this subset of patients, when testing would be extremely helpful, test performance does not direct management conclusively.

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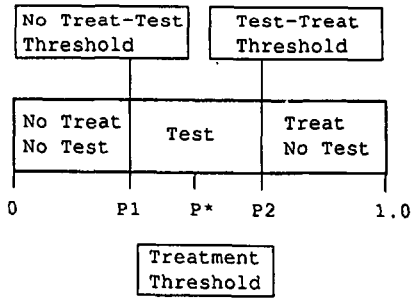
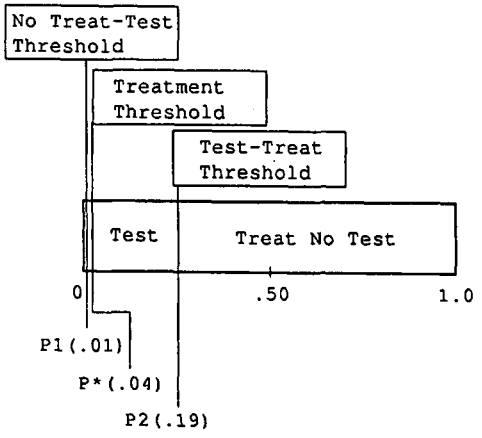


PROBABILITY OF DISEASE
Figure 1 (Adapted from Sox[2])



PROBABILITY OF MALIGNANT HYPERTHERMIA SUSCEPTIBILITY
Figure 2

CRITICAL RESPIRATORY EVENTS IN THE PACU

DK Rose, Dept. of Anaesthesia, St. Michael's Hospital, MM Cohen, Clinical Epidemiology Unit, Sunnybrook Health Science Centre, Toronto Ontario

INTRODUCTION:

Previous studies have documented the frequency of respiratory problems in the PACU (Post Anaesthetic Care Unit) but used nonspecific definitions of the outcome (e.g. all respiratory events) or did not investigate etiological factors.[1,2] We determined the frequency of PACU critical respiratory events - CRE (*desaturation* requiring ventilation or intubation, *hypoventilation* corrected by narcotic antagonists, assisted ventilation or intubation and *airway obstruction* requiring jaw thrust, airway insertion, racemic epinephrine or intubation) and the associated modifiable risk factors. We followed all patients admitted to our PACU (a unit which does not admit electively ventilated patients) for a 15 month period.

METHODS:

CRE were defined directly on PACU charts and nurses were trained to record their occurrence. After Ethics Committee approval for the study, copies of all OR and PACU records containing information on preoperative patient data, anaesthetic techniques, monitors, drugs and events were examined in a prospective manner and then entered into a computerized database. From the database, we first analyzed variables which have been shown to influence respiratory problems namely general anaesthesia, sex, age, ASA status and operative procedure in patients who had CRE and those who did not. All CRE occurred following general anaesthesia. The case-mix of patients with CRE was found to be markedly different from the general surgical population making the study of modifiable risk factors difficult. Therefore we used a matched analysis with control patients being similar in preoperative case-mix to the CRE cases. Thus for each patient with CRE, 4 controls who also had general anaesthesia were chosen from the non-CRE patients and matched by sex, age <60 or >60, ASA status <2 or 3+, and surgical procedure (13 categories).

Intraoperative techniques and drugs, and other associated postoperative outcomes were compared for the CRE groups versus their matched controls. The relationship between each potential risk factor and CRE was determined by calculating the relative odds (and 99% CI) of having the risk factor for the CRE group versus their matched controls.[3]

RESULTS:

15,779 patients (98.5% of all OR patients who were not electively ventilated postoperatively) were admitted to PACU during the 15 months. One or more CRE occurred in 217 patients (1.4%). They included *desaturation* episodes (30), *hypoventilation* (64), and *airway obstruction* (183). Reintubation was necessary in 17 cases, only 2 of whom were extubated prior to PACU discharge. Fifteen of the CRE patients required admission to ICU for unplanned postoperative ventilation.

CRE patients were more likely than controls to have hypotension (relative odds = 2.1), hypertension (2.4), tachycardia (9.6) and dysrhythmia (8.0) $p<0.05$. Anaesthetic factors associated with increased risk for CRE as compared to controls (Table) included morphine premedication (relative odds = 1.7), being intubated (4.5), having received fentanyl >2μg/kg/hr in the OR (2.4), or having received atracurium >.25mg/kg/hr (2.1) or pancuronium >.025mg/kg/hr (2.4).

Factors not associated with increased risk for CRE were non-narcotic premedication, duration of anaesthesia, choice of inhalational agent, use of monitors, rapid sequence induction, and difficult intubation.

DISCUSSION:

CRE were found in 1.4% of cases admitted to our PACU and while small in number, these were great in terms of management. These patients also were more likely to suffer from other adverse events in the PACU. Using the matched analysis, we were able to determine that various potentially modifiable risk factors were associated with an increased risk of CRE. These included techniques and drug choices which are under the control of the anaesthetist. Further studies at our hospital will consider modifications to our anaesthetic management to determine if the rate of CREs can be reduced.

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TABLE Anaesthetic factors associated with CRE (p<.01)

ANAESTHETIC TECHNIQUE	RELATIVE ODDS RATIO
Morphine Premedication any dose	1.7
Intubation	4.5
Intraop Fentanyl >2μg/kg/hr	2.4
* Atracurium >.25 mg/kg/hr	2.1
* Pancuronium >.025 mg/kg/hr	2.4

* administered to patients who were mechanically ventilated

USING CLINICAL ASSESSMENT TO PREDICT DIFFICULT DIRECT LARYNGOSCOPY

C.P. Bellhouse M.B.,B.S.,F.F.A.R.A.C.S., Caroline Dore, B.Sc.

Murwillumbah Hospital, Murwillumbah, 2484, NSW, Australia. Clinical Research Centre, London U.K.

INTRODUCTION: Because it would help to reduce morbidity and mortality, clinicians (1-3) have attempted to improve the predictability of difficult intubations, even though one recent study concluded that it was not possible to identify the difficult patients without the false positive rate increasing unacceptably (3). In this study, we examine a combination of criteria that seemed most promising from earlier studies in an attempt to devise an improved system of predictability which might be put to widespread use.

METHOD: Institutional Committee approval was obtained for this study. One hundred and thirty one patients aged over 17 requiring laryngoscopy at anesthesia were studied over a 9 month period, and to obtain sufficient numbers of grades 3 and 4 difficult laryngoscopy patients, 19 randomly selected patients of grade 3 and grade 4 who had been examined and laryngoscoped at an earlier period were added. The criteria chosen for study were, tongue size (1) extension of head on neck [V21 (2) and AOW], mouth opening measured with all dentures removed [I.G.(3)], chin size [V16 (2) (estimate)] and maximal protrusion forward of the lower incisors beyond the upper incisors [SLux (3)]. Head extension (AOW) was assessed as follows: "with the patient lying down, flex the head and neck as far as possible, hold the hand under the neck to keep it in position, and then extend the head as far back as possible (ensuring with the hand under the neck there is no neck movement) estimate whether there is about 30 degrees of extension at the AO joint, about 15 degrees, or virtually no movement." (*Personal communication M.E. Wilson.) Acceptable measures and points allocated for unfavourable findings were as follows: tongue size, grade 2 or better (allow 1 point for each grade worse); head extension, grade 2 or better or AOW 30 degrees or better (allow 1 point for each grade worse or each 15 degrees reduction), mouth opening 5 cm (allow 1 point for each 0.5cm reduction to maximum of 2 points), chin size 2.5cm (allow 1 point for each 0.5 cm reduction to maximum 2 points) lower teeth protrusion, SLux 0 mm (allow 1 point for each 2 mm reduction to maximum 2 points). The pharyngo-laryngeal view was also graded (4). Macintosh laryngoscopes size 3 and 4 were used and external pressure was applied to the larynx where necessary, attempting to improve the view.

RESULTS: 2 out of 37 patients (6%) with no points for unfavourable criteria were difficult to laryngoscope (grade 3 or 4 laryngeal view). 6/38 patients (16%) of those with 1 unfavourable criterion point were difficult. 9/29 patients (31%) with 2 unfavourable points were difficult, and 26/46 patients (57%) with 3 or more unfavourable points were difficult to laryngoscope.

CONCLUSIONS: Prediction of difficult laryngoscopy still cannot be done with absolute precision; occasionally a patient will be falsely predicted as unlikely to be difficult. But the results that can be obtained make the exercise well worthwhile. In the same way that obstetricians approach labour, anesthesiologists should cautiously approach every intubation as a 'trial of intubation', especially in those patients with one or more points for unfavourable criteria. This is particularly applicable if the patient is at risk of regurgitation, or if the anesthesiologist suspects there could be difficulty with pulmonary ventilation.

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Controlled Hypotension and Blood Transfusion for Lefort I Osteotomy

William E. Code, MD, FRCPC, T.W. Rachwal, MD, D.T. Lanigan, DMD, MD, Raymond Yip, MD, FRCPC, Peter G. Duncan, MD, FRCPC
Departments of Anaesthesia and Dentistry, University of Saskatchewan, Saskatoon, Saskatchewan, Canada, S7N OXO

INTRODUCTION: Controlled hypotensive anaesthesia is frequently used to reduce blood loss in elective Lefort I Maxillary Osteotomy. A review of the literature reveals no studies specifically testing the value of controlled hypotension in this surgical procedure. It could be suggested controlled hypotension may have increased or decreased benefit because of the surgery being done on very vascular bone. In addition, many centres have switched to autologous blood collection and transfusion to reduce homologous transfusion. Our first hypothesis is that controlled hypotension reduces blood loss and a second hypothesis is that autologous transfusion minimizes the need for homologous transfusion.

The Lefort I Maxillary Osteotomy is a standardized surgical procedure of major proportions performed in a very vascular area. The risk of a life-threatening haemorrhage from this procedure is less than one per cent, although such cases have been reported.[1,2] Since the increasing popularity of autologous blood collection blood transfusion practices have changed in our institution, despite the same two surgeons having done all the cases. An audit of our results may enhance our understanding of controlled hypotension and transfusion practices.

METHODS: A retrospective audit included all patients undergoing Lefort I Maxillary Osteotomy over a ten year period in our institution. Controlled hypotension was defined as a 20% or greater reduction in mean blood pressure from the baseline recorded at rest on the ward. Each anaesthesia record was reviewed by a single anaesthetist (WEC) to ascertain if hypotension was employed. Parameters collected included demographics such as age, sex, transfusions and perioperative hemoglobins. Data was evaluated statistically with the Mann-Whitney test using normal two-tail approximation with a p value of 0.05 or less denoted as significant.

RESULTS: Orthognathic surgery, which included a Lefort I osteotomy was performed on 45 patients prior to the institution of an autotransfusion program (see Group 1, table I). The diagnoses included 1) midfacial/maxillary retrusion/maxillary hypoplasia, 21 patients (46.7%) 2) long face syndrome (maxillary alveolar hyperplasia), 14 patients (31.7%), 3) apertonathia, 7 patients (15.6%), and 4) other, 3 patients (6.6%).

Eighty-one patients underwent a similar procedure after an autotransfusion program was instituted. The combinations of diagnoses requiring the procedure was the same as above with the exception of three patients for malunited facial fractures.

The blood loss in Group I ranged from 100 cc to 4,900 cc with an average blood los of 700 cc. The average blood loss values according to the kind of anaesthesia for both groups are given in Table II. The blood loss for the 81 patients undergoing surgery following institution of the autotransfusion program (Group II) ranged from 55 cc to 1800 cc, with an average loss of 528.5 cc. There was a statistically significant decrease with the use of hypotensive anaesthesia (p = .0165). Also, there was generally a decrease in the blood loss in those prepared by autologous transfusion compared to their historic controls. Four of 45 patients (8.3%) in Group I were transfused; the reasons were the low postoperative haemoglobin in one patient, and excessive intraoperative bleeding in three patients. Fourteen of 81 patients in Group 2 were transfused, (17.2%) all with autologous blood: two patients had a low postoperative haemoglobin, and 12 had perceived excessive intraoperative blood loss. The effect of controlled hypotensive anaesthesia can be seen in Table II, which reveals reduced blood loss in the patients that underwent hypotension (p = 0.0165).

DISCUSSION: Our results demonstrate, for the first time, that controlled hypotensive anaesthesia significantly decreases blood loss during elective Lefort I Osteotomy surgery. Also, none of the patients managed by autologous donation required homologous transfusion, evidence which supports the benefit of an autologous transfusion program for this surgery. Two questions which require further study are whether controlled hypotension is indicated in the presence of autologous blood donation and is autologous blood administered too frequently when it is available. Further investigation is required to evaluate these questions.

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TABLE I

	Age Range	Mean Age	Male	Female	Total Patients
Group I	14-57 yrs.	24.5 yrs.	8	37	45
Group II	14-57 yrs.	22.4 yrs.	38	43	81

TABLE 2: The average blood loss values accordingly to the kind of anaesthesia (p = .0165)

Kind of Anaesthesia	Mean blood loss during surgery
Hypotensive 93 pts	530.6 ± SE 53.7 ml
Normotensive 33 pts	706.2 ± SE 86.5 ml

OBESITY POSES A RISK FOR ADVERSE ANAESTHESIA OUTCOMES.

Duncan PG, Cohen MM
Dept. of Anaesthesia, Univ. of Saskatchewan, Saskatoon SK and
the Clinical Epidemiology Unit, Sunnybrook Health Science Centre, Toronto ON.

INTRODUCTION: Obesity is highly prevalent in western society, yet its role in the genesis of adverse anaesthetic outcomes remains undefined. Previous work has focused upon the morbidly obese undergoing abdominal procedures; the few studies of non-obesity surgery have confirmed only an increased risk of wound infections and thrombophlebitis. We sought to define what risk, if any, is associated with obesity and whether such risk is independent of co-existent cardiorespiratory disease.

METHODS: For each adult, non-obstetric patient provided inpatient anaesthetic services in four Canadian teaching hospitals in a 12 month period (88-89), a record was completed of demographics, medical illnesses, and factors affecting the conduct of anaesthesia. The anaesthetist documented any intraoperative events, while PACU nurses and research nurses recorded adverse postoperative events. Measures to ensure reliability and validity of the data, as well as population definitions have been presented earlier (1).

Patients were designated as "obese" if, in the opinion of the responsible anaesthetist, the body mass index was greater than normal. The crude rate of occurrence of measured outcomes was then calculated for "obese" versus "non-obese" subjects, and expressed as a relative risk of having the defined complication relative to the non-obese. The data was then reexamined by multiple logistic regression where those with or without associated cardiorespiratory (and other preoperative illnesses) and those undergoing equivalent surgical procedures could be prepared. The analysis also controlled for differences in age, gender and physical status. Due to multiple comparisons, statistical significance was accepted at the $P \leq 0.01$ level.

RESULTS: Of 27,195 inpatients, 3,577 (13.2%) were deemed obese. These patients had an age distribution (centred around 40-60 years), female predominance (65%) and physical status score (III-40% vs. 31%) greater than the non-obese. The obese had an increased frequency of perioperative problems especially in the cardiac and respiratory systems, including both medically important outcomes and those significant to patient comfort (Table). This increased relative risk persisted when the analysis was controlled for preoperative cardiorespiratory illness, age, gender and physical status.

CONCLUSIONS: Obese patients, when compared to non-obese individuals, are at increased risk of adverse anaesthetic outcomes during and after anaesthesia. Moreover, the absence of associated cardio-pulmonary or other diseases such as diabetes, does not reduce this risk to levels found in non-obese comparison subjects.

REF: Can J Anaes 1991:38:A51-A53.

Table I - Significant Adverse Outcomes

OR	Adjusted Relative Odds
↓ BP	1.36
↑ BP	1.43
Bronchospasm	3.20
Upper Respiratory	2.64
Lower Respiratory	2.49
PACU	
Nausea/Vomiting	1.31
Respiratory	1.70
Post-op	
Nausea/Vomiting	1.21
Sore Throat	1.78
Backache	2.32
↑ BP	0.75
Atelectasis	1.33
Bronchospasm	2.62
Lower Respiratory	1.55

Obese/non-obese $P \leq 0.01$

CAFFEINE-HALOTHANE CONTRACTURE (CHC) TEST: A COMPARISON OF TWO PROTOCOLS

J.B. Derdemezi MD FRCPC, B.A. Britt MD FRCPC
Department of Anaesthesia, The Toronto Hospital, Toronto General Division, 200 Elizabeth St., Toronto, Ontario M5G 2C4

INTRODUCTION

The only reliable test available at present for the diagnosis of MH is the invasive CHC test[1]. However, two separate and substantially different protocols for this test exist, namely the North American (NA)[1] and the European (E)[2]. Our aim is to compare these two methods.

METHODS

Skeletal muscle has been obtained from 139 patients who have been classified into two groups, MH Suspects (MHS) and Controls. The patients in the MHS group are individuals who have exhibited an MH reaction, family history of MH, or chronic elevation of CK in combination with muscle pain, while those in the control group have no personal or family history of MH. In the NA protocol[1], separate muscle fascicles are exposed to either 1, 2, or 3% halothane or to incremental doses of caffeine (0.5, 1, 2, 4, 8, 32 mMol). However, with the E protocol, doses of halothane are added cumulatively to one strip (0.5, 1.0, 1.5, 2.0) as are the doses of caffeine (0.5, 1.0, 1.5, 2.0, 3.0, 4.0, and 32 mM). Parameters calculated for halothane and for caffeine are as follows: the amplitude of halothane contracture in grams for the NA protocol; the dose of halothane required for a threshold contracture for the E protocol; the dose of caffeine required for a 1.0 Gm contracture (CSC) for the NA protocol; and the dose of caffeine required for a threshold contracture for the E protocol.

