Abstracts

Haemodynamic and metabolic changes after aortic cross-clamping for thoraco-abdominal aneurysm resection

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During thoraco-abdominal aortic aneurysmectomy, the aorta is replaced from the left subclavian artery to the aortic bifurcation. We wished to describe the haemodynamic events occurring during clamping and unclamping of the thoracic aorta and the metabolic changes associated with the interruption of organ perfusion beyond the left subclavian artery.

Methods

We studied 11 patients (58–77 years) undergoing thoraco-abdominal aortic aneurysm resection without the use of cardiopulmonary bypass. All patients had normal left ventricular systolic function. No patient had angina.

Diazepam, fentanyl, pancuronium, air/O_2 anaesthesia was used. An arterial line, a Swan-Ganz catheter and a left double lumen endobronchial tube were inserted. The left lung was collapsed to facilitate surgical exposure. Immediately prior to the application of the thoracic aortic cross-clamp, sodium nitroprusside was infused in an attempt to eliminate excessive hypertension at the time of cross-clamp. This was continued for the duration of the cross-clamp (mean 72 minutes) to maintain systolic arterial pressures between 150–200 mmHg. An IV infusion of five per cent sodium bicarbonate was given to achieve a serum bicarbonate of 30–35 mmol·L^{-1} prior to unclamping of the aorta.

Results

Haemodynamic results (Table I)
Cross-clamping of the thoracic aorta produced an immediate increase in mean arterial blood pressure (MAP). This reverted back to preclamp levels with removal of the clamp. Mean pulmonary artery pressure (MPAP) increased significantly with clamp application and this increase persisted after removal of the clamp. There was no significant change in either systemic vascular resistance (SVR) or pulmonary vascular resistance (PVR). Cardiac indices (CI) were not affected by clamp application but increased significantly after clamp removal. Both the central venous (CVP) and pulmonary capillary wedge pressures (PCWP) increased with clamp application and these changes persisted after clamp removal.

Metabolic results (Table II)
An average of 791 mmol of sodium bicarbonate (range 240–1545 mmol) was infused during the time of cross-clamp. Unclamping of the aorta with re-establishment of circulation to liver, gut, and kidneys produced an acid wash out, resulting in a highly significant drop in pH ($p < 0.001$) and plasma bicarbonate. PCO_2 rose significantly

TABLE I Haemodynamic results (mean ± 2 SEM)

n = 11	*PreClamp*	*PostClamp*
MAP mmHg	98 ± 9	126 ± 18†
MPAP mmHG	21 ± 3	28 ± 7§
CVP mmHg	10 ± 3	14 ± 3*
PCWP mmHg	15 ± 3	22 ± 4‡
SVR dynes·sec·cm^{-5}	1346 ± 327	2367 ± 1297¶
PVR dynes·sec·cm^{-5}	76 ± 21	76 ± 21¶
CI L·min^{-1}·m^{-2}	3.0 ± 0.5	3.0 ± 1.0¶

N = 11	*PreUnclamp*	*PostUnclamp*	*End of Proc.*
MAP mmHg	120 ± 14†	103 ± 11¶	103 ± 12¶
MPAP mmHG	29 ± 6†	27 ± 2‡	31 ± 5*
CVP mmHg	16 ± 3*	15 ± 2‡	18 ± 3*
PCWP mmHg	23 ± 4†	21 ± 2§	22 ± 4‡
SVR dynes·sec·cm^{-5}	1401 ± 380¶	1005 ± 173‖	1103 ± 272¶
PVR dynes·sec·cm^{-5}	72 ± 21¶	62 ± 20¶	83 ± 21¶
CI L·min^{-1}·m^{-2}	3.7 ± 1.0¶	4.0 ± 0.7‡	3.8 ± 0.9¶

*$p < 0.001$; †$p < 0.005$; ‡$p < 0.01$; §$p < 0.02$; ‖$p < 0.05$; ¶NS.

TABLE II Metabolic results (Mean ± 2 SEM)

n = 11	*PreClamp*	*PostClamp*	*PreUnclamp*
pH	7.41 ± 0.04	7.44 ± 0.04‡	7.53 ± 0.04†
PCO_2 mmHg	33 ± 2	32 ± 3§	35 ± 2§
HCO_3 mmol·L^{-1}	21 ± 2	22 ± 3§	32 ± 2*
Anion Gap	8 ± 1	8 ± 2§	13 ± 2†

n = 11	*PostUnclamp*	*End of Proc.*	*6 hrs post op*
pH	7.31 ± 0.04*	7.40 ± 0.04§	
PCO_2 mmHg	49 ± 5*	38 ± 2†	
HCO_3 mmol·L^{-1}	26 ± 2*	24 ± 1‡	26 ± 2†
Anion Gap	15 ± 3*	14 ± 2*	11 ± 2§

*$p < 0.001$; †$p < 0.005$; ‡$p < 0.05$; §NS.

after unclamping. The anion gap increased during the cross-clamp and returned to baseline six hours after the end of the operation.