RESULTS & DISCUSSION

T-tests, ANOVAs and correlation coefficients have shown significant differences between the two methods. Also, partial disagreement in diagnosis has been observed in 42 of 139 patients and complete disagreement in diagnosis has been observed in 6 of 139 patients. All of the latter have been positive by the NA method and negative by the E method. Additionally, with the E method, repeated additions of incremental doses of halothane to the same strip fatigues the muscle. Thus, with higher doses of halothane, the contracture amplitudes often decline rather than increase. This fatigue may have contributed to a higher incidence of false negatives using this method. The measurement of halothane threshold contractures which have been arbitrarily set at 0.2 mM in the E protocol is considerably more difficult and less accurate than is the measurement of contracture amplitudes in the NA protocol because of the flatter curves with the former technique. The clinical groups derived by the CHC test using the NA protocol are HC, H, C and N (normal) while those from the E method are MHS, MHE (equivocal) and MHN (normal). The term "equivocal" is very confusing to both patients and physicians. Is such a patient positive or negative? Some of our patients with a history of typical MH reactions were diagnosed as MHE. Therefore, a more definitive term should be used in order to avoid confusion.

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CONCLUSION

From this study it appears that the European method is less reliable once diagnostic discrimination is less and there are more false negative results.

IS SUCCESS IN ANAESTHESIA PRACTICE AFFECTING RESIDENT EDUCATION?

Duncan PG, Cohen MM, Yip R
Dept. of Anaesthesia, Univ. of Saskatchewan, Saskatoon SK and
the Clinical Epidemiology Unit, Sunnybrook Health Science Centre, Toronto ON.

INTRODUCTION: The modern practice of anaesthesia has successfully reduced the rate of associated morbidity and mortality. In addition, technologic advances in surgery combined with considerations of resident workload and the need for didactic instruction, have modified current anaesthesia resident experience. This study questions whether current anaesthesia training affords sufficient opportunity to develop clinical expertise in the specialty.

METHODS: For a 12-month period in 1988-89, we conducted an outcome study in four teaching hospitals in Canada (1). Data was collected from all adult, non-obstetric patients describing case-mix, operative procedure, anaesthetic deployed and outcomes occurring intraoperatively, in the PACU or within 72 hours of the procedure. We determined the frequencies of patient case-mix, anaesthetic techniques and index events then estimated the exposure of an "average" resident over a one and four year period by determining the proportion of cases attended by a resident and dividing by the number of residents.

As a basis for comparison, the Program Directors of the 16 accredited Canadian anaesthesia programs were surveyed, and the averages of the responses adapted as the consensus of the experience (i.e. the number of encounters during training) necessary for "independent" (safe) and "consultant" (specialist) practice. Comparison of the residents' experience and the Program Directors was done using the unpaired t-test ($P \leq 0.05$).

RESULTS: Of 37,665 patients in the study, approximately 50% were attended by an anaesthesia resident. While the rate of high risk patients and adverse events varied, there was no hospital which had consistently higher rates. The total number of residents doing clinical anaesthesia rotations was 28; of the 16 Program Directors survey, 8 (50%) responded.

The actual number of high-risk patients, anaesthetic procedures and adverse events encountered by the "average" resident, together with the consensus number needed to be "safe" or act as a "consultant" is given in the Table. Except for the technical aspects of invasive monitoring (i.e. arterial line or CVP), anaesthesia residents appear to be getting less than the desired exposure to complex patients and various adverse events.

DISCUSSION: Clinical experience has been demonstrated to correlate positively with success at specialty examinations in anaesthesiology (2). Clinical expertise, not usually assessed by the examination process, has also been associated with experience and development of "illness scripts" (3). However, due to the low rate of adverse events seen in today's practice, residents appear not to be receiving the exposure we have assumed necessary. We conclude that the content of current clinical training in anaesthesia should be examined with respect to the competencies achieved, and alternative educational strategies developed to compensate for the deficiencies induced by the specialty's success.

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Table: The desired vs actual number of events for an "average resident"

Patient Variables	Desired Experience		Actual Experience	
	Safe	Consultant	12 months	48 months
Hypertension	13.3	30.7	27.1	108.5
Renal Disease	7.8	23.1	4.9	19.5*
MI < 6/12	6.6	16.4	2.7	10.9*#
Adverse Anes Hx	8.5	16.3	3.3	13.1*
Trauma	13.3	34.4	3.9	15.4*#
Anaesthesia Techniques				
Plexus Block	12.2	31.8	4.1	16.3*#
Spinal	21.9	58.8	21.1	48.3*
CVP	11.3	26.9	17.1	68.2
P.A. Cath	10.9	39.4	9.2	36.9*
Art line	14.4	39.1	27.0	108.0
Adverse Outcomes				
Diff Intubation	13.3	29.1	2.2	8.8*#
Cardiac Arrest	6.6	18.6	1.2	4.8*#
Aspiration	2.3	9.1	1.0	4.0*
Drug Incident	2.9	7.8	1.1	4.3*#
PACU Respiratory	9.1	25.0	3.3	13.1*#
Awareness	1.2	2.9	1.0	4.0

* Actual < desired for 4 years
\# $p \leq 0.01$

HISTAMINE RELEASE BY INTRAVENOUS OPIOID ANALGESICS

D.E. Withington, FFARCS, F. Reynolds, FFARCS, A. Patrick FFARCS, W. Man, PhD*
St. Thomas Hospital, London, England
Hammersmith Hospital, London, England*

INTRODUCTION

Diamorphine and morphine are strong opioid analgesics routinely used for post-operative pain relief in the UK. Significant histamine release has been demonstrated after morphine and diamorphine administration in the dog (1) and after morphine in man (2). However, these drugs have not been compared clinically in man with respect to histamine release.

METHODS

Ethical committee approval was obtained. The study was double-blind and randomised. All patients were scheduled for abdominal surgery and received temazepam pre-medication. Fentanyl was used for pre-operative analgesia. Post-operatively a baseline blood sample was taken from an in-dwelling cannula and when analgesia was requested the patients were randomised to receive either morphine 0.16mg/kg or diamorphine 0.08mg/kg intravenously. Blood samples were taken 1, 2.5, 5, 10, 15 and 20 minutes after drug administration into EDTA tubes on ice and spun at 2000rpm for 10 minutes. The plasma was stored at -20°C until assayed by the single isotope radio-enzymatic technique (3). Histamine release was defined as a plasma concentration of >1ng/ml or a rise of >400% over baseline. Pain was assessed by linear analogue scores.

RESULTS

Thirty-six patients gave informed consent, 17 receiving morphine and 18 diamorphine. The 2 groups were comparable in terms of demographic factors. Analgesia was similar in the 2 groups. Using the above criteria histamine release occurred in 6/17 (35.3%) patients receiving morphine (Figure 1) and 6/19 (31.6%) patients (Figure 2) receiving diamorphine. Substituting the criteria of a rise of >1000% histamine release occurred in 17.6% of morphine subjects and 26.3% of diamorphine subjects. There was no significant difference between the groups on chi-squared testing.

Pharmacokinetic parameters were examined. Histamine release occurred earlier in the diamorphine group with a mean Tmax of 1.17 minutes compared to 6.83 minutes for morphine ($p<0.01$). There was no significant difference in Cmax between the groups. In each group one patient produced extremely high peak histamine concentrations (diamorphine: 23.1 ng/ml; morphine: 48.47 ng/ml). Area under curve (Auc) was 8.7 ng.min/ml for diamorphine and 10.31 ng.min/ml for morphine

DISCUSSION

Morphine and diamorphine cause histamine release in approximately one third of patients receiving intravenous boluses. There is thus no apparent difference between the histamine releasing properties of these 2 analgesics. The difference in time course of histamine release correlates with the different pharmacokinetics of the two drugs, diamorphine being more fat soluble. Previous work on dogs has failed to demonstrate histamine release from basophils in vitro but has suggested release from lung mast cells (1). These findings would be compatible with our results as basophil degranulation is not affected by fat solubility whereas access of drugs to mast cells is. The time course demonstrated in this study would therefore suggest that opioid-induced histamine release is from mast cells.

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PLASMA HISTAMINE AFTER MORPHINE BOLUS

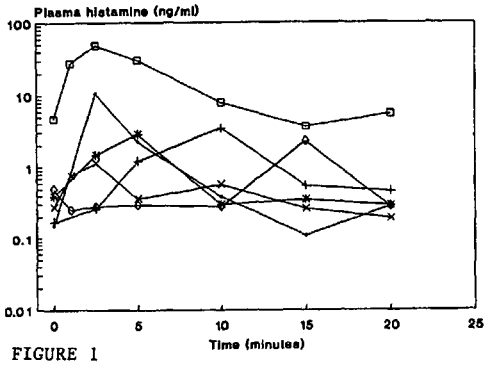

FIGURE 1

PLASMA HISTAMINE AFTER DIAMORPHINE BOLUS

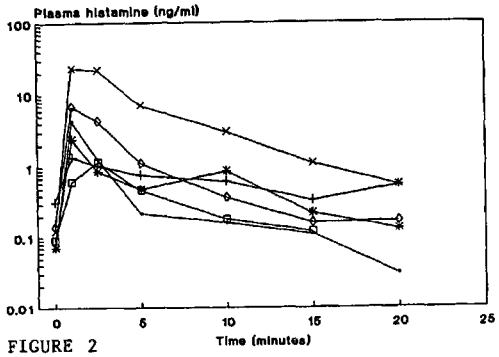

FIGURE 2

ASSESSMENT OF CONTINUOUS BLOOD PRESSURE MEASUREMENTS BY ARTERIAL TONOMETRY (N-CAT) IN RAPID ATRIAL FIBRILLATION

N.R. Searle, M.D., J. Perrault, Ph.D., H. Ste-Marie, R.N.
Department of Anaesthesia, Montreal Heart Institute, 5000 Belanger East, Montreal, Quebec, Canada H1T 1C8

INTRODUCTION: Comparing invasive and noninvasive methods of blood pressure measurements places the latter method at a disadvantage, especially with respect to accuracy and continuous beat to beat pressure recording. New technology and improvement in software made it possible to conceive monitors able to accurately depict beat to beat systemic blood pressure noninvasively. Arterial tonometry (TBP) is a newly developed noninvasive method able to reproduce the blood pressure waveform and calculate its systolic, diastolic and mean pressure values.[1] A reported correlation of 0.83-0.91 for arterial tonometry to the invasive method (IBP) has recently been published.[2] This correlation, though decreased in the same study to 0.70-0.81 under controlled hypotension. We were interested in assessing the accuracy of TBP during rapid atrial fibrillation.

METHODS: After ethic committee approval, 8 patients were included in the study. All were postoperative cardiac patients with rapid atrial fibrillation (H.R. > 100/min) but were hemodynamically stable. The IBP was recorded from cannulation of the radial artery with a 20-gauge catheter which was linked to a Sorensen arterial transducer (Abbott Critical Care). All arterial transducers were calibrated and zeroed before each study. Radial artery pressure was read every minute from data stored in the Siemens 1281 monitor. The contralateral radial artery was used for tonometric readings. TBP was recorded by the N-CAT monitor (Nellcor Inc., Hayward, CA). Similarly, TBP were read every minute from stored N-CAT data. Paired values for systolic, diastolic and mean pressures were analyzed by Student's t-test for differences between the two blood pressure methods and correlation coefficients were obtained for systolic, diastolic and mean arterial pressures between the two methods. We also determined the accuracy of the N-CAT by measuring its bias (mean prediction error) and precision (mean absolute error) according to references.[2,3]

RESULTS: Descriptive data between IBP and TBP during rapid atrial fibrillation are illustrated in Table 1. The systolic and diastolic blood pressures were statistically different. The figure presents the graphic representation with the correlation coefficients obtained for individual blood pressures. The correlation coefficient range from 0.52-0.84 and all are statistically significant. Finally, Table 2 lists bias and precision values between the two methods.

DISCUSSION: Although the systolic and mean blood pressures are statistically different between the two methods, these differences are not clinically relevant. Our correlation coefficients for systolic and mean blood pressure values are significant and are consistent with those reported by Kemmotsu[2] for patients under controlled hypotension. While our paired diastolic readings were not statistically different, they revealed a very low correlation coefficient. This may be attributed to the way diastolic reading are obtained. The continuous noninvasive diastolic blood pressure is not a measured pressure but rather is a calculated value. Our diastolic correlation coefficient was lower than those reported by Kemmotsu.[2] Finally, the bias and precision values obtained in this study are well within the requirements for equivalency to invasively determined arterial pressure established by the Association for the Advancement of Medical Instrument. In view of the specific study design, we believe that the TBP is able to reliably approximate IBP during rapid atrial fibrillation. We also believe that more investigative work should be done to evaluate these monitors under various pathological states where there might be a tendency to malfunction.

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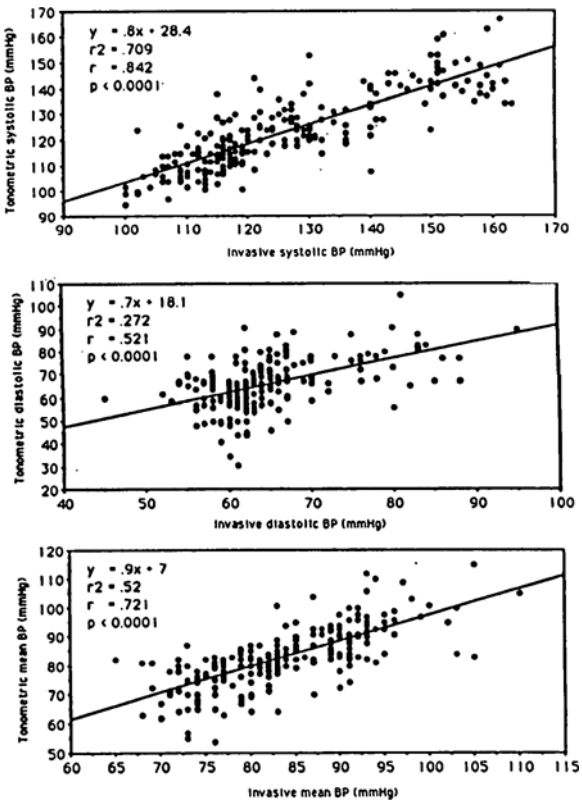
Table 1 Descriptive data between IBP and TBP

	IBP Mean (SD)	TBP Mean (SD)	p (value)
Systolic	125.7 (16.0)	122.8 (14.3)	0.0001
Mean	83.7 (8.0)	82.9 (10.1)	0.0440
Diastolic	64.3 (7.2)	65.5 (10.2)	0.0680

Table 2 Bias and precision values between IBP and TBP

	Systolic Mean (SD)	Diastolic Mean (SD)	Mean Mean (SD)
Bias	-2.83 (4.47)	1.30 (5.02)	-0.64 (2.06)
Precision	6.72 (2.71)	6.84 (3.1)	5.19 (1.78)



SEDATION FOR COLONOSCOPY: A DOUBLE-BLIND COMPARISON OF DIAZEPAM, MIDAZOLAM AND PROPOFOL

Mark A. Kostash, MD, Richard Johnston, MD, R. J. Bailey, MD
Departments of Anaesthesia and Gastroenterology,
University of Alberta, Royal Alexandra Hospital, 10240 Kingsway, Edmonton, AB, T5H 3V9

INTRODUCTION

Colonoscopy can be performed without sedation under certain circumstances; however, the majority of patients require benzodiazepines or narcotics to tolerate the procedure (1). The effects of sedation often persist long into the recovery period. Complications may arise when sedation is too generous or stimulation subsides, leaving a patient at risk of significant respiratory depression and hypoxemia. The purpose of this study was to compare three sedation techniques using the following criteria: reliability of sedation, speed of recovery and severity of oxygen desaturation.

METHODS

Approval was obtained from the Ethical Review Committee. 60 consecutive patients scheduled for elective colonoscopy agreed to participate and were randomized into three intravenous sedation groups. The study was a prospective, double-blind clinical trial. Diazepam, midazolam and propofol were diluted to equipotent concentrations using intralipid. Continuous pulse oximetry (SpO2) and non-invasive blood pressure were measured. All patients were sedated to 3 or 4 on a 5 point scale (2) (see Table 1). Group D received diazepam plus meperidine, Group M received midazolam plus fentanyl, and Group P received propofol plus fentanyl followed by a continuous infusion of propofol at 50μg/kg/min. Groups D and M were given an infusion of intralipid as a control. Oxygen was administered if the SpO2 dropped below 85% for greater than 15 seconds. Following the procedure, Aldrete scores (3) were calculated every 15 minutes. After one hour, patients completed a questionnaire regarding side effects and adequacy of sedation. Statistical analysis included ANOVA for oxygen saturations, recovery times and vital signs. Pooled estimate of proportions were calculated for side effects.

FIGURE 1: DECREASE IN SpO2 AFTER SEDATION

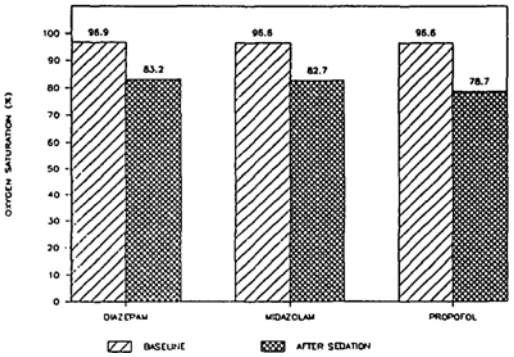


TABLE 1: SEDATION SCALE

Level 1 - Fully awake and oriented
Level 2 - Drowsy
Level 3 - Eyes closed but rousable to command
Level 4 - Eyes closed but rousable to mild physical stimulation
Level 5 - Unrousable to mild physical stimulation

RESULTS

Fifty seven patients completed the study. There were no significant differences in patient demographics or baseline vital signs between the groups. Group D required a total of 0.12mg/kg of diazepam and 2.0mg/kg of meperidine. Group M received 0.07mg/kg of midazolam and 2.2μg/kg of fentanyl. Group P required 1.3mg/kg of propofol and 2.2μg/kg of fentanyl, plus a mean propofol infusion of 76.5μg/kg/min. No differences were measured in rate of recovery following the three sedation techniques. A significant decrease in SpO2 occurred following sedation in all groups (see Figure 1). Only 5 of the 57 patients maintained an oxygen saturation above 90% throughout the procedure while 11 patients dropped below an SpO2 of 75%. Oxygen was required in a total of 12 patients, 7 of whom were in Group P. 15 patients complained sedation was inadequate, 8 in Group M. In each group 40% of patients experienced moderate to severe pain during colonoscopy.

DISCUSSION

Midazolam and propofol were not superior to the established combination of diazepam and meperidine for sedation during colonoscopy. While reports describe a faster recovery from propofol when compared to diazepam and midazolam (4), our study did not support this conclusion. The contribution of narcotic agents to residual sedation may explain this disparity. Despite relatively high doses of sedatives and narcotics, over one quarter of patients were not satisfied with the sedation and analgesia provided. The study revealed a significant decrease in SpO2 in all three sedation groups. When patients are elderly or have underlying cardiopulmonary pathology, hypoxemia can be particularly dangerous. Therefore, we recommend that supplementary oxygen be administered to all colonoscopy patients.

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ORGAN DONOR PROBLEMS AND THEIR MANAGEMENT: A FOUR YEAR REVIEW OF A CANADIAN TRANSPLANT CENTRE

M.J. Ali MD, G. Wood MD, A.W. Gelb MD,
Department of Anaesthesia and Program in Critical Care, University Hospital,
339 Windermere Road, London, Ontario N6A 5A5

INTRODUCTION

Effective perioperative management of medical problems in the donor has significant impact on organ availability for transplantation and graft function in the recipient. In order to document the type and frequency of medical problems encountered by anaesthetists in adult donor management, we conducted a retrospective chart review.

METHOD

Charts from 43 local adult donors between 1986 and 1990 were reviewed. Only local donors were included in the study as donor information and problems were more accurately recorded. Each chart was reviewed for demographics, cause of death, haemodynamic data, inotropic requirements, fluid and electrolyte data, respiratory problems, anesthetic management and organs harvested. Results are presented as mean ± sd.

RESULTS

There were 18 females and 25 males with a mean age of 35.8 ± 13.9 years. Subarachnoid haemorrhage and head injury were the commonest cause of brain death (Fig 1). Hypotension requiring inotropic support and central diabetes insipidus (CDI) requiring fluid and antidiuretic hormone therapy were the commonest problems (Fig 2). Other problems included electrolyte (especially in patients with CDI) and temperature disturbances, arrhythmias, high oxygen or peep requirements and coagulopathy. Intraoperative data are shown in Table I. Muscle relaxants were required to control the viscero-somatic reflexes that can result in complex muscular movements. Some patients required narcotic and/or inhalational agents to control the viscero-visceral reflexes that cause hypertension. Large amounts of crystalloid, and in some patients, blood was required. Central venous pressure provided adequate monitoring in most patients and Swan Ganz catheters were used only in a few patients. Multiple organs were harvested from each donor.

CONCLUSIONS

Organ donors have complex medical problems. The attending anaesthetist needs to be cognizant of these problems and be fully prepared to manage them in the OR so as to prevent organ loss or damage.

TABLE I

PRE AND INTRAOPERATIVE DATA (N = 43)

Anesthetic Time (mins)	225.4 ± 69.6
Urine output (mls/hr)	282.3 ± 258.8
Crystalloids required (mls)	4617.4 ± 2934.6
Blood Transfused (units)	2 ± 3.4
CVP monitored in	32
CVP (mmHg)	11.3 ± 4
Swan Ganz monitored in	5
Relaxant required in	32
Narcotics/inhalationals required in	19
Inotropes (μg/kg/min):	
- Dopamine <10	18
- Dopamine >10 or Epinephrine or Norepinephrine used in	13
Organs Harvested: Kidneys	34
Livers	31
Hearts	28
Others (corneas, skin, bone)	16

Fig 1

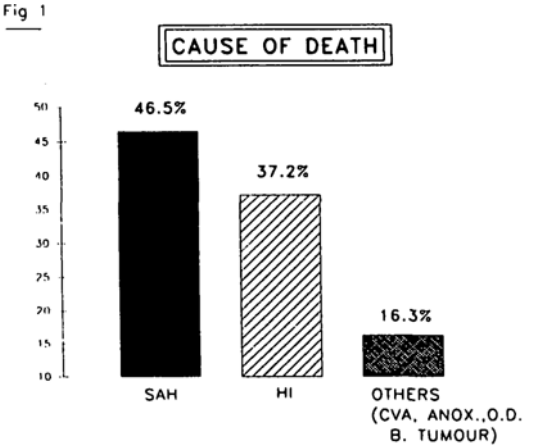
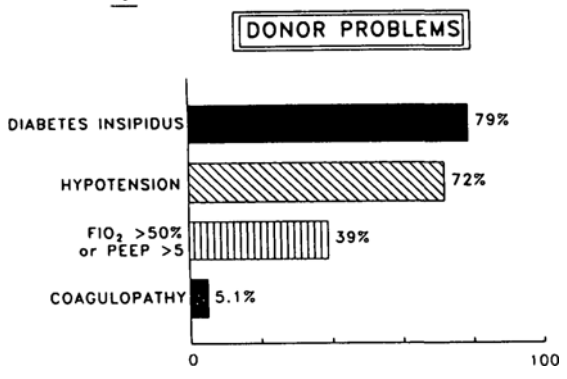


Fig 2



CYCLOSPORIN POTENTIATES VECURONIUM BLOCKADE AND PROLONGS RECOVERY TIME IN HUMANS

MD SHARPE FRCPC, AW GELB FRCPC
Department of Anaesthesia/Critical Care, University Hospital,
University of Western Ontario, London, Ontario N6A 5A5

INTRODUCTION

Cyclosporin (CsA) is an important immunosuppressive agent administered to most transplanted patients. Recent clinical reports have implicated CsA in prolonging neuromuscular blockade post-operatively.[1,2,3] Gramstad el al have shown the augmentation of neuromuscular blockade by CsA in cats.[4] Therefore, we studied the effects of CsA upon augmentation and recovery from vecuronium induced neuromuscular blockade in humans.

METHODS:

With Ethics Committee approval and signed consent 4 patients undergoing donor related kidney transplantation were studied. Anaesthesia was induced with thiopentone (4-5 $mg.kg^{-1}$), lidocaine 1.0 $mg.kg^{-1}$, fentanyl (3 $\mu g.kg^{-1}$) and tracheal intubation facilitated with succinylcholine (SxCH, 0.5 $mg.kg^{-1}$). Maintenance anaesthesia consisted of oxygen/nitrous oxide (FIO_2 0.30-0.40) to maintain $SaO_2 \geq$ 96%, and isoflurane (1.0%, end-tidal). Positive pressure ventilation was used to maintain normocapnea (Nellcor capnograph). Using a Datex NMT-221 monitor (Puritan-Bennett) a continuous electromyogram (EMG) was recorded with surface electrodes over the hypothenar muscles in response to train-of-four supramaximal stimulation of the ulnar nerve at a frequency of 2Hz. 30 min was allowed to elapse following SxCH. Vecuronium was then administered (0.03-.04 $mg.kg^{-1}$) to induce paralysis and the block was allowed to recover spontaneously. The recovery time (time from T4/T1 ratio of 0.25 to 0.75) was recorded and served as our control. Subsequently, a vecuronium infusion was titrated to maintain a steady-state level of neuromuscular blockade at approximately 50% depression of the first twitch height. A CsA infusion (3 $mg.kg.^{-1}$ hr^{-2}) was then started and its effects on the level of blockade was recorded. Once initiated, the CsA infusion was constant for 24 hrs. The vecuronium infusion was then stopped and the neuromuscular blockade allowed to recover spontaneously. The recovery time was again measured. For statistical analysis, comparison of recovery time before and during CsA infusion was made using paired Student's t-test. Results are expressed as mean ± SD.

RESULTS:

The initiation of the CsA infusion caused an augmentation of neuromuscular blockade in all patients (range 17-64%). As well, the recovery time was significantly increased from 16.7 ± 2.7 to 27.6 ± 3.9 min ($p<0.05$). (see Figure)

DISCUSSIONS:

This study confirms in humans the ability of CsA to augment neuromuscular blockade as well as prolong the recovery time. This study emphasizes i) the need for monitoring of neuromuscular blockade, particularly in patients taking cyclosporin and ii) the potential for CsA to potentiate residual neuromuscular blockade in the recovery room and cause "recurarization". This may result in the need for re-intubation / ventilation.

REFERENCES:

1. Can J Anaesth 37:543-8, 1990
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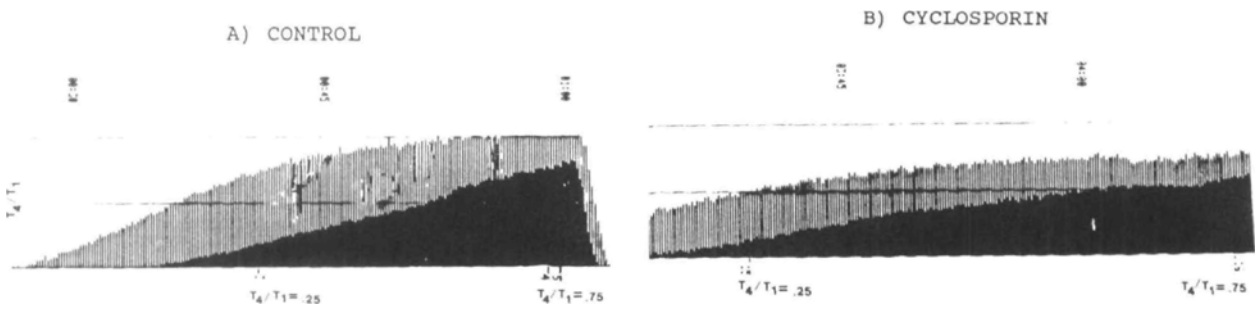
FIGURE:

Figure demonstrates the prolongation of recovery time during CsA (b) infusion compared to control (a).



AMINOGLYCOSIDE PHARMACOKINETICS IN POST-OPERATIVE SURGICAL AND NEUROSURGICAL PATIENTS

R.P. Woda DO, M. Haug Pharm D, P. Slugg MD, J Lockrem MD, G. Barnett, MD
The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, Ohio 44195, U.S.A.

INTRODUCTION

The use of aminoglycoside antibiotics for the management of various infections occurs frequently in the post-operative critical care setting. The etiology of such infections are quite variable as are the surgical procedures performed. The purpose of this study is to determine the pharmacokinetic profile of aminoglycoside antibiotics in different types of postoperative intensive care patients.

METHODS

General surgical patients were compared to neurosurgical patients in two separate intensive care units. Pharmacokinetic data was determined on post-operative surgical and neurosurgical patients for the first three days of therapy with gentamicin or tobramycin. All patients on aminoglycoside antibiotics were admitted to the study. Collected data included patient's age, height, weight, surface area, and gender along with aminoglycoside dosing schedule and serum levels. Serum creatinine values were determined and creatinine clearances were calculated for each patient. Aminoglycoside pharmacokinetics were calculated using a computer program developed at the University of Southern California. One-hundred and eleven general surgical patients and seventy neurosurgical patients comprised the two groups.

RESULTS

Height, weight and surface area of the study population were not significantly different. (See Table). There were more males in the general surgery group. The general surgical population was also older compared to the neurosurgical group. Baseline serum creatinine values were higher in the general surgical group and calculated creatinine clearances were lower. The volume of distribution was higher and the half life of the chosen aminoglycoside was longer in the general surgery group. The post-operative general surgery patients required 12.5% larger doses to obtain similar peak aminoglycoside levels compared to neurosurgical patients.

DISCUSSION

Appropriate serum levels of aminoglycoside antibiotics are essential for maximizing therapeutic intervention [1]. Pharmacokinetic data is very useful in determining dosing regimes as patient populations are very different [2]. This study shows that general surgical post-operative patients require higher doses and longer dosing intervals than post-operative neurosurgical patients. The explanation for this variation is based on differences in the pathophysiology of disease states in the two populations. The results of this study support the use of population kinetics in determining dosing guidelines for specific patient groups. Traditional dosage guidelines based on patient body weight may provide inadequate serum levels of aminoglycoside antibiotics.

TABLE

	SICU	NICU	P
Number	111	70	
Height (kg)	171±11	170±10	NS
Weight (cm)	74±17	73±16	NS
Surface area(m2)	1.9±.24	1.86±.25	NS
Males/Females	69/111	39/70	< 0.01
Age (yrs)	63±13	58±16	< 0.01
Serum creat.(mg%)	2.1±1.6	1.1±1.2	< 0.001
Creatinine clearance (ml/min/m2)	47±32	80±34	< 0.001
Volume of distribution (L/kg)	.36±.08	.32±.08	< 0.01
Half-life (hrs)	9.7±8.9	4.5±4.5	< 0.001

REFERENCES

[1] The American Journal of Medicine 77:657, 1984.
[2] Intensive Care Medicine 16:303, 1990.

POST BYPASS CA^{++}: EFFECTS ON LV DIASTOLIC FUNCTION AND HAEMODYNAMICS.

B.A. Finegan FRCPC(C), M. Robertson MD, D. Taylor MD, G. Frost RDCS,
S. Fossey BSc N, A. Koshal MD.
University of Alberta, 8440 - 112 Street, Edmonton, Alberta T6G 2B7

INTRODUCTION

An adequate intracellular Ca^{++} concentration is essential for normal systolic ventricular function. Diastolic ventricular relaxation however, requires active uptake of Ca^{++} into the sarcoplasmic reticulum. Ischemia is associated with disruption in this process and abnormalities of relaxation are early and sensitive markers of ventricular ischemia. Ca^{++} is frequently administered at the termination of cardiopulmonary bypass (CPB) with the aim of acutely increasing cardiac output (CO) and afterload. Increasing extracellular ionized Ca^{++} levels in a recently reperfused heart may impede ventricular relaxation. In this study we measured the effects of such treatment on post CPB left ventricular (LV) diastolic function and haemodynamics.

METHODS

Patients undergoing elective coronary artery bypass (by AK) were considered for inclusion in the study. The presence of significant valvular or congenital heart disease, atrial or ventricular dysrhythmias, or oesophageal pathology constituted preoperative exclusion criteria. If patients required pacing or were not in sinus rhythm post CPB they were also excluded. Anaesthesia was induced and maintained pre and post CPB with midazolam and sufentanil. Following induction, a 5 MHz single plane ECHO probe (Toshiba) was inserted to allow Doppler recording of mitral valve inflow velocities. These data were recorded on tape and subsequently analyzed off-line (Dextra 200 analysis system) to determine the E/A velocity ratio and the E-slope. The initial haemodynamic, blood gas, plasma ionized Ca^{++}, ST segment and Doppler measurements were performed post CPB following protamine administration (control). Ca^{++}, 10 $mg \cdot kg^{-1}$, was infused over 1 min and the subsequent measurements recorded 5 min later (post Ca^{++}). Data were subject to ANOVA for repeated measures and in the case of proportional data to Chi-squared tests.

RESULTS

To date, five patients have completed the study. Plasma ionized Ca^{++} were significantly different following treatment. No differences between control and post Ca^{++} values were observed in absolute and derived haemodynamic values, ST segments and blood gases. Ca^{++} did not alter either E/A velocity ratio or the E-slope. Two patients had reversed control E/A velocity ratios suggesting abnormal diastolic function. The E/A ratio or the E-slope in these patients did not change with Ca^{++} administration.

DISCUSSION

We have seen in the limited number of patients studied so far, no deleterious consequences of Ca^{++} administration post CPB. The post Ca^{++} haemodynamic data however, indicates that bolus Ca^{++} has only a transient effect on function. This confirms data of Shapira *et al.*.[1] The absence of effect on Doppler derived indices of LV relaxation may be a reflection of the rigid inclusion criteria. To measure E/A ratios and E-slope sinus rhythm is essential. Sinus rhythm post CPB preselects a group of patients less likely to have suffered ischaemic damage. Whether bolus Ca^{++} administration post CPB would have similar benign effects on diastolic function in the presence of ischemic reperfusion injury remains to be determined. This preliminary data does question the usefulness of bolus Ca^{++} post CPB.