Discussion

Major haemodynamic changes can be effectively curtailed during thoraco-abdominal aortic aneurysm repair with aggressive afterload reduction. Bicarbonate loading during the cross-clamp, with resulting metabolic alkalosis can prevent a profound metabolic acidosis from acid washout after unclamping.

Serum catecholamine responses to anaesthetic induction with fentanyl and sufentanil

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Catecholamine release may influence the haemodynamic response to anaesthetic induction with narcotics in patients with coronary disease.[1] Previous studies have yielded conflicting results regarding serum catecholamine responses to narcotic anaesthesia.[1–4] We have noted unexplained, potentially deleterious, increases in heart rate (HR) and arterial pressure (AP) in occasional patients during induction with high-dose fentanyl.[5] Therefore we tested the hypothesis that catecholamine release accompanies anaesthetic induction with potent narcotics.

Methods

Institutional approval was obtained and all patients gave informed consent. Thirty-three patients with preoperative left ventricular ejection fraction >0.50 who underwent elective coronary artery surgery participated in a randomized double-blind study. Patients received either fentanyl (F) 100 $\mu g \cdot kg^{-1}$ or sufentanil (S) 15 $\mu g \cdot kg^{-1}$. Antianginal medications were continued until the time of surgery. Premedication was morphine 0.1 $mg \cdot kg^{-1}$ IM and scopolamine 0.006 $mg \cdot kg^{-1}$ IM, 1 h preoperatively. In the operating room intravenous, radial arterial and pulmonary arterial catheters were inserted under local anaesthesia. Patients breathed 100 per cent O_2 by mask for 5 min, following which metocurine 0.06 $mg \cdot kg^{-1}$ IV was given. Two min later anaesthesia was induced with fentanyl 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$ or sufentanil 1.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Following loss of consciousness metocurine 0.36 $mg \cdot kg^{-1}$ IV was given over 2 min. End-tidal PCO_2 was monitored and ventilation controlled to maintain normocarbia. Arterial CO_2 ($PaCO_2$) was measured at C, and after 5 and 10 min of narcotic infusion. After 10 min of narcotic infusion the trachea was intubated. Blood for serum epinephrine (E) and norepinephrine (NE) was drawn at control (C), after 2, 4, 6, 8, 10 min of narcotic infusion, 1 min post-intubation (PI) and 1 min post-sternotomy (PS). Serum was stored at −70° C until analyzed by high performace liquid chromatography and electrochemical detection. Catecholamine levels are not normally distributed so statistical analysis was performed on log-transformed data using analysis of variance (ANOVA). Comparisons with control were made by least squares means procedure using Bonferroni's correction for multiple comparisons. A p-value of ≤0.05 was regarded as significant.

TABLE Serum NE ± SEM, $pg \cdot ml^{-1}$ (*p ≤ 0.05 vs C)

	C	2'	4'	6'	8'	10'	PI	PS
S	462 ±77	515 ±114	605 ±124	734* ±125	847* ±167	635 ±149	611 ±134	638 ±201
F	281 ±44	418* ±27	355* ±37	468* ±39	431* ±36	490* ±65	395* ±42	332 ±36

Results

Seventeen patients received S and 16 received F. Serum E was unchanged in either group. Serum NE increased significantly with both drugs ($p < 0.001$) peaking after 6–10 min of narcotic infusion (Table). The NE response to induction did not differ significantly between groups. Six patients developed increases in HR > 30 per cent during induction, but prior to intubation. In no patient did $PaCO_2$ exceed awake levels by ≥5 mmHg.

Discussion

Our results indicate that endogenous NE release accompanies induction with either F or S. This response may prevent hypotension during induction, but occasional potentially harmful hyperdynamic responses may result. Since equipotent doses of S and F cause similar increases in NE it seems likely that opioid receptors participate in this response. Differences between our study and others which do not demonstrate increases in NE[3,4] may reflect differences in anesthetic adjuvants, narcotic dose regimen, and/or duration of mask ventilation. Ongoing studies should clarify these issues.