REFERENCE

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PROPOFOL OR PROPOFOL/ALFENTANIL COMPARED TO THIOPENTONE/SUCCINYLCHOLINE FOR INTUBATION OF HEALTHY CHILDREN

Grant E.Rodney, MB, Clayton C. Reichert, MD, Desmond N. O'Regan, MB, Derek Blackstock, MB, David J. Steward, MB.
British Columbia Children's Hospital, Vancouver, British Columbia

INTRODUCTION: Propofol has been shown to depress pharyngeal and laryngeal reflexes more effectively than does thiopentone, allowing visualization of the vocal cords when given alone.(1) Intubation of adults, given propofol without muscle relaxants, has been reported.(2,3) This study was designed to evaluate intubation conditions in children after induction with propofol alone, propofol and alfentanil, or thiopentone and succinylcholine.

METHODS: After institutional approval and informed written consent, seventy-five unpremedicated children aged two to seven years were entered into a prospective, randomized, double-blind study. Intravenous access was gained prior to induction. Patients received atropine 0.02 mg/kg and were randomized to one of three groups.
Group 1(P) received Propofol 3.5 mg/kg.
Group 2(P/A) received Alfentanil 0.02 mg/kg followed by Propofol 3.5 mg/kg.
Group 3(T/S) received Thiopentone 5 mg/kg followed by Succinylcholine 2mg/kg.
Induction doses were given over 20 s. Patients were ventilated with 100% oxygen for 30 s, before intubation by one of two "blinded" anaesthetists. Blood pressure and heart rate were measured at one-minute intervals for five minutes. Anaesthesia was maintained by manual ventilation with 67% nitrous oxide and 1.5% halothane, to an end tidal CO2 of 40-60 mm.Hg, until spontaneous respiration resumed. The period of apnoea was recorded.
Ease of intubation was graded as follows:
Grade 1: Easy laryngoscopy and intubation, no movement of the patient or vocal cords, no pharyngeal, laryngeal or cough reflexes.
Grade 2: Successful laryngoscopy and intubation, some movement but no gagging or coughing.
Grade 3: Successful laryngoscopy and intubation, but resulted in gagging or coughing.
Grade 4: Failed intubation due to patient movement.
Grade 4 patients were given a further dose of propofol 0.5 mg/kg or thiopentone 1 mg/kg and succinylcholine 1-2 mg/kg.to facilitate laryngoscopy and intubation.

RESULTS: The groups were similar with regard to age, weight (Kruskal-Wallis tests) and sex (Chi square tests).

Table 1 shows the results of intubation. Intubation grades were significantly lower in the group (T/S) (p=0.0001). In groups (P) and (P/A) combined, 90% of intubations were successful. Intubation conditions (grade 1&2 combined) were better in group (P/A) than in (P).[8 vs 0 patients, p=.004, Chi square test].

Mean blood pressure was significantly higher at all times for thiopentone versus propofol groups.(figure 1) Results for heart rate, systolic and diastolic blood pressures were similar.

DISCUSSION: Tracheal intubation with propofol alone is not recommended for children as intubating conditions are poor.
The addition of alfentanil to propofol improves conditions and may be useful for the intubation of healthy, unpremedicated children, especially when it is necessary to avoid succinylcholine.
Of additional note is the cardiovascular stability following intubation with propofol and alfentanil.

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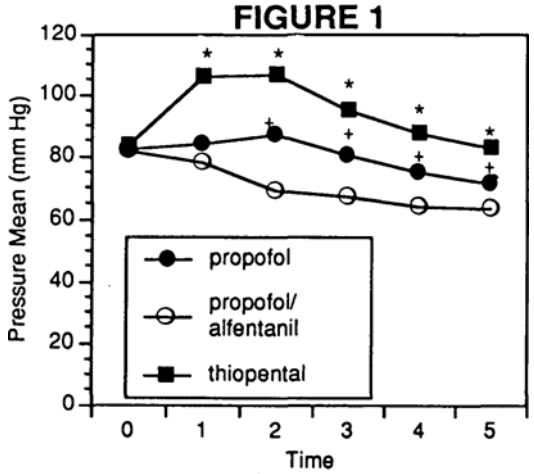
TABLE 1: INTUBATION GRADE

ease of intubation	propofol	prop/ alfent	thiopental
grade 1	0	5	22
grade 2	0	3	2
grade 3	21	16	1
grade 4	4	1	0

FIGURE 1



Statistical Difference= * (p=0.001)T vs. P & P/A
+(p=0.001)P vs. P/A

ENDOTRACHEAL INTUBATION OF TRAUMA PATIENTS: TECHNIQUES AND COMPLICATIONS

Richard Wenstone MB ChB FFARCS, J Hugh Devitt MD MSc FRCPC, Ellen Harrington BA RN
Department of Anaesthesia, Sunnybrook Health Science Centre University of Toronto, Toronto, Ontario

INTRODUCTION: The airway management of trauma patients remains controversial with no particular mode of tracheal intubation proven to be superior [1,2]. It is our impression that airway management in the acute resuscitation setting differs from the operating room. We undertook a retrospective study of patients admitted to our tertiary referral trauma centre to document and quantify any differences.

METHODS: The study took place between May 1990 and October 1991, inclusively. All patients who required tracheal intubation within 24 hours of injury were included. Data collected included: age, Injury Severity Score (ISS), technique, route, indications, complications, whether the patient was awake or asleep (use of induction and/or neuromuscular blocking agents) for intubation, location and by whom intubation was carried out. We analyzed separately those patients who required tracheal intubation as part of their resuscitation (Group I) and those whose tracheas were intubated as part of general anaesthesia and surgery (Group II). All data was collected on a standardized form and checked for accuracy with the individual performing the intubation where necessary. A "*difficult intubation*" was defined as one felt to be difficult by the individual performing the procedure and/or requiring more than one attempt. A "*complication*" was defined as vomiting, sinus bradycardia, epistaxis or cardiac arrest. Groups I and II were compared with respect to age, ISS, frequency of awake intubations, incidence of reported difficulties and complications. Age and ISS were compared using an unpaired t-test while frequency of awake intubation, reported difficulties and complications were compared using Chi square or Fisher's exact test where indicated. A p value <0.05 was considered significant.

RESULTS: Three hundred and ninety-six patients were entered into the study. Data were incomplete for three individuals and not analyzed further. Two hundred and thirty-one patients required endotracheal intubation as part of their resuscitation (Group I) and 162 underwent tracheal intubation for anaesthesia and surgery (Group II). There was no difference between mean ages (36.2 vs 34.0), but ISS was significantly greater in Group I (29.8 vs 19.9, $p<.0001$). Method of intubation (awake vs asleep), incidence of difficulties and complications is presented in Table 1. The frequency of awake intubation was greater in the resuscitation group ($p<0.001$). More complications were reported during resuscitation than in the operating room. There was a significantly higher incidence of intubation difficulties in the resuscitation group when tracheal intubation was assisted with induction or neuromuscular blocking agents ($p<0.01$). No cases of epistaxis were reported during this study. The methods of tracheal intubation used in different locations are shown in Table 2.

Table 1
Method of Intubation, Difficulties and Complications

	Number	Difficult	Complication
Group I Asleep	36	12	0
Group I Awake	195	32	9
Group II Asleep	112	10	0
Group II Awake	50	5	0
	p<0.001	p<0.01	

Table 2
Method of Intubation by Location

	Referral Hospital	Trauma Room	Operat Room
Laryngoscopic Asleep	29	8	112
Laryngoscopic Awake	68	25	16
Bronchoscopic	0	3	21
Blind Nasal	72	24	13
Surgical	2	0	0

DISCUSSION: Tracheal intubation was more difficult or carried a much higher complication rate when performed in the resuscitation setting especially when induction or neuromuscular blocking agents were used. Patients who undergo tracheal intubation in the operating room appear to constitute a very different population from those requiring intubation as part of their resuscitation. Awake intubation in the operating room had fewer complications than when performed in the trauma room, probably because personnel are more skilled in airway management, more sophisticated equipment such as the fiberoptic bronchoscope is readily available and patients were less severely injured. Clearly in the trauma patient, the approach to airway management in the resuscitation and anaesthesia settings is different.

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Does Bupivacaine Reduce Pain in Children After Tonsillectomy?

A. Wong, M.D., B. Braude MB, BCh., D. Fear, M.D., B. Bissonnette,M.D.
Dept. of Anaesthesia, The Hospital For Sick Children, Toronto, Ont.

Introduction: Post-tonsillectomy pain in children is a difficult management problem. A previous study using topical lidocaine on the tonsillar beds showed a statistically significant improvement in pain control in the immediate postoperative period compared to the use of intramuscular codeine [1]. The use of topical or infiltration of bupivacaine in the tonsillar beds may be even more advantageous because of its longer duration of action thus potentially reducing the postoperative analgesic requirements [2]. Although previous studies have been done to separately assess the use of topical or infiltration anaesthesia, no previous study, to our knowledge has compared the two modalities in children [3,4]. The purpose of this study is to investigate and compare the effects of topical and infiltration of bupivacaine on post-tonsillectomy pain in children.

Methods: After approval from the Human Ethics Committee and informed parental consent, 45 children (ASA 1-2), between 2 to 10 years of age scheduled for elective tonsillectomy and adenoidectomy were enrolled in this study. With routine monitoring, all children were induced with intravenous atropine, 0.02mg/kg, sodium thiopental 5 mg/kg, and tracheal intubation was facilitated with succinylcholine 2 mg/kg. Anaesthesia was maintained with 70% N2O in oxygen and maintained on isoflurane. They were then randomly assigned to one of three groups: Group A received a total of 0.5 cc/kg of normal saline spray divided between each tonsillar bed, Group B received a total of 2 mg/kg of 0.5% bupivacaine with 1:200,000 epinephrine infiltrated in each tonsillar bed and Group C received a total of 2 mg/kg of 0.5% bupivacaine with 1:200,000 epinephrine sprayed on both tonsillar beds. In all three groups, the treatment was applied after the tonsils were removed. At the end of surgery the children were all extubated awake. They were then returned to the recovery room where they were assessed according to the Objective Pain Scale (OPS) [5],by a nurse unaware of the treatment and given codeine (1.5 mg/kg im.)for OPS≥6 and acetaminophen (15 mg/kg rectally) given for OPS≤5. These observations were continued on the ward every 4 hours until discharge the next morning from the hospital. The three groups were compared with respect to immediate postoperative pain score, average ward pain score, total postoperative analgesic requirements and intraoperative blood loss.

Results: Nine patients have been thus far enrolled in the study, three in each group. There were no significant differences in age or weight amongst the three groups. Preliminary results indicate that Group B, (infiltration of bupivacaine) had lower immediate postoperative pain scores in the recovery room than the other groups (OPS 3 versus 8 in groups A and C). This was also reflected in lower postoperative analgesic requirements in the recovery room compared to Groups A and C (0.5 mg/kg codeine versus 1.5 mg/kg codeine in groups A and C). The beneficial effects appeared to be sustained only for the immediate postoperative period as the average ward pain scores were similar amongst the three groups.(OPS 3-4). Despite this, Group A still required greater amounts of acetaminophen on the ward than the other two groups.(30 mg/kg versus 15 mg/kg). The average intraoperative blood loss was lower in Group B than in Group A or C. There were no complications noted in any of the groups.

Discussion: Infiltration of 0.5% bupivacaine with 1:200,000 epinephrine in the tonsillar beds appears to be a safe method of providing improved post-tonsillectomy pain control compared to topical bupivacaine spray or placebo. There also appears to be a reduction in intraoperative blood loss with this technique.

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HAEMODYNAMIC CONSEQUENCES OF ABDOMINAL INSUFFLATION WITH CO_2 DURING LAPAROSCOPIC CHOLECYSTECTOMY

Craig W. Reid, M.D., Raymond J. Martineau, M.D., Kathryn A. Hull, R.N., Donald R. Miller, M.D.
The Department of Anaesthesia, Ottawa General Hospital and The University of Ottawa, Ottawa, Ontario

INTRODUCTION: The technique of laparoscopic cholecystectomy is becoming increasingly widespread, and appears to confer major postoperative benefits by obviating the need for upper abdominal incision. The procedure, however, is not without potential hazard, as the induced pneumoperitoneum may cause significant changes in heart rate (HR) and systolic blood pressure (SBP).[1] During laparoscopy for gynaecologic surgery, there have been several reports of cardiac arrest.[2,3] As a result of concerns regarding the prolonged period of abdominal insufflation during this new procedure, we undertook a study to evaluate the haemodynamic effects of laparoscopic cholecystectomy in healthy subjects under balanced anaesthesia.

METHODS: Ten ASA Class I,II, and III patients scheduled to undergo laparoscopic cholecystectomy were enroled in this study which was approved by the Hospital Human Experimental Procedures Committee. All subjects were between 17-60 years of age, had a normal body mass index, and were free of major cardiovascular disease. Following premedication with oral diazepam 0.1-0.15 $mg \cdot kg^{-1}$, anaesthesia was achieved with a combination of 70% N_2O, isoflurane, fentanyl and muscle relaxant. Following abdominal insufflation, the end-tidal concentration of isoflurane was unaltered in order to minimize the confounding influence of varying depths of anaesthesia on the observed haemodynamic changes. Minute ventilation was also held constant during the period of insufflation unless end-tidal CO_2 ($P_{ET}CO_2$) exceeded 40 mmHg. Heart rate and systolic blood pressure were measured with a Dinamap 1846SX vital signs monitor. Stroke volume index (SVI), cardiac index (CI), end-diastolic volume index (EDVI), and ejection fraction (EF) were measured noninvasively using the BoMed NCCOM3 bioimpedance cardiac monitor. Haemodynamic data and $P_{ET}CO_2$ values were recorded immediately prior to abdominal insufflation with CO_2 (BL), and at 5, 10, 20, and 30 minutes post-insufflation. Changes with time for each parameter were analyzed using repeated measures analysis of variance, with significance assumed when $P<0.05$.

RESULTS: Abdominal insufflation pressures were maintained at 15 mmHg throughout the study period, while there was a linear increase in $P_{ET}CO_2$ from 30.6±4.3 to 35.3±3.0 mmHg. Heart rate increased from 59±8 to 72±12 min^{-1} ($P<0.05$), associated a progressive increase in SBP ($P<0.05$, Figure). Modest but significant ($P<0.05$) decreases in both SVI and CI occurred within the first 5 minutes of insufflation. These changes were followed by a gradual increase in CI as HR and SVI values rose, despite a significant decrease in EDVI (from 85±15 to 71±15 $ml \cdot m^{-2}$, $P<0.05$). Ejection fraction was initially unchanged, but gradually increased over time from 54±4 to 59±3% ($P<0.05$).

DISCUSSION: The decrease in cardiac output and stroke volume indices associated with pneumoperitoneum result from a decrease in ventricular preload (EDVI), without impairment of left ventricular ejection fraction in these healthy subjects. This preload reduction was most likely due to diminished venous return as intrabdominal pressure increased during insufflation. A compensatory increase in heart rate may account for the gradual increase in cardiac output to pre-insufflation values. The observed increase in systemic blood pressure may have resulted from the combined influences of the stimulation of trocar manipulation, and increased sympathetic outflow related to rising CO_2 values. While these changes were well tolerated in this group of patients with normal cardiac function, the haemodynamic derangements accompanying prolonged abdominal insufflation of gas may jeopardize the patient with significant coronary artery disease or left ventricular systolic dysfunction.

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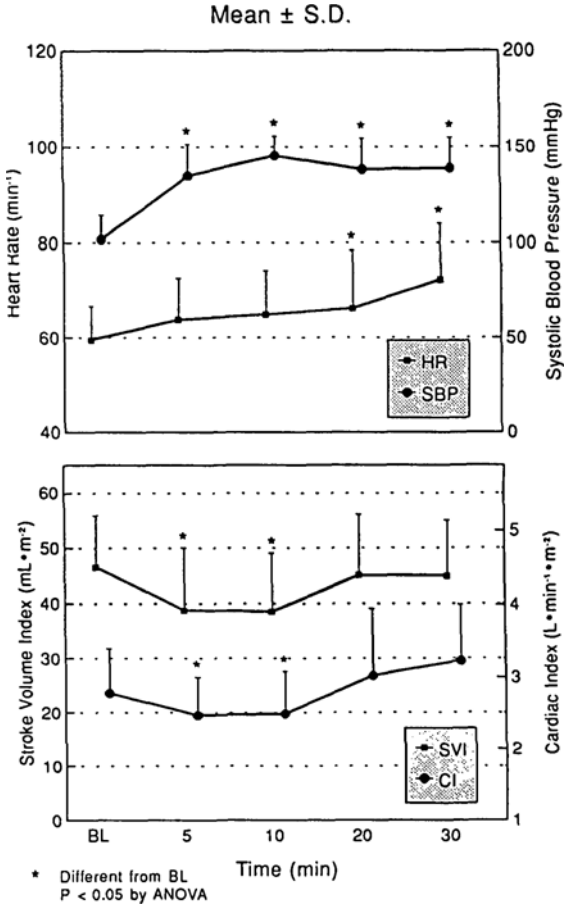
FIG HAEMODYNAMIC CHANGES



LOWER ICU MORTALITY IN SEPTIC SHOCK DUE TO UROSEPSIS COMPARED TO NON-UROSEPSIS.

David T. Wong MD*, Douglas P. Wagner PHD †, William A. Knaus†.
*Department of Anaesthesia, Toronto Western Hospital, 399 Bathurst St., Toronto, Ontario. M5T2S8.
†ICU Research, The George Washinton University Medical Center, Washington DC, USA

INTRODUCTION

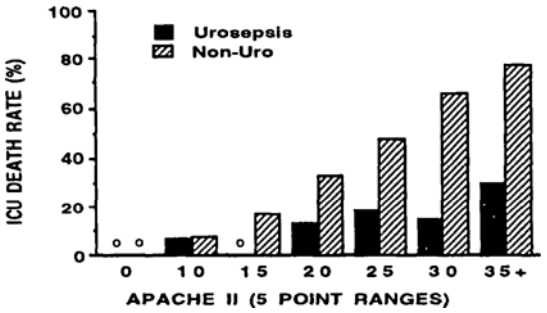
Death rate (DR) from septic shock (SS) varies from 10 to 90% and is influenced by diagnosis, comorbidity and severity of illness (1). We prospectively studied the impact of source of sepsis and APACHE II (AP2) score in explaining wide variations in ICU DR among SS patients.

METHODS

During 1988-89, we collected data for 17457 consecutive ICU admissions at 40 American hospitals, 26 of which were randomly selected. For each patient, we recorded age, diagnosis, chronic health status, day 1 AP2 score and survival at ICU and hospital discharge. SS was defined as hypotension and a clinical diagnosis of sepsis. Patients were divided into two groups; urosepsis (US) and non-urosepsis (NUS). For the whole SS group and subsequently for the US and NUS subgroups, the ICU DR corresponding to incremental AP2 5 point ranges were obtained.

RESULTS

There were 518 SS patients from 17457 ICU admissions. Among all SS patients, for AP2 ranges 0-9, 10-14, 15-19, 20-24, 25-29, 30-34 and >35, the ICU DR was 0, 7, 12.9, 29.4, 42.2, 53.3, and 69.5% respectively. For 104 US patients, mean AP2 was 22.6 and ICU DR 11.5%. For 414 NUS patients, mean AP2 was 23.1 and ICU DR 36.2%. The ICU DR was significantly lower in the US compared to the NUS group ($p<0.001$, chi-square). The ICU DR in the US and NUS subgroups stratified by 5 point AP2 ranges is shown below:



DISCUSSION

Variation in DR among SS patients is directly related to the AP2 score. After controlling for severity of illness using AP2 scores, urosepsis is still associated with a lower ICU death rate compared to non-urosepsis. Further analysis is needed to identify the mechanism to explain this difference in death rate.

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POSTOPERATIVE HYPOXEMIA IN AMBULATORY SURGERY

S.Yogendran MD.,G.McGuire MD.,M Gomez MD..V.Chan MD.,F.Chung MD.
Department of Anaesthesia, The Toronto Hospital (Western Division),University of Toronto, 399 Bathurst Street, Toronto, Ontario. M5T 288, Canada.

Introduction

Hypoxemia (oxygen saturation <90% or PAO2 <60 mm Hg) in the postoperative period is well known and has been documented in the past few years with the introduction of the pulse oximeter (1,2). Postoperative hypoxemia can cause prolonged recovery, confusion,myocardial ischemia and cardiac dysrhythmias. Our investigation evaluated the incidence of hypoxemia in the ambulatory surgery post anaesthetic care unit (PACU) and on discharge home.

Methods

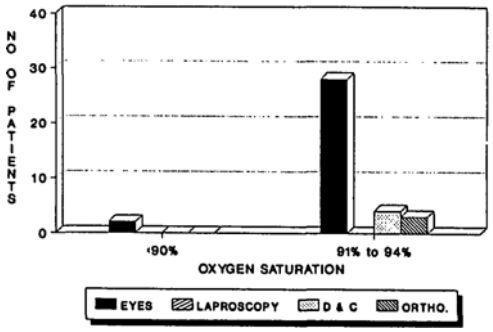
After institutional approval and informed consent all patients (ASA 1 to 3) scheduled for ambulatory surgery were studied. The study design was prospective and single blinded. It included all patients in ophthalmology, D&C suction, laparoscopy and orthopaedic surgery. Exclusion criteria included: patient refusal or preoperative saturation $\leq$ 90%. Preoperatively baseline oxygen saturation was documented in the ambulatory centre breathing room air. Post operatively the PACU nurse determined the patient to be sufficiently recovered from anaesthesia, using a standard protocol, the oxygen mask was removed. Oxygen saturation level was blinded from the nurse so as not to influence the decision to discontinue oxygen. Oxygen saturation was monitored five minutes and ten minutes after the removal of the oxygen mask and prior to discharge home.

Results

Baseline oxygen saturation in all patients were 97% $\pm$ 2. The incidence of oxygen desaturation was 22% in the ophthalmology patients, 8% in the orthopaedic patients and 2% in the D&C suction patients.(table). Five ophthalmology patients had oxygen saturation < 90% was noted in any of our patients. Eleven percent of patients were discharged home at oxygen saturation between 90% - 94%. In these there were 28 ophthalmology patients, 4 D&C patients and 3 orthopaedic patients(fig). There was no correlation between oxygen desaturation and risk factors such as age, obesity or smoking.

	EYES	ORTHOPAEDIC	LAPAROSCOPY	D&C	TOTAL
NO.OF PATIENTS	124	34	11	146	315
AGE (MEAN)	65	42	32	28	
M:F	52:72	22:12	0:11	0:146	
OBESE	6	3	0	7	16
CHEST DISEASE	11	3	0	5	19
SMOKING	15	9	2	19	45

OXYGEN SATURATION AT DISCHARGE



Discussion

Patients discharged at oxygen saturation between 90 - 94% may have further risk of hypoxemia. Most of the PACU discharge criteria do not include oxygen saturation. Measuring oxygen saturation in PACU and at discharge,may identify the high risk patients.

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CAPNOGRAPHY AND THE LARYNGEAL MASK AIRWAY IN CHILDREN

I. SPAHR-SCHOPFER MD, B. BISSONNETTE MD, E HARTLEY MD.
Department of Anaesthesia, The Hospital for Sick Children, Toronto, Ontario.

INTRODUCTION

The laryngeal mask was designed for adults but is now available for use in children. The use of capnometry is mandatory during anaesthesia. In infants and children interpretation of the value of end-tidal carbon dioxide (ETCO2) is more difficult than in adults because the combination of high fresh gas flows (FGF) and small tidal volumes tends to dilute the expired carbon dioxide, leading to an underestimation of the arterial carbon dioxide pressure (PaCO2).[1] This study was designed to determine the accuracy and the best site of sampling of ETCO2 measurements as an estimate of $PaCO_2$ in anaesthetized infants and children breathing spontaneously through a laryngeal mask.

METHODS

After approval of the Human Review Committee and obtaining informed parental consent, 16 unmedicated infants and children, ASA I and II, weighing between 11-25 kg were enrolled in the study. All children were scheduled for elective minor surgery requiring general mask anaesthesia and lasting less than 1 hour. Exclusion criteria were patients at risk of aspiration of gastric contents and with known abnormal airway anatomy. Blood pressure, ECG, oxygen saturation, end-tidal gases and axillary temperature were recorded. All patients were studied in the supine position and received atropine 0.02 mg/kg. Anaesthesia was induced with either intravenous thiopentone or halothane inhalation and maintained with halothane 2% and 70% N_2O in O_2. Spontaneous respiration was maintained. A size 2 laryngeal mask airway (LMA), modified to allow placement of an $ETCO_2$ sampling catheter, was inserted under direct vision to ensure its correct placement. Fresh gas flow was provided with an Ayre's T piece and was determined according to: 3 x (1000 + (100 x body weight in kg)).[2] Presence or absence of rebreathing was noted. If rebreathing occurred, FGF was increased until no rebreathing was noted. At completion of surgery, the inspired fraction of halothane was maintained at 2% and, under steady state conditions, end-tidal carbon dioxide pressures were recorded by a Datex 255 infrared capnometer (Puritan-Bennet) calibrated before each study with dry gas of known composition (5% CO2 and 36% N2O). All values of ETCO2 were corrected to BTPS.[3] The measures of peak end-tidal CO_2 were taken in random order at predetermined distances from the elbow connector down the LMA shaft using a #19 gauge central venous catheter inserted through the luer lock port at the elbow connector. The distances were : proximal = at the elbow; 1. = 4.5 cm from the elbow; 2. = 6 cm from the elbow; 3. = 11 cm from the elbow(halfway down the shaft of the LMA); distal = 17 cm from the elbow (distal end of the LMA); tracheal = 20 cm from the elbow (3 cm into the trachea). An arterial blood sample was drawn. Respiratory rate and tidal volume were recorded with a Wright Pediatric Respirometer. Parametric data were analysed with repeated measures ANOVA and the Student-Neuman-Keuls tests for multiple comparisons. $p<0.05$ was accepted.

RESULTS

Sixteen patients scheduled for minor surgery lasting less than 60 min. were enrolled in the study. Mean age and weight of the children were 3.8 years (SD±1.62) and 16.3 kg (SD±3.4) respectively. One child developed a brief episode of laryngospasm during LMA insertion, treated with positive pressure ventilation. There were no other episodes of oxygen desaturation due to placement or removal of the LMA. Mean respiratory rate was 45/min (SD±7) and mean tidal volume was 2.3 ml/kg/breath (SD±0.83) giving a mean minute ventilation of 100 ml/kg/min.(SD±28.3). At the more distal sampling sites, rebreathing of 4-5 mmHg CO_2 was noted which could not be eliminated by increasing FGF. Mean PaCO2 was 61.3 mmHg (SD±10.35). Measured $ETCO_2$ rose progressively as sampling became more distal from the elbow (Fig.) $ETCO_2$ measured in the trachea was not significantly different than $PaCO_2$ but all the other sites of sampling showed significantly lower values (the mean difference between arterial-ETCO2 measured at elbow was 13±10.7 mmHg).

DISCUSSION

Studies have shown that $ETCO_2$ measurements are well correlated with $PaCO_2$ at any site of sampling in the endotracheal tube for ventilated children weighing more than 12 kg.[4]. Our results showed that only the $ETCO_2$ sampled directly in the trachea closely approximate $PaCO_2$ and that FGF gradually dilutes $ETCO_2$ in the shaft of the LMA. Tracheal sampling is inconvenient. The most accurate site to measure $ETCO_2$ within the LMA is at the distal end, although the value is significantly lower than $PaCO_2$.

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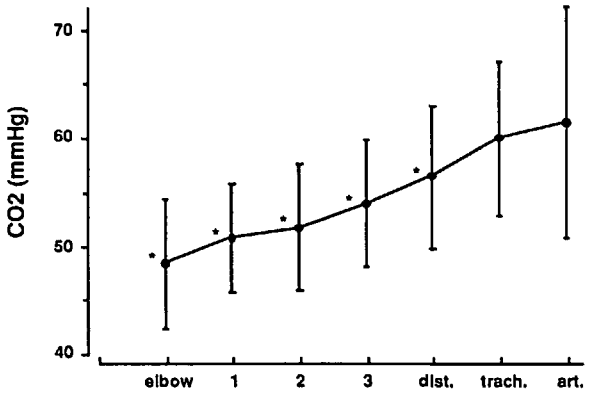

THE RELATIONSHIPS BETWEEN MALIGNANT HYPERTHERMIA, CHRONIC MUSCLE PAIN AND CREATINE KINASE ELEVATIONS.

Beverley A. Britt, M.D., F.R.C.P.(C), Professor, Depts. of Anaesthesia and Pharmacology, University of Toronto; Senior Staff Anaesthetist, Toronto General Hospital, Toronto, Ontario M5G 2C4.

INTRODUCTION

We have observed that some, but by no means all malignant hyperthermic (MHS) patients complain of migratory type muscle pains, cramps and/or stiffness. Some of these individuals also have persistent elevations of their creatine kinases (CK) even in the absence of unusual exercise or other muscle disorders. Such association of anaesthetic induced MH with muscle pain and elevated CK has also been reported by other workers (1,2). We have, therefore, in recent years, accepted for performance of the caffeine halothane contracture test (CHCT) individuals who have had not anaesthetic history, but rather have had a history of chronic migratory muscle pain and/or creatine kinase elevations. Most of these patients, at least in more recent years, came to our clinic labelled as having chronic fatigue immuno deficiency (CFS). In addition to muscle pain and an elevated CK most also had chronic fatigue, blinding headaches and episodes of excessive sweating in the absence of any external heat stimulus. These will, therefore, be termed CFS.

METHODS

The patients were divided into the following three groups: control patients who had had no history of a malignant hyperthermic reaction in themselves or in their relatives; MHS patients who had a history of an anaesthetic-reaction in themselves; CFS patients who had no anaesthetic history in themselves or in their relatives. Each of these three subgroups were subdivided according to the presence of muscle cramps, elevated CKs or muscle cramps plus elevated CKs.

The CHCT was performed on each individual according to the North American Malignant Hyperthermia Registry protocol (3). The parameters measured were: 3% halothane contractures in grams (normal $\leq$ 0.7 grams); and mM caffeine required to raise the resting tension by 1.0 gram, ie. the caffeine specific concentration (CSC) (normal $>$ 4.0 mM).

The data was compared using unpaired T tests, analyses of variance and analyses of covariance.

RESULTS

In all three groups 3% halothane contractures were greatest and CSCs were least in those with a combination of muscle pain and a CK elevation, intermediate in those with either muscle pain or a CK elevation and least in those with neither muscle pain nor a CK elevation.

Within each subgroup there were no significant differences in 3% halothane contractures or in CSCs between the MHS and the CFS group. However, comparison of the MHS group and the CFS groups with the control group revealed that for each of the former two groups the 3% halothane contractures were greater and the CSCs were less than in the control group.

DISCUSSION

Whether the patients with only a history of muscle pain and/or CK elevation are truly identical to the patients with an anaesthetic history of MH reactions is not determined by this study. Such information will have to await the outcome of ongoing genetic restriction fragment length polymorphism and sequencing studies. In the interim, safety decrees that patients complaining of chronic muscle pain should be biopsied for MH, particularly if the CK is also substantially elevated.

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REDUCTION OF POST CARDIOPULMONARY BYPASS BLEEDING WITH TRANEXAMIC ACID.

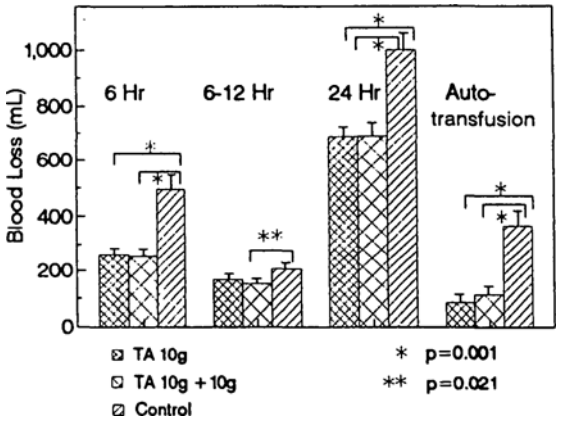
J.M. Karski M.D, S.J. Teasdale M.D, P. Norman M.D, P. Young, R.N.,J. Carroll R.N., K. Van Kessel BSc., R. Weisel M.D., M. Glynn M.D.
The Toronto Hospital, General Division, University of Toronto, 200 Elizabeth Street, Toronto, Ontario, M5G 2C4.

INTRODUCTION: Patients undergoing cardiac surgery with cardiopulmonary bypass (CPB) are at risk of postoperative bleeding, which contributes to morbidity, mortality and re-operation (3-5%). Platelet dysfunction, fibrinolysis, release of plasminogen activator and activation of the complement system are thought responsible. Fibrinolysis has been estimated to cause at least 12 to 25% of post CPB bleeding. We have used the antifibrinolytic agent, tranexamic acid (TA), as an intravenous infusion in the pre-bypass period to prevent fibrinolysis. TA is ten times more potent than epsilon-aminocaproic acid, binds more strongly to plasminogen, has a longer half-life and is less expensive. Experience using TA before CPB is limited.

METHODS: We collected, in a double blinded, placebo controlled, prospective, randomized fashion, data on 146 consenting patients undergoing aorto-coronary bypass and valvular surgery surgery with CPB. 48 patients received 10g of TA over 20 minutes prior to CPB, 49 received 10g TA over 20 minutes prior to CPB plus 10g infused over 5 hours and 49 were not pretreated (control). Demographics did not differ. Patients were anesthetized with high dose fentanyl, pavulon and valium. The initial dose of heparin was 300 U/kg and ACT was maintained above 400 sec. Heparin was reversed with protamine sulfate (1mg per 100 U of heparin). Mediastinal and pleural drains were employed to collect blood which was autotransfused up to 6 hours post operatively. We collected and analyzed the following postoperative data; blood loss over 6, 12 and 24 hours, blood and blood products transfused, hemostatic and coagulation profiles.

STATISTICS: Analysis of variance (ANOVA), two-way ANOVA and post hoc Tukey multiple comparison tests and Chi Square tests were used, (Systat, Systat INC). Three patients reoperated upon for surgical bleeding were excluded.

RESULTS: Postoperative blood loss and autotransfusion per group are presented in **Table I.**



Transfusion requirements among groups did not differ due to effectiveness of autotransfusion in preserving blood loss.