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Cardiac function during abdominal aortic surgery. Preoperative assessment of the need for pulmonary artery catheterization

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It has recently been suggested that a poor correlation between PCWP and CVP exists in patients undergoing coronary artery surgery, in whom the ejection fraction (EF) is less than 0.5, when preload is altered.[1] The purpose of this study was to determine whether a knowledge of EF is able to predict the correlation between PCWP and CVP during aortic surgery when both the preload and afterload are altered.

Methods

Following hospital approval 23 ASA physical status Class II–III patients underwent preoperative MUGA scanning to determine EF. Premedications included diazepam 0.1 $mg \cdot kg^{-1}$ PO one and one-half hour preoperatively, morphine 0.1 $mg \cdot kg^{-1}$ and scopolamine 0.005 $mg \cdot kg^{-1}$ IM one hour preoperatively. After insertion of a Swan Ganz catheter under local anaesthesia, anaesthesia was induced with fentanyl 10 $\mu g \cdot kg^{-1}$ IV and thiopentone 1–2 $mg \cdot kg^{-1}$ IV. Muscle relaxation was obtained with pancuronium 0.1–0.15 $mg \cdot kg^{-1}$ IV. Anaesthesia was maintained with 70 per cent N_2O:30 per cent O_2 and 0.5 per cent to one per cent halothane under normocapnic conditions.

Changes in cardiac filling pressure (preload) were induced by ±24° table tilt. Changes in arterial resistance (LV afterload) were induced by aortic cross-clamp. CVP and PCWP were measured in the horizontal (control), ±24° positions for the awake, post-induction, pre-crossclamp, post-crossclamp and pre-declamp periods.

Data were analysed as a single population and as subgroups of good LV function (LVEF > 0.5): Group I, and poor LV function (LVEF < 0.5): Group II. Regression analysis and the appropriate paired t-tests were performed on all the data. The following relationships were explored: (1) CVP and PCWP for each patient pre- and post-crossclamp; (2) change in CVP (ΔCVP) and change in PCWP (ΔPCWP) associated with table tilt, for all patients at each measurement period, and (3) LVEF and the results of regression analysis from (1). $P < 0.5$ = statistically significant.

Results

Fourteen patients had good ventricular function, nine had poor ventricular function. Patients were comparable in all other respects. Thirteen of 23 patients failed to show a significant relation of CVP and PCWP at some time prior to or after aortic cross clamp. In one patient this occurred in both periods.

There was no statistically significant difference between slopes of ΔCVP and ΔPCWP for the awake, post-induction, pre-cross clamp and post-cross clamp periods. For Group I, knowledge of ΔCVP enabled prediction of ΔPCWP ± 6 mmHg. For Group II, the predictability of ΔPCWP form ΔCVP was as poor as ±12.5 mmHg after cross clamping. The regression analysis of "r" versus LVEF and slope versus LVEF demonstrated a horizontal line ($r = 0.5 \times 10^{-2}$ to 0.4). There was no statistically significant difference between slopes pre- and post-crossclamp.

Discussion

Preoperative knowledge of the LVEF does not help in predicting a relationship between CVP and PCWP in patients undergoing aortic surgery. Indeed in 53 per cent of our patients there was no significant relationship before and/or after crossclamp. When a relationship existed, it was not altered by application of aortic crossclamp. However, the spread of values that can be calculated by the 95 per cent confidence intervals makes prediction of PCWP from CVP clinically impractical. Therefore we suggest that both CVP and PCWP must be independently measured to assess ventricular filling pressures during aortic surgery.

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Oxygen consumption and carbon dioxide production in patients following open heart surgery

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Despite attempts to adequately rewarm patients after hypothermic cardiopulmonary bypass (CPB), they routinely arrive in the intensive care unit (ICU) with a nasopharyngeal temperature (NPT), ranging from 34–36° C. The metabolic changes that occur as a result of their subsequent rewarming, such as increased O_2 consumption and CO_2 production are undesirable in these patients. We wished to measure the actual change in these parameters during the first four hours post-CPB, a period during which these changes have been suggested to be

maximal, and to assess if the rate of rise of NPT or the presence of shivering are contributing factors. We also wished to assess the value of measuring mixed venous O_2 saturation ($S\bar{v}O_2$) as an indicator or the adequacy of tissue perfusion during the same period.