CONCLUSIONS: Our results indicate that pretreatment with the antifibrinolytic agent tranexamic acid significantly reduces post CPB blood loss in patients undergoing heart surgery. Increasing the dose over 10g of TA achieved minimal increase in blood loss reduction at 12 hours.

MECHANISMS OF EXCESSIVE BLEEDING AFTER CARDIOPULMONARY BYPASS.

J.M. Karski M.D, S.J. Teasdale M.D, P. Norman M.D, J. Carroll R.N., M. Glynn M.D.
The Toronto Hospital, General Division, University of Toronto, 200 Elizabeth Street, Toronto, Ontario, M5G 2C4.

INTRODUCTION: Excessive postoperative bleeding after cardiopulmonary bypass (CPB) presents a significant clinical problem and contributes to morbidity and mortality. A small proportion of patients bleeding excessively (10%) will require reoperation. In 50% of these no defined surgical cause will be found. Development of coagulopathy during CPB seems to be responsible for this bleeding. Currently it is not possible to predict occurrence of post CPB bleeding. In this study we investigated the frequency of excessive bleeding after CPB and defined its mechanisms.

METHODS: In the Phase I of the study we retrospectively collected data on 89 patients undergoing first time CABG surgery to identify percentage of excessively bleeding patients. In the Phase II in a prospective manner we collected data on 48 consenting patients undergoing CPB. Patients were anesthetized with high dose fentanyl, pavulon and valium. The initial dose of heparin was 300 U/kg and ACT was maintained above 400 sec. Heparin was reversed with protamine sulfate (1mg per 100 U of heparin). Crystalloid hemodilution and a membrane oxygenator were used during CPB. Mediastinal and pleural drains were employed to collect blood which was autotransfused up to 6 hours post-operatively. We collected and analyzed the following data; blood loss over 6 and 24 hours, blood and blood products transfused, hemostatic and coagulation profiles.

STATISTICS: Analysis of variance (ANOVA) and Chi Square tests were used, (Systat, Systat INC). Patients reoperated upon for surgical bleeding were excluded. Basic demographics like CPB time, degree of hypotermia did not differ.

RESULTS: In the Phase I we identified 14 (17 %) of patients bleeding over 750 cc in first 6 hours (1311+-511 vs 361+-163 p=0.001). Blood (RBC) requirement in these 14 patients was (635+-599 vs 236+-342 p=0.001) compared to these not bleeding.
In Phase II we found that 9 patients (18 %) bled over 750 cc in 6 hours (1029+-280 vs 395+-131 p=0.001) and required blood (RBC) (305+-273 vs 150+-213 p=0.07). Coagulation parameters measured in Phase II are presented in Table I and Table II.

DISCUSSION: These data indicates the presence of ongoing fibrinolysis in the patients with excessive postoperative bleeding. The concentration of fibrinogen although reduced ,is not sufficiently low to impair hemostasis but the effect of plasmine on the platelets membrane are likely responsible for the compromised platelet function as evidenced by the prolonged bleeding time.

CONCLUSIONS:

1. 18 % of patients undergoing CPB bled extensively (>750 ml in 6 hours)) in the postoperative period (300% increased blood loss) and will required increased amount of blood (RBC) (200-300%) more then control.
2. The major difference between patients who bled excessively and these who did not is the presence of excess fibrinolysis and, in particular,the effect of plasmin on the blood platelets of these patients.
3. There is need for a study to predict who will bleed extensively postoperatively to target prophylactic use of pharmacologic agents for selected patients.

	PRE-OP	POST-OP 2 HOURS	POST-OP 12 HOURS
PT >750 ml	10.4±1	17±1.5	14.7±1.3
<750 ml	11.1±3	15±2.2 p=0.005	13.6±1.3 p=0.026
PTT	31.6±7	40±7	37±8
	31.5±12	34±6 p=0.02	31±5 p=0.02
PLT	250±31	210±21	137±25
	240±64	185±46	136±40
Bleeding Time	5±1	11±4	24 HOURS 8±3
	4±1	7±3 p=0.002	5±2 p=0.001

>750ml - Bleeding in 6 hours
<750ml

Table legend: PT - protrombin time
PTT - tromboplastin time
PLT - platelets

>750ml <750ml	PREOP	POSTOP 2 HOURS	POSTOP 12 HOURS
Plasminogen Activity	0.95±0.07	0.44±.1	0.44±.1
	0.94±0.3	0.58±.1 p=0.037	0.63±.1 p=0.009
Plasminogen Antigen	0.1±0.03	0.053±.01	0.06±0.03
	0.1±0.1	0.066±.01 p=0.06	0.07±0.03
Fibrinogen	3.3±.7	1.369±0.5	2.9±1
	3.2±1.0	2.078±0.7 p=0.021	3.6±1
Alpha 2	1.09±0.1	0.53±0.08	N/A
	1.04±0.1	0.68±0.1 p=0.01	

>750ml
<750ml Bleeding in 6 hours

Cardiovascular Complications in the Post-Anaesthetic Care Unit

RJ Smyth MSc, MD, N Takla MD, D Cheng FRCPC, F Chung FRCPC

Western Division, The Toronto Hospital, University of Toronto, 399 Bathurst Street, Toronto, Ontario. M5T 2S8

INTRODUCTION:
Despite the exceedingly low incidence of intraoperative events, postoperative complications remain a significant challenge to total anaesthetic care. There remains a paucity of data examining postop cardiovascular (CVS) complications in large patient populations. This study represents a 4 year examination of all CVS complications occurring in the immediate postop period in a large University hospital.

METHODS:
Over a 4 year period (1986-90) CVS complications were prospectively studied in all surgical patients experiencing CVS problems in the postanaesthetic care unit (PACU). Their anaesthetic and surgical data, cardiac risk factors and the timing, duration, etiology, treatment and outcome of all CVS complications were documented. Complications were defined by ASA criteria:
i) hyper/hypotension (SBP ≥ 200/≤ 70 mmHg)
ii) tachy/bradycardia (≥ 100/≤ 60 bpm)
iii) arrhythmia
iv) MI/suspected MI
v) angina
Good outcome was defined as post-recovery transfer to a ward or day bed unit, whereas transfer to an ICU or death was considered a poor outcome.

RESULTS:
In a total of 46,672 anaesthetics, 121 CVS complications occurred in PACU (0.26%). Figure 1 shows the incidence of postop CVS complications for each surgical service: Urology-0.80%, Orthopedics-0.72%, Opthalmology-0.27%, General-0.15% and Other- 0.06%. The most frequently encountered complications were hypotension (59/121) and bradycardia (37/121). Thirty percent of the bradycardia group experienced concomitant hypotension. Orthopedic patients had the highest number of arrhythmias (38.9%), tachycardias (62.5%), angina (40.0%) and MI/Suspected MI (72.7%). Urology patients were the largest group experiencing hypertension (37.5%), with preop hypertension as the most common etiology (75.0%). Underlying cardiac disease was frequently considered the etiology in MI/Suspected MI (81.8%), angina (60.0%), arrhythmia (55.6%) and bradycardia (27.0%). Hypovolemia was the most common cause of postop hypotension (56.7%). Cardiac risk factors were present in 91% of the patients with postop MI/Suspected MI and in 100% of patients with postop hypertension. Outcome was considered good for only 28% of the MI/Suspected MI group and 60% of angina patients, whereas the remaining groups showed a good outcome 91% of the time (Tables 1 and 2).

CONCLUSION:
Urological and orthopaedic patients had the highest incidence of CVS complications in the PACU. Hypotension and bradycardia were the most frequently encountered complications with hypovolemia and vasovagal/oculocardiac reflexes considered the most common etiologies of these complications. Cardiac risk factors were present more frequently in patients with postop hypertension or MI/Susp MI which may contribute to the poor outcome in the MI/Susp MI group. Outcome was regarded as good in all groups except those with postop angina or MI/Susp MI.

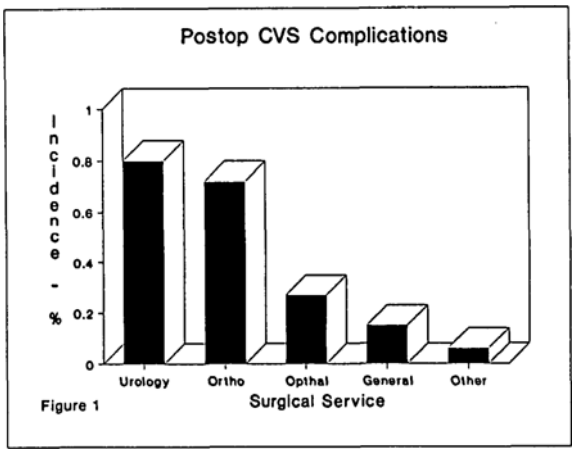


Figure 1

Table 1

	BRADYCARDIA	ARRHYTHMIA	TACHYCARDIA
N	37	18	16
Age	67.1 ± 12.8	70.9 ± 15.2	59.3 ± 21.7
Sex (M:F)	22:15	10:8	8:8
ASA I	3	2	1
II	23	10	10
III	9	6	5
IV	2	0	0
Cardiac Risk Factors (%)	65%	67%	56%
Treatment (%) (Y:N)	87:13	39:61	75:25
Outcome (%) (Good:Poor)	86:14	95:5	88:12

Table 2

	HYPOTENSION	MI/SUSP. MI	ANGINA	HYPERTENSION
N	59	11	10	8
Age	70.1 ± 13.3	62.8 ± 19.1	71.4 ± 9.2	70.4 ± 21.5
Sex (M:F)	32:27	5:6	5:5	5:3
ASA I	2	1	0	0
II	41	5	6	8
III	15	4	4	0
IV	1	1	0	0
Cardiac Risk Factors (%)	73%	91%	70%	100%
Treatment (%) (Y:N)	100:0	100:0	75:25	97:3
Outcome (%) Good:Poor	88:12	28:72	60:40	100:0

A SIMPLE CLASSIFICATION OF THE RISK IN CARDIAC SURGERY: THE FIRST DECADE

N.A. Tremblay, M.D., J-F Hardy, M.D., J. Perrault Ph.D., M. Carrier, M.D.
Departments of Anesthesia, Research and Surgery, Montreal Heart Institute, 5000 Belanger East, Montreal, Quebec, Canada H1T 1C8

Introduction. Since 1980, the risk of early mortality in all our cardiac surgical patients is assessed preoperatively. In light of reports[1-4] on the changing cardiac surgical populations, we reexamined our practice and risk classification.

Methods. In 1989 and 1990, 2110 consecutive cardiac surgical patients were prospectively grouped using our previously established risk classification[5] based on risk factors (RF) (Table 1): normal risk patients = no RF, increased risks = one RF and high risks >1 RF. 2024 patients were compared to the previously reported 1980 series of 500[5]; 86 excluded patients had (new) surgery not reported in 1980.

The patient's characteristics, the risk classes and their relationship to intrahospital mortality were studied. Data were analysed with ANOVA, chi-square and Z-proportion. $P < .05$ was considered significant.

Results. From 1980 to 1990, the proportion of high risk patients doubled at the expense of normal risks (Table 2). The incidence of advanced age, emergency surgery and reoperation increased (Table 1). In coronary surgery (CS) patients, the incidence of poor LV function and of unstable angina/recent MI decreased while the incidence of obesity and of other systemic disorders increased. In noncoronary surgery (NCS) patients, the incidence of heart failure increased.

Complex surgery (double valves, CS combined with other corrections) carried a higher mortality than single surgery in 1980 (8.7% vs 2.6%) and in 1990 (11.5% vs 4.2%). In 1990, new surgical procedures also carried a higher mortality than other surgical procedures (16.3% vs 4.9%).

The difference in mortality among the risk classes has remained significant and mortalities have not changed (Table 2).

Discussion. Compared to 1980, in 1990 cardiac surgical patients were sicker yet mortality did not increase. This can be attributed to improved therapeutic measures. The risk classification continues to reliably indicate the expected outcome in cardiac surgical patients. It is a practical, easy to use, clinical tool; the required data is readily available at the preanesthetic visit. The classification can also be used to assess quality of care. A new RF ("complexity/new surgery") is found, taking into account the evolution of surgical practice.

References.

1. Miller DG, et al. J Thorac Cardiovasc Surg 85:197-213, 1983
2. Cosgrove DM, et al. J Thorac Cardiovasc Surg 88:673-684, 1984
3. Naumheim KS, et al. J Am Coll Cardiol 11:494-498, 1988
4. Jones EL, et al. J Thorac Cardiovasc Surg 101:108-115, 1991
5. Paiement B, et al. Can Anaesth Soc J 30:61-68, 1983

Table 1: Incidence of risk factors in coronary and non-coronary surgery in the 1980 and 1990 populations

	Coronary surgery				Non coronary surgery			
	1980 (n = 370)		1990 (n = 1606)		1980 (n = 130)		1990 (n = 418)	
Risk factor	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Left ventricular EF < 0.3	34	(9.1)	37	(2.3)*	7	(5.4)	7	(1.7)
Unstable angina or recent (< 6 week) MI	78	(21.0)	143	(8.9)*	0	(0.0)	2	(0.5)
Heart failure	5	(1.3)	23	(1.4)	7	(5.4)	56	(13.4)*
Age > 65 years	37	(10.0)	561	(34.9)*	15	(11.5)	126	(30.1)*
Obesity (body mass index > 30)	36	(9.7)	327	(20.4)*	15	(11.5)	38	(9.1)
Emergency surgery	10	(2.7)	137	(8.5)*	2	(1.5)	19	(4.6)*
Reoperation	21	(5.7)	179	(11.1)*	15	(11.5)	187	(44.7)*
Other systemic disorders	22	(5.9)	873	(54.4)*	32	(24.4)	267	(63.8)

* significant difference between 1990 and 1980

Table 2: Distribution of all patients and of nonsurvivors in the 1980 and 1990 populations according to preoperative risk classification

	All patients				Non-survivors (mortality)			
	1980 (n = 500)		1990 (n = 2024)		1980 (n = 500)		1990 (n = 2024)	
Risk class	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Normal	251	(50)	410	(20) *	1	(0.4)	2	(0.5)
Increased	159	(32)	683	(34)	5	(3.1)	24	(3.5)
High	90	(18)	931	(46) *	11	(12.2)	74	(7.9)

* significant difference between 1990 and 1980
° significant difference between risk classes within each population

DETERMINANTS OF ARTERIAL-END TIDAL CARBON DIOXIDE DIFFERENCES AFTER CARDIAC SURGERY

AJ Davies MB FFARCS, T Nakagawa MD, B Kavanagh MB MRCPI, A Sandler MB, FRCPC
Department of Anaesthesia, The Toronto Hospital (General Division), Toronto, Ontario.

INTRODUCTION: The immediate post-operative period after hypothermic cardio-pulmonary bypass is a time of potential respiratory instability. Respiratory acidosis is common. Capnometry allows easier detection of rapid changes in arterial CO_2 ($PaCO_2$) than intermittent arterial blood gas sampling. The relationship between $PaCO_2$ and end-tidal CO_2 (ET-CO_2) is complex. A previous study has suggested that the arterial-end tidal CO_2 difference [D(a-ET)CO_2] increases immediately after CPB but measurements were not continued into the post-operative period[1]. It has been shown that once established, [D(a-ET)CO_2] remains constant following cardiac surgery[2]. However, intra-individual variation of [D(a-ET)CO_2] may be wide[3]. None of these studies have assessed capnometry in extubated cardiac patients. The aims of this study were to determine the factors responsible for the magnitude of [D(a-ET)CO_2] following cardiac surgery, and to assess the difference in accuracy of [D(a-ET)CO_2] in these patients whilst intubated and following extubation.

METHODS: Following Ethical Committee approval and completion of written consent, 30 patients undergoing hypothermic CPB were studied. Data was collected at three points after the patient was transferred to the ITU;
Phase 1: during IPPV, core temperature <36.5 °C
Phase 2: during IPPV, core temperature >36.5 °C
Phase 3: after extubation. The following measurements were taken three times, at half hourly intervals in each phase: ET-CO_2, cardiac index (CI), arterial blood gases, core temperature.
Physiological dead-space (Vd/Vt), venous admixture (Qs/Qt) and CO_2 production (V CO_2) were calculated in 10 patients during Phases 1 and 2 only.

Statistical analysis included calculation of simple linear regression, bias and precision, and multivariate analysis and was processed using the "Statview II" statistical package.

RESULTS: Agreement between $PaCO_2$ and ET-CO_2 was close in all phases, but was best in Phases 1 and 2 (see Table 1). [D(a-ET)CO_2] was greater in Phase 1 than in Phase 2. There was no significant difference in Vd/Vt or in Qs/Qt between Phase 1 and Phase 2 (see Table 2). CI and V CO_2 were significantly greater in Phase 1 than in Phase 2: however there was no correlation between either of these variables and [D(a-ET)CO_2].

DISCUSSION: Correlation beween ET-CO_2 and $PaCO_2$ in post-operative cardiac patients is best when they are intubated but remains close after extubation. [D(a-ET)CO_2] is greater in these patients during IPPV when hypothermic than when normothermic.
Ventilation-perfusion (V/Q) inequality, particularly increased Vd/Vt, is generally regarded as the main determinant of [D(a-ET)CO_2]. Increased V CO_2 has been shown to reduce [D(a-ET)CO_2] in exercising human subjects[4]. We were not able to explain the changes seen in [D(a-ET)CO_2] in cardiac surgical patients in terms of either V/Q imbalance or V CO_2 production, and would suggest that other factors govern [D(a-ET)CO_2].

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(1)Anesth Analg 1987;66:690
(2)Can J Anaesth 1991;38(1):15
(3)Can J Anaesth 1990;37(5):560
(4)J Appl Physiol 1979;47(5):954

Table 1

	Phase 1	Phase 2	Phase 3
No of determinations	78	86	59
R D(a-ET)CO_2 v $PaCO_2$	0.808	0.838	0.629
D(a-ET)CO_2 (SEM)	3.1** (0.3)	1.8** (0.3)	4.4** (0.5)

** p = <0.01

Table 2

	Phase 1	Phase 2
No of determinations	25	29
CI (L/min/m^2) (SEM)	2.60** (0.08)	2.87** (0.06)
Vd/Vt (SEM)	0.52 (0.1)	0.49 (0.01)
Qs/Qt (SEM)	0.296 (0.02)	0.301 (0.02)
V CO_2 (SEM)	0.185* 0.001	0.211* 0.006

**p = <0.01
* p = 0.01

INTRAVENOUS MIDAZOLAM INFUSION FOR POST-OPERATIVE SEDATION FOLLOWING CARDIAC SURGERY

FE Ralley, FFARCS; JG Ramsay, FRCPC; GR Robbins, FRCPC; FC Salevsky, FRCPC.
Departments of Anaesthesia, McGill University and Royal Victoria Hospital, Montreal, H3A 1A1

INTRODUCTION. After cardiac surgery, the need for adequate sedation whilst maintaining hemodynamic stability must be weighed against the risk of prolonging recovery time. Previously, this has been attempted with the use of bolus injections of diazepam; disadvantages of which include venous thrombosis and a long elimination half-life (30-90 h). Midazolam is a water-soluble, short-acting benzodiazepine with twice the potency of diazepam and an elimination half-life of 2-4 h, thus making it suitable for administration by a continuous intravenous infusion. At present, there is a wide range of dosage regimen suggested in the ICU setting, probably due to either different patient populations or different sedation end points. The aim of this study is to establish a safe and effective dosage regimen for the continuous intravenous (iv) infusion of midazolam for sedation of patients following cardiac surgery and high-dose narcotic anaesthesia.

METHODS. After informed written consent, 45 patients scheduled for elective cardiac surgery (single procedure) were entered into this double-blind randomized study. Premedication consisted of morphine and scopolamine. Routine invasive monitoring was inserted. All patients received a standard anesthetic of sufentanil (5-10 μg/kg), enflurane and vecuronium. At the start of hypothermic CPB patients received midazolam 0.035 mg/kg. Full hemodynamic profiles were recorded before induction, on arrival in ICU, then with each sedation rating.

In the ICU, after reversal of muscle relaxation, once patients responded to verbal commands, they were assigned to one of three groups. Each received a 2 ml bolus of midazolam 0.03 mg/kg (Group 1), 0.06 mg/kg (Group 2) or 0.1 mg/kg (Group 3), followed by a midazolam infusion at 0.5 μg/kg/min (Group 1), 1.0 μg/kg/min (Group 2) or 1.5 μg/kg/min (Group 3). Level of sedation was assessed just prior to initial bolus, at 15 and 30 min after start of infusion, then at 30 min intervals for 6 h. Infusion rate was titrated every 30 min to achieve a predetermined sedation level. Time from initial bolus to "ideal" sedation score (i.e., calm, rousable) obtained was recorded. Morphine was used for analgesia. Hypertension was treated with nipride or labetolol. Time from arrival in ICU to start of weaning, extubation and discharge was recorded. Total dose of analgesia during the first 24 h was also recorded.

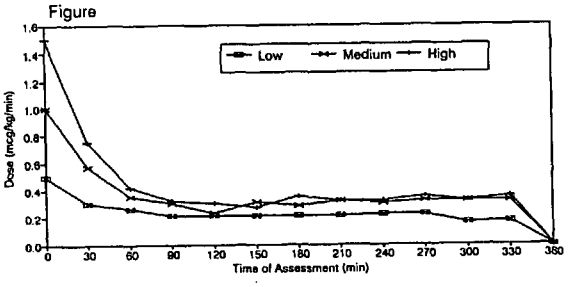
RESULTS. There was no difference in demographic data between the 3 groups. By 90 min the infusion dose of the 3 groups was very similar (0.21, 0.30 and 0.32 μg/kg/min respectively), after which the mean rate in each group remained fairly constant (Figure). Time to reach optimal sedation was 100.7 min, 143.5 min and 142.4 min respectively. There were 6 cases of hypotension associated with the initial bolus [0 (Group 1), 1 (Group 2), 5 (Group 3)]. All responded to a fluid bolus and/or ephedrine. No other significant changes in hemodynamic parameters during the study period were seen. As patients were receiving similar doses at end of infusion, post-infusion data was pooled to make one group. Mean time to start of weaning was 123.2 ± 15.5 min and to extubation 285.5 ± 33.4 min. There was no difference in the total dose of morphine given in the first 24 h between groups. By 24 h 60% of patients had been discharged from ICU.

DISCUSSION. This technique was an effective method of postoperative sedation with high acceptability by both patients and nursing staff. We recommend an initial bolus of 0.03 mg/kg followed by a continuous infusion at 0.2-0.3 μg/kg/min. This should then be titrated to effect. The small initial bolus may help reduce the possibility of hypotension at this time. With this dosage, patients are able to request analgesia if necessary, whilst accepting the endotracheal tube. We found patients could start weaning within 2 h after the end of the infusion, and therefore recovery time was not significantly prolonged. Unlike a previous study [1], we saw no reduction in analgesia requirement.

Reference

1. Anesthesiology 67: 257-62, 1987.

Figure



EFFECTS OF INTRAVENOUS (I.V.) PREMEDICATION ON OXYGEN SATURATION IN OUTPATIENT AND A.M. ADMISSIONS

Charul A. Munshi, M.D., S. Gandhi, M.D., S. Gandhi, Research Assistant, N. Nimphius, M.S.
Department of Anesthesiology, Medical College of Wisconsin, Milwaukee, WI 53226, USA

INTRODUCTION

With the advent of outpatient and a.m. admissions for surgical procedures, intravenous sedation in the O.R. holding area has largely replaced preop oral or intramuscular premedication. For a period of two weeks, oxygen saturation and pulse rate were measured in our O.R. holding area to assess the effects of I.V. premedication on oxygen saturation.

METHODS

Oxygen saturation and pulse rate (Criticare 501+) were measured on all outpatients and a.m. admissions on arrival to the holding area. All I.V. medications were given at the discretion of the anesthesia personnel responsible for the patient and they did not know the results of pulse oximetry.

A total of 101 patients were studied. Patients were divided into three groups. Group I - no sedation (n=18), group II - I.V. midazolam (2.0±1.1mg)(n=65), group III - midazolam (2.1±1mg), and fentanyl (55.6±22μg)(n=18). Only peripheral I.V. lines and radial artery catheters were placed during this period.

DATA ANALYSIS

Desaturation was defined as decrease in oxygen saturation of 2% or more from the baseline.

Levels of desaturation and change in heart rate between the three treatment groups, gender groups, and age groups (over 60 years vs. under 60 years) were evaluated by 3-factor analysis of variance with Scheffe's test. Incidence of desaturation was evaluated using Chi-square analysis.

RESULTS

There were significantly more incidents of desaturation in the midazolam with fentanyl group (78% of patients) than in the midazolam only group (34%) and the nonmedicated group (11%)($P<0.001$). Average saturation on departure from the holding area in Group I was 96±2%, Group II 96±3%, and Group III 94±3%. Mean decrease in saturation in Group I was 0.3±8%, Group II 1.2±1.8% and Group III 2.8±1.9% (Figure 1). In the midazolam with fentanyl group, desaturation was significantly greater in patients over 60 years (4.8±1.7%) than those under 60 years (2.3±1.5%)($P=0.007$)(Figure 2). Of the patients that desaturated (decrease in saturation of ≥2%), those in Group I desaturated 2±0%, Group II 3.3±1.7%, and Group III 3.6±1.3%. Age did not affect saturation in the unmedicated or midazolam only groups. Gender did not affect saturation. There were no significant changes in heart rate betwee treatment, gender, or age groups.

CONCLUSION

There was significantly more incidence of desaturation in patients who received I.V. sedation than the patients who did not. Patients who received midazolam and fentanyl had significantly higher incidence of desaturation which was more pronounced in patients over 60 years. With increasing I.V. premedication, use of midazolam with fentanyl should be carefully monitored especially in patients over 60 years of age who may have significant cardiovascular and respiratory disease. I.V. sedation in the holding area can cause oxygen desaturation, requiring O_2 supplement. For safe I.V. premedication, pulse oximetry should be available in the holding area and supplemental O_2 administered when necessary.

Figure 1

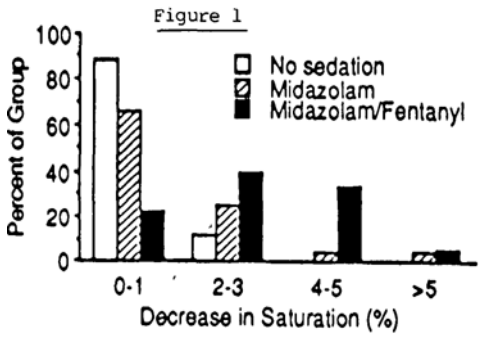
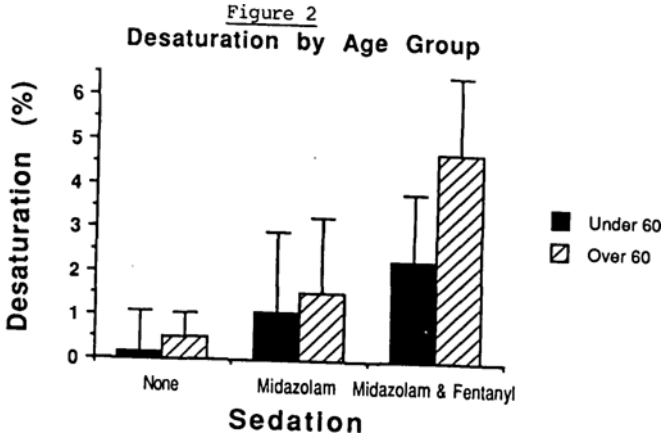


Figure 2



MEASUREMENT OF RESPIRATORY MECHANICS USING THE PURITAN-BENNETT 7200a VENTILATOR

Daniel Chartrand MD PhD, Bernard Dionne M Ing, Christian Jodoin, Michel Lorange PhD, Alain Lapointe DScA

Hôtel-Dieu de Montréal, Dept of Anaesthesia and Biomedical Engineering, 3840 St-Urbain, Montréal, H2W 1T8

INTRODUCTION

Many modern ventilators can measure the compliance and the resistance of the respiratory system. However, for most of these ventilators, no independent study has validated the measurements of respiratory mechanics. In our intensive care unit, clinicians perform more than 95% of the measurements of respiratory mechanics with the Puritan-Bennett 7200a ventilator equipped with the optional 30/40 module. The aim of this study was to validate the respiratory parameters measured and calculated by this ventilator.

METHODS

Two ventilators were studied immediately after a thorough preventive maintenance performed according to Puritan-Bennett specifications. They were then connected to a mechanical model of the respiratory system and submitted to 54 different ventilatory conditions by modifying the respiratory rate (10, 20 or 30 $\cdot min^{-1}$), the tidal volume (0.5, 1.0 or 1,5 L), the inspiratory flow rate (20, 60 or 100 $L \cdot min^{-1}$) and the resistance of the model (7 or 9-mm endotracheal tubes). The respiratory parameters measured by the ventilators (constant inspiratory flow rate, tidal volume and pressure) and calculated by the optional 30/40 module (compliance and resistance) were compared to those obtained by our reference equipment at the opening of the respiratory model.

At the opening of the model, the flow rate was measured with a pneumotachometer (Jaeger PT-36) and the pressure was measured with a piezoresistive transducer (Micro Switch 143PC03D). These signals were amplified (Hewlett Packard 8802A), low-pass filtered at 80 Hz (Frequency Devices 902LPF), digitized at a sampling rate of 200 Hz (Data Translation 2801A A/D converter) and stored on the hard disk of a microcomputer. The analog pressure and flow signals of the ventilator were also digitized and stored on the computer. These four signals were then analyzed (Asystant+ scientific software) in order to obtain the tidal volume, the steady-state inspiratory flow rate, the peak inspiratory pressure, the plateau pressure and the PEEP. Using these measured parameters, the compliance and the resistance were calculated. For each of these measured and calculated parameters, the comparisons between the values obtained from the ventilator and those obtained from the reference equipment were made by linear regression. Statistical significance was assumed when $P < 0.05$.

RESULTS

Although the ventilators underestimated the inspiratory flow rate by only 2.8 and 3.7 $L \cdot min^{-1}$ respectively, this constant absolute error resulted in an important relative error at an inspiratory flow of 20 $L \cdot min^{-1}$. The tidal volume (expiratory flow integrated over time) was measured with a mean error of less than 10 ml and no significant difference was found between the ventilators and the reference equipment.

The two ventilators overestimated the plateau pressure by 7 and 10%, respectively. This error in the calibration of the pressure transducers was also observed in the measurement of the peak inspiratory pressure. Furthermore, the measurement of this dynamic pressure was also affected by another source of overestimation: the pressure gradient due to the resistance of the inspiratory limb of the breathing circuit. This pressure gradient reached as much as 6 cm H_2O at 100 $L \cdot min^{-1}$. Although PEEP was measured within 1 cm H_2O in most instances, large differences (up to 10 cm H_2O) occurred between the opening of the respiratory model and the ventilator when a residual expiratory flow was observed (intrinsic PEEP of the model).

Using the parameters measured by the ventilators, our calculations of the compliance underestimated the "true" compliance of the model (C_{model}) by more than 7% in average. Furthermore, using the automatic measurement feature of the 30/40 module, the compliance calculated by this optional module ($C_{30/40}$) was:

$$C_{30/40} = (C_{model} \cdot 0.7275) + 38.5 \text{ ml} \cdot \text{cm } H_2O^{-1}.$$

Using the parameters measured by the ventilators, our calculations of the resistance overestimated systematically the "true" resistance of the model (R_{model}). For example, at an inspiratory flow rate of 100 $L \cdot min^{-1}$, the resistance of the model was overestimated by 4.2 cm $H_2O \cdot L^{-1} \cdot s$ in average. A large part of this overestimation was due to the overestimation of the peak inspiratory pressure by the ventilator and was dependent of the inspiratory flow rate. Furthermore, using the automatic measurement feature of the 30/40 module, the calculation made by this module was not only overestimating systematically R_{model} but, at 100 $L \cdot min^{-1}$, was also sporadically much higher (> 6 cm $H_2O \cdot L^{-1} \cdot s$) than our calculation made with the same signals. As the pressure signal was often presenting several artifacts at this flow rate, this second source of overestimation of the resistance was probably related to an erroneous selection of the peak airway pressure by the 30/40 module .

DISCUSSION

This study has identified the limitations of a modern mechanical ventilator commonly used for measuring respiratory mechanics in the intensive care setting. However, this does not imply that other ventilators would perform better for that particular purpose. Furthermore, this study was limited to one aspect and no conclusion is made about the overall performance of the Puritan-Bennett 7200a ventilator.

Knowing that the margins of tolerance accepted by the manufacturer during preventive maintenance are 15% for the inspiratory flow and 20% for the tidal volume, a clinician should already appreciate the level of precision he could expect. Furthermore, as the airway opening pressure is not directly measured by the ventilator, one can predict that an error will be introduce by the breathing circuit (filters and tubes).

Knowing their limitations, we believe that the measurements of respiratory mechanics made with these ventilators should be interpreted with extreme caution. Similar studies should be conducted on several other ventilators offering automatic measurement of respiratory mechanics. For the time being, we prefer to use our research equipment for the measurement of respiratory mechanics in the intensive care setting.

LIGHT-GUIDED VS. LARYNGOSCOPIC INTUBATION IN SURGICAL PATIENTS: CLINICAL TRIAL OF A NEW LIGHTWAND DEVICE.

Orlando R. Hung, FRCPC, Sarah C. Stevens, MD, Geoffrey Hawboldt.
Department of Anaesthesia, Dalhousie University and Victoria General Hospital, Halifax, NS B3H 2Y9.

INTRODUCTION:

The placement of tracheal (ET) tubes under direct vision using a rigid laryngoscope has been the standard method for intubation. However, there is a need for alternative techniques of intubation, since the incidence of difficult laryngoscopy is approximately 2% and the existing methods of preoperative airway assessment (Mallampati classification and Wilson scores) are inadequate.[1] Transillumination through the tissues of the neck using a strong light from a special stylet (lightwand) has been demonstrated to be of great use in the placement of ET tubes.[2,3] A new design of the lightwand device incorporates several modifications: a brighter light bulb at the tip of the stylet with a conveniently placed light switch; a longer stylet; a side clip to hold the ET tube in place; and a retractable inner wire trocar. These modifications make the device suitable for both orotracheal and nasotracheal intubation. Although the transillumination technique has been found useful in various environments including the ambulance[2], the emergency room and the operating theatre [3], clinical testing of this new device in elective surgical patients requiring intubation would possibly broaden the application of this valuable technique. This study reports the results of a comparative study of conventional direct laryngoscopic (DL) and light-guided intubation using the new "Stewart Tracheal Lightwand" (STL) design.