Methods

Sixteen patients undergoing open heart surgery were studied. After premedication with diazepam, morphine and scopolamine, routine monitoring lines were inserted under local anaesthesia. A fibreoptic, triple lumen, pulmonary artery catheter was also inserted for continuous monitoring of $S\bar{v}O_2$. Anaesthesia was induced with fentanyl 40 $\mu g \cdot kg^{-1}$ and pancuronium 0.15 $\mu g \cdot kg^{-1}$, and maintained with 100 per cent O_2 and isoflurane as required. During CPB, patients were cooled to a NPT of 26–28° C, then rewarmed to 37° C NPT prior to termination of CPB. O_2 consumption ($\dot{V}O_2$) was measured using the Fick principle and CO_2 production ($\dot{V}CO_2$) by measuring the fractional expiratory CO_2 concentration of timed, measured collections of expired gases. Both measurements were determined at 30 min intervals from 90 min (control) to 4 hrs post-termination of CPB, and divided by the BSA in an attempt to standardize the measurements. A temperature probe was placed in the nasopharynx and changes in NPT recorded for each 30 min interval. Mean values of each parameter were calculated for each time interval. The presence of shivering was recorded by the nurse in charge of the patient.

Results

Four patients in the study were noted to be shivering. These patients had more marked changes than the twelve patients who did not shiver. By 180 min post-CPB, $\dot{V}O_2$ increased maximally to 62 per cent above control values and was still 37 per cent above control values by 4 hrs (Table). In the group who shivered, the $\dot{V}O_2$ during the first 2 hrs in the ICU was a further 50–60 per cent increased compared to the group who did not shiver. By 4 hrs the $\dot{V}O_2$ was the same in both groups. $\dot{V}CO_2$ showed less marked changes, and was virtually constant in the non-shivering group, but again was 60–70 per cent greater in the shivering group, compared to the non-shivering. There was no correlation with $\dot{V}O_2$ and the rate of rise of NPT, nor at what temperature the patient started to shiver, although > 85 per cent of patients with $\dot{V}O_2 >$ 300 $ml \cdot min^{-1}$ had a NPT > 36° C. The patient with the highest $\dot{V}O_2$ and $\dot{V}CO_2$ was shivering to such a degree that he required pancuronium to maintain IPPV. The probability of a patient shivering could not be predicted.

Discussion

Patients are normally ventilated to normocarbia post CPB, but if the metabolic changes that occur during rewarming are not identified, this may lead to hypercarbia and respiratory acidosis. At the same time $\dot{V}O_2$ is also increased and shivering causes a marked further increase. This increase may initially be matched by a rise in cardiac output; however, when the rise in $\dot{V}O_2$ outstrips the ability of this compensatory mechanism, the $S\bar{v}O_2$ begins to fall and anerobic metabolism, with the onset of lactate acid production and metabolic acidosis, will become evident when the $S\bar{v}O_2$ falls below 50 per cent. The temperature at which these increased metabolic demands are maximal is unpredictable but they appear to develop during the first 4 hrs post-CPB. Shivering further increases these demands and it may be advisable to consider the use of muscle relaxors in these cases to reduce the possibility of both respiratory and metabolic acidosis developing at the same time. We believe that continuous monitoring of $PE\bar{C}O_2$ and $S\bar{v}O_2$ may aid to the early detection of these metabolic changes as the $PE\bar{C}O_2$ can detect the increased metabolic activity and the ability of the system to meet these increased demands is monitored by the $S\bar{v}O_2$.

TABLE Results (mean)

		Minutes post CPB					
		90	*120*	*150*	*180*	*210*	*240*
	AP	107.4	139.8	155.8	179.9	165.6	147.6
$\dot{V}O_2$/BSA	S	143.0	201.3	220.8	228.6	185.8	145.2
$ml \cdot min^{-1} \cdot m^{-2}$	NS	96.2	126.2	139.3	157.9	150.7	147.6
	AP	101.9	110.7	—	105.8	108.5	109.6
$\dot{V}O_2$/BSA	S	136.5	161.3	—	132.0	124.0	124.0
$ml \cdot min^{-1} \cdot m^{-2}$	NS	88.1	88.3	—	95.2	102.9	107.5
	AP	2.5	2.6	2.8	2.9	2.7	2.7
C.I.	S	2.9	3.2	3.4	3.4	3.2	2.7
$L \cdot m^{-1}$	NS	2.3	2.4	2.6	2.7	2.6	2.6
	AP	63.2	63.1	61.5	62.5	61.5	60.5
$S\bar{v}O_2$	S	54.5	52.0	50.3	54.3	56.3	57.5
(%)	NS	67.1	68.0	66.0	65.8	64.0	61.5

AP = all patients; S = shivering; NS = non-shivering.