METHODS:

After obtaining institutional approval and informed consent, patients scheduled for elective surgical procedures requiring intubation were studied. All were interviewed prior to surgery and clinical evaluations of their airways using the criteria suggested by Mallampati[4] and Wilson[5] were carried out. Intravenous catheter and routine monitors (blood pressure cuff, EKG, and O_2 saturation) were placed on the patients upon arrival in the operating room. After preoxygenation, induction of anaesthesia was induced with an anaesthetic and muscle relaxant of the clinician's choice. The method of intubation was chosen by opening a sealed envelope drawn randomly from the study supply. The time for intubation was recorded for both techniques from the time of insertion of the laryngoscope or STL into the patients mouth to the time when these devices were removed from the patients. Any trauma or bleeding during the intubation was noted. Patients were reexamined and interviewed within 24 hours to determine the incidence of sore throat and trauma to the soft tissues or teeth. The data were analyzed using unpaired t-test and Chi-square analysis of contingency table where appropriate with $p<0.05$.

RESULTS:

Seventy adult patients were studied. Twenty-eight patients were intubated utilizing DL and forty-two using STL (Table 1). There was no difference between the groups with respect to age or weight. The mean ($\pm$SD) time-to-intubation (TTI) was 24.7 $\pm$ 31.0 sec with DL and 20.5 $\pm$ 14.0 sec with STL. These were not statistically significant. However, there was evidence that longer time was required to intubate patients with Mallampati class 3 or higher using DL. There was no association between the time-to-intubation and Mallampati classification using the STL device. One patient was intubated utilizing the STL after several unsuccessful attempts with DL. There were no statistically significant differences in the incidence of sore throat or trauma in these 2 groups of patients.

DISCUSSION:

Intubation utilizing the light-guided STL appears to be a useful alternative technique for placement of the endotracheal tube. The preliminary results of this study also suggest that this technique may have advantages over the conventional method of intubation using DL for patients with potentially difficult airways.

REFERENCES:

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2. Ann Emerg Med 14:324, 1985.
3. Anesthesiology 64:824, 1986.
4. Can Anaesth Soc J 32:429-434, 1985.
5. Br J Anaesth 61:211-216, 1988.

Table 1.

Intubation Technique	STL	DL
Patient Number (M/F)	20/22	11/17
Age (Mean $\pm$ SD)	51.1$\pm$16	43.7$\pm$20
Weight (Mean $\pm$ SD)	75.2$\pm$21	71$\pm$23
TTI (Mean $\pm$ SD)	20.5$\pm$14	24.5$\pm$31
Number of Sore Throat	4	5
Number of Trauma	0	1
Other Technique used	0	1

DYE DILUTION CARDIAC OUTPUT MEASUREMENTS USING PULSE OXIMETER SENSORS; A FEASIBILITY STUDY.

GA Volgyesi, PEng, H Reimer, MD
Department of Anaesthesia and the Research Institute, The Hospital For Sick Children and the University of Toronto, 555 University Avenue, Toronto, Ontario, M5G-1X8

Introduction:

Cardiac output measurements provide physiologic information that is useful in the clinical management of selected patients. In adults, the dye dilution method has been largely replaced by the less accurate, but technically easier thermal dilution method. However, the latter method may be difficult or impossible to perform in infants and young children. In an attempt to develop a simple and less invasive technique applicable to pediatric patients, we have investigated the possibility of performing dye dilution cardiac output measurements using a standard pulse oximeter sensor for the non-invasive detection of the dye dilution curve.

Methods:

An electronic circuit(EC) was designed and built to enable a Nellcor pulse oximeter sensor to transilluminate the patient's finger and to detect the unabsorbed red light(R). In order to display and record a normal dye curve after the bolus injection of indocyanine-green dye, the R signal has to be amplified, filtered and inverted. In order to assess the feasibility of this method, preliminary experiments were performed on a rabbit. After inhalation induction with halothane, the rabbit was intubated and ventilated to maintain normocapnia. Femoral arterial and venous catheters were introduced in order to perform cardiac output determinations with the dye dilution method using a Waters densitometer and a Harvard syringe pump. A Nellcor adult finger probe was placed on the ear of the rabbit and the probe was connected to the EC. The outputs from the densitometer and from the EC were displayed on a Gould strip-chart recorder and recorded on an H/P FM tape recorder for subsequent analysis. After baseline measurements, the cardiac output of the rabbit was increased by administering isoproterenol and then lowered by increasing the halothane concentration and administering propranolol. Three cardiac output determinations were obtained at each level of cardiac output. The dye curves obtained from the densitometer and from the EC were transferred to a Macintosh computer where areas under the curves were calculated after extrapolation of the exponential portions to the baseline. Linear correlation analysis was then performed on the reciprocal of the areas.

Results and Discussion:

Although there are significant baseline variations in the dye curves obtained from the EC due to respiration, their shapes appear similar to those from the densitometer. A typical set of dye curves obtained simultaneously by the two methods is shown in fig.1. The good correlation found between the reciprocal of the areas obtained from the two methods(Fig.2) in this preliminary study indicates that simple dye dilution cardiac output measurements may be possible using ordinary pulse oximeter sensors. The best method of signal smoothing and calibration has yet to be determined.

Fig.1

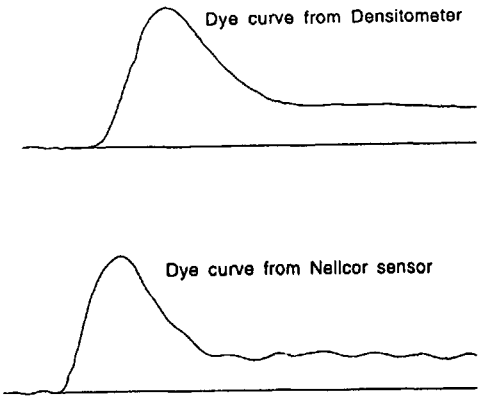
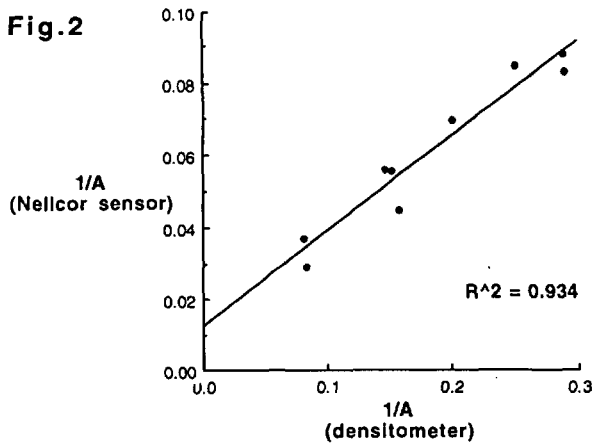


Fig.2



A PORTABLE DEVICE FOR IN VITRO TESTING OF PULSE OXIMETERS

G.A.Volgyesi, PEng, J. Lerman MD
Department of Anaesthesia and the Research Institute, The Hospital For Sick Children and the University of Toronto, 555 University Avenue, Toronto, Ontario, M5G-1X8

Introduction:
A simple in vitro device for testing pulse oximeters has been described recently[1,2]. The finger shaped device, called Manual Pulse Simulator (MPS) by the authors, modulates the thickness of a thin film of blood, enabling the pulse oximeter to provide an SpO_2 reading, which can be compared to saturation estimations obtained from a Hemoximeter. Although their device is much simpler than that described by another group[3], the MPS still requires blood and additional equipment, so it is not practical for routine testing.
We have developed an improved MPS which requires neither blood nor additional equipment for its operation and therefore may be useful for routine testing of sensors or comparison of pulse oximeters.
Materials and methods:
The new MPS is constructed from two ordinary glass microscope slides, sealed together at the edges by silicone rubber and spaced parallel to each other. The 1 mm space between the slides is filled with a liquid compound filter, consisting of an aqueous solution of a mixture of two compounds, one of which absorbs radiation in the red (R), and the other in the infra-red(IR) regions of the spectrum. When one end of the MPS is inserted in the sensor of a pulse oximeter and the other end is squeezed rhythmically between the thumb and index finger (fig.1), the thickness variations of the compound filter induce the required fluctuations in the detected R & IR light to enable the pulse oximeter to provide an SpO_2 reading. By altering the relative concentrations of the R and IR absorbers in the compound filter contained within the MPS, any SpO_2 from 0 to 100% can be obtained. Ten MPS's were constructed to provide a range of simulated SpO_2 values from 40 to 100%. In order to test the utility of these devices, the set of new MPS's were used to compare SpO_2 estimations from 3 commonly used pulse oximeters. Because of the slow evaporation of water from the MPS's over time, the apparent SpO_2 values increased gradually, enabling us to obtain a large number of comparisons over a period of two months.
Results and discussion:
The new MPS's fit the Nellcor adult finger sensor and the Criticare ear sensor well. However, for proper fit, the Ohmeda finger sensor had to be modified by shaving off some of its soft silicone finger padding. The apparent SpO_2 obtained with each MPS on each pulse oximeter was highly reproducible. The slow changes in SpO_2 caused by the evaporation of water from the MPS's could easily be reversed by simply replacing the lost water. The comparison of SpO_2 readings obtained with the three pulse oximeters is shown on fig.2. The low scatter of points obtained in this study indicates that the new MPS may be useful in testing sensors or comparing pulse oximeters, and may render in vivo testing less necessary.
References:
1. Can J Anaesth 37(4), S67, 1990
2. Anesthesiology 73(3A), A427, 1990
3. IEEE Transact Biomed Eng 36(6), 1989

Fig.1

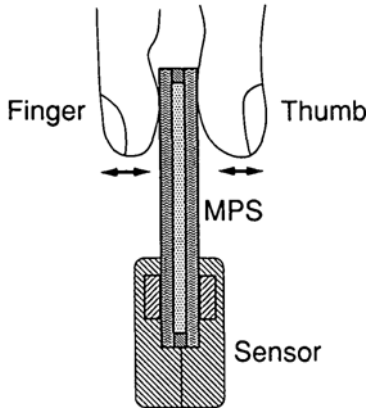
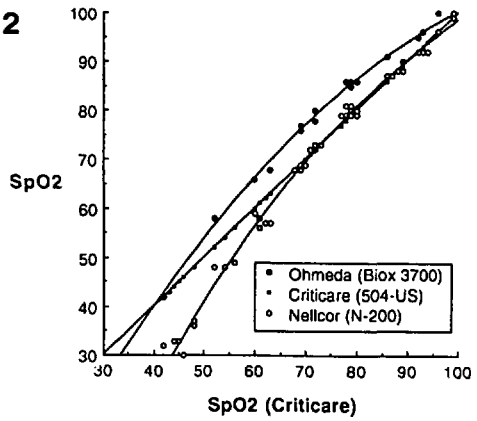


Fig.2



LARYNGOSCOPES, LIGHTS, AND FIELDS OF VISION

Guy Tousignant MD FRCPC and Michael J. Tessler MD FRCPC
Department of Anaesthesia, Sir Mortimer B. Davis - Jewish General Hospital
and McGill University, Montreal, Canada.

INTRODUCTION: We believe that the intensity of light and the scope of illumination from a laryngoscope affect one's ability to visualize the larynx during endotracheal intubation. We evaluated several brands of laryngoscopes and various laryngoscope blade sizes in order to identify differences in direct and reflected light intensity and the field of illumination for each model.

METHODS: Non-single use laryngoscopes from Heine optotechnik, Penlon, Rusch, and Welch-Allyn were assessed. Disposable laryngoscopes from Vital Signs and North American Medical Products, Inc. as well as the Tube-Stat endotracheal intubation stylet (Concept, Inc.) were evaluated. The tests were conducted on either new instruments, sample models, or used but thoroughly cleaned laryngoscopes. New industrial grade batteries, 1.5 V, that were checked before and after use for full charge were our power sources. Trials were performed in a photographer's dark room. There were three parts to the study. Part 1-direct light intensity- Each laryngoscope was inserted into a rigid clamp system that was set up to maintain the beam of light in a constant position. The laryngoscope was positioned such that the light was aimed directly into the middle of a Minolta Flash meter III, a device that measures light intensity from continuous light sources, with the tip of the blade resting on the Flash meter spherical diffuser. This was done to standardize the distance from the light source to the meter. The room lights were turned off to eliminate ambient light and a reading of the laryngoscope blade light intensity was obtained. Each blade and laryngoscope handle were tested three times in this manner. The results record only the most intense light measured for each handle and blade. Part 2- reflected light - The laryngoscope blade was placed in the clamp system and directed at a nonreflective cream-coloured wall. The tip of the laryngoscope touched the wall. The Minolta Flash meter III was positioned so that it was level with the laryngoscope light source, one meter away from the wall and at a 45^{o} angle to both the laryngoscope and the wall. The laryngoscope was turned on and off three times. Each time a new reading was taken and the most intense reflected light measured was recorded. Par 3 - area of illumination - The laryngoscopes were placed against the wall as they had been to test for reflected light, and photographs were taken to illustrate the pattern of light illumination. A 10 cm ruler was placed within the field of illumination to measure the range. A field of illumination was considered narrow (N) if its diameter was less than 4 cm, average (A) if between 4 and 7 cm, and wide (W) if its diameter was greater than 7 cm.

RESULTS: No two laryngoscope blades were alike for all three measurements. (see Table)

DISCUSSION: We think the differences among these laryngoscope blades in terms of direct light intensity, quality of reflection, and field of illumination are significant. We conclude that the Penlon laryngoscope blade with the incandescent light bulb, when attached to a regular handle, provides the best features for lighting for endotracheal intubation, because of its bright direct light and wide field of illumination.

TABLE

Laryngoscope model	F.o.I.	D.L.I. (lux)	R.F.I. (lux)
Heine Fibreoptic			
Macintosh 3	N	2743.8	85.8
Macintosh 4	A	2560.0	60.8
Penlon Incandescent			
Regular handle			
Macintosh 3	W	3377.5	260.0
Macintosh 4	W	3377.5	320.0
Miller 3	A	5487.5	320.0
Short handle			
Macintosh 3	-	1371.8	113.3
Macintosh 4	-	1371.8	121.3
Miller 3	-	2388.5	121.3
Welch-Allyn Fibreoptic			
Regular handle			
Macintosh 3	-	1371.8	130.0
Macintosh 4	-	844.5	105.5
Miller 3	-	1371.8	121.3
Miller 4	-	844.5	98.5
Pencil handle			
Macintosh 3	-	1114.3	121.3
Macintosh 4	-	640.0	98.5
Miller 3	-	970.0	130.0
Miller 4	-	686.0	121.3
Rusch Fibreoptic			
Regular handle			
Macintosh 3	N	2228.5	105.5
Short handle			
Macintosh 3	-	422.3	34.8
Vital Signs			
Macintosh 3	W	4777.3	298.5
Macintosh 4	W	2560.0	298.5
North American Medical Products			
Macintosh 3	N	905.0	113.3
Miller 2	A	844.5	105.5
Tube Stat	W	6303.5	298.5

F.o.I.-Field of Illumination D.L.I.-Direct Light Intensity, R.L.I.-Reflected Light Intensity
One lux=illumination created by one candle one meter away in all directions

NITROUS OXIDE ENVIRONMENTAL POLLUTION

A COMPARISON BETWEEN FACE MASK, LARYNGEAL MASK AND ENDOTRACHEAL INTUBATION

R. Barnett MBBS FFARACS, B. Gallant, S. Fossey RN, B. Finegan FRCP(C)
University of Alberta, 8440 112 St., Edmonton, Alberta T6G 2B7

INTRODUCTION

The laryngeal mask airway (LMA) has been rapidly accepted into clinical practice because of its ability to control the airway both in the routine case and in the anticipated difficult intubation. One disadvantage of the LMA may be an increase in environmental pollution because the seal is only effective to airway pressures less than 15 cm H_2O. The purpose of this study was to compare environmental levels of nitrous oxide (N_2O) when the Magill mask (MM), the LMA or endotracheal intubation (ETT) were used during anaesthesia.

METHODS

Thirty ASA I and II patients undergoing peripheral orthopaedic procedures were randomized to one of three groups. Anaesthesia technique was standardized with each patient being induced with propofol 2 mg/kg and fentanyl 1.5 ug/kg, maintained with N_2O (3 l/min), O_2 (2 l/min) and Isoflurane. The ETT group also received vecuronium (0.8 mg/kg) and IPPV was instituted to maintain normocarbia. The anaesthetist was blinded as to the degree of N_2O spillage. Trace levels of N_2O were measured throughout the case by an infra-red N_2O analyser (FOREGGER 410) and recorded by a chart recorder (CANLAB Bi-channel). The sampling tube of the N_2O analyser was positioned 30 cm above the front right corner of the anaesthetic machine. Statistical analysis was performed using paired T tests.

RESULTS

There were 10 patients in each group. No differences were found with regard to age, sex, or weight. There was greater environmental pollution in the MM group than with either the LMA or ETT groups ($p < 0.05$). There was no difference in pollution between the LMA and ETT groups.

Interestingly, only in the MM group was the average level of N_2O pollution greater than the NIOSH and CAS standard of 25 ppm.

CONCLUSION

This study shows that not only is the LMA an acceptable airway, but also it has significant advantages over conventional face mask in terms of environmental pollution. We would recommend the LMA be used when prolonged spontaneous ventilation is anticipated (>30 min) in order to minimize environmental pollution.