A comparative study of continuous and intermittent epidural analgesia for labour and delivery

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Epidural analgesia administered by intermittent "top-up" doses of a local anaesthetic agent through an indwelling catheter is routinely used to provide pain relief during childbirth. Recently, continuous administration of the drug using mechanical infusion pump has gained popularity.[1,2]

TABLE I VAS Pain score (0–10)

	Group A (n = 29)	*Group B (n = 30)*
Before labour	8.6	9.0
After epidural	1.8	2.9
At delivery	2.4	3.4
Labour } as assessed	1.4	2.6
Delivery } next day	1.9	3.6

This study was undertaken to compare the two methods of administration of the same drug in equal doses, with regard to efficacy and outcome.

Methods

Sixty healthy, primigravid patients aged 18–35, gestation >37 weeks, who wished epidural analgesia for labour participated in the study after signing informed consent. The epidural catheter was inserted at L2-3, when labour was well established. All patients received an initial dose of 12 ml 0.25 per cent bupivacaine. The patients were randomized into two groups: Group A (29 patients) received 8 ml 0.25 per cent bupivacaine per hour by infusion and Group B (30 patients) received 8 ml 0.25 per cent bupivacaine hourly on a p.r.n. basis as determined by their nurse. At hourly intervals sensory block was assessed using pinprick, and motor block using the Bromage scale. Unblocked segments were noted. Pain level was scored on a visual analogue vertical scale (VAS) before the epidural was inserted, 30 min after effective pain relief had been obtained and after the delivery. A trained observer interviewed the patient the next day and scored the level of satisfaction with pain relief for both labour and delivery. Levels of bupivacaine in the mother's blood and the baby's cord blood at delivery were measured in six patients in each group.

Results

The two groups were well matched for age, height, weight, gestation and length of labour. The babies' weight, Apgar scores and cord blood gases were similar in the two groups. The mean height of the sensory block was T8 in both groups and the incidence of motor block was similar in the two groups. Eleven patients in each group recorded missed segments at some time during labour. VAS pain scores are shown in Table I. Before labour both groups scored pain in the 8–9 level on a vertical scale of 0 (no pain) to 10 (worst pain I've ever experienced). Group A scored consistently lower than Group B after the epidural both during labour and at delivery; however, the difference was not statistically significant ($p = 0.06$).

The mode of delivery in each group is shown in Table II. The number of C-Sections was the same in each group.

TABLE II Mode of delivery

	Group A (n = 29)	*Group B (n = 30)*
Vaginal delivery	6	15
Outlet forceps	12	6
High forceps	3	1
C-section	8	8

TABLE III Bupivacaine blood levels (mean ± SD)

	Group A (n = 6)	*Group B (n = 6)*
Maternal ($ng \cdot L^{-1}$)	770 ± 220	1427 ± 765
Cord ($ng \cdot L^{-1}$)	155 ± 94	272 ± 184

However, in Group A more patients required outlet forceps than in Group B. The mean amount of bupivacaine administered was significantly larger in Group A (165 mg ± 74) than in Group B (88.5 mg ± 53) ($p < 0.001$). Table III shows the mean (± S.D.) blood levels of bupivacaine. Even though Group A received nearly twice as much bupivacaine as Group B the maternal and cord blood levels at delivery tended to be lower but the difference was not statistically significant.

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Warming intravenous fluids and the incidence of shivering during Caesarean sections under epidural anaesthesia

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Shivering is a common side-effect of epidural anaesthesia for Caesarean section. It is distressing to the patient, interferes with monitoring and causes a rise in oxygen consumption. This study was designed to assess the effect of warming the intravenous fluids on the incidence of shivering and to determine if shivering is related to changes in body temperature.

Methods

Forty patients receiving epidural anaesthesia for elective Caesarean section were studied, after giving informed

consent. An epidural catheter was inserted into the lumbar epidural space. Then two litres of normal saline were infused intravenously over the next 20 minutes. Patients were randomly assigned to receive either warm (34° C) or unwarmed (room temperature) fluids. Carbonated lidocaine, two per cent, was injected into the epidural space in small increments, starting ten minutes after the start of the infusion. Core and skin temperatures were measured with probes in an aural canal and at four skin sites (calf, thigh, upper arm and lateral chest). Measurements were made prior to the infusion of the intraveneous fluids and at ten-minute intervals thereafter. Mean skin and mean body temperatures were calculated using Holdcroft's method.[1] The patients were assessed for shivering by an observer who was blind to the type of fluid administered. Shivering was scored on a scale 0–3 (0 – no shivering, 1 – mild, 2 – moderate and 3 – severe shivering).

Results

The overall incidence of shivering was 45 per cent. It was 55 per cent in patients receiving warmed fluids and 35 per cent in those receiving unwarmed fluids. Of the warmed patients, three of twenty, 15 per cent, had severe shivering. Five of 20, 25 per cent, of the unwarmed patients had severe shivering. There were no patients shivering at time zero. The onset of shivering coincided with the start of the epidural injection (Table I). Patients in both the warmed and unwarmed groups showed a fall in core temperature and a rise in mean skin temperature (Table II). Those who received warmed fluids maintained a higher mean body temperature, although this was not statistically significant. Both the shivering and the non-shivering groups showed a fall in core temperature. The patients who shivered had a higher core temperature at time zero (37.5 ± 0.1° C vs 37.2 ± 0.06° C; p = 0.013). During the first 20 minutes, core temperature fell by 0.7 in patients who shivered and by 0.6° C in those who did not. The difference was not statistically significant.

Discussion

Warming the intravenous fluids has no protective effect on the incidence of shivering during Caesarean section under epidural anaesthesia. It does not prevent a fall in core temperature. Although shivering is a phenomenon that occurs in response to cold, it may be modulated by other factors such as apprehension and the presence of cold solution in the epidural space.[2] This study is consistent with the hypothesis that patients who are predisposed to shivering need to maintain a higher core temperature.

TABLE I Time of onset of shivering

Time (mins)	*0*	*0–10*	*10–20*	*20–30*	*30–40*	*40–50*
No. of patients	0	3	13	1	1	0

TABLE II Temperatures °C (mean ± SEM)

Time (mins)	*0*	*10*	*20*	*30*	*40*
Warmed					
Core	37.4 ± 0.1	37.2 ± 0.06	37.0 ± 0.06	36.9 ± 0.08	36.7 ± 0.1
Mean skin	33.7 ± 0.2	34.1 ± 0.3	34.1 ± 0.2	34.3 ± 0.2	34.7 ± 0.2
Mean body	36.2 ± 0.14	36.1 ± 0.2	36.0 ± 0.15	36.0 ± 0.16	36.0 ± 0.14
Unwarmed					
Core	37.3 ± 0.08	37.0 ± 0.06	36.6 ± 0.06	36.5 ± 0.06	36.4 ± 0.06
Mean skin	33.5 ± 0.2	33.4 ± 0.7	33.7 ± 0.25	33.8 ± 0.25	34.2 ± 0.24
Mean body	36.0 ± 0.16	35.8 ± 0.4	35.6 ± 0.16	35.6 ± 0.15	35.6 ± 0.15

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Reflex bronchodilatation induced by laryngeal stimulation in humans

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Recent work has shown that in cats laryngeal stimulation reflexly evokes non-adrenergic, non-cholinergic bronchodilatation.[1] The aim of this study was to estabish if the same reflex can be demonstrated in humans. Subjects were premedicated with 80 μg of inhaled ipratropium bromide, 0.6 mg IV atropine and 10 mg IV propranolol. A flexible 6 mm bronchoscope was introduced via a nostril and positioned just above the epiglottis with a direct view of the vocal cords. Lung resistance (RL) was measured before and after the introduction of the bronchoscope by the technique of Amdur and Mead. The subjects then inhaled a histamine aerosol producing an increase in RL of 423 ± 196 per cent (mean ± SD) of control. The larynx was then mechanically irritated by a standard bronchoscopy brush introduced through the channel of the bronchoscope while RL was continuously recorded. One minute after the laryngeal stimulation, the bronchoscope was withdrawn and measurements of RL continued for 10 min. The results of 15 experiments performed in four subjects showed that following laryngeal stimulation, RL decreased from 423 ± 196 per cent of control to 265 ± 117 per cent ($p < 0.001$). This decrease in RL was independent of the slight cough produced by laryngeal irritation (two subjects).

The adequacy of beta-adrenergic blockade was examined in one subject. The increase in pulse (25 beats/min) and inpulse pressure (30 mmHg) produced by 16 ng·kg^{-1}·min^{-1} of isoproterenol IV was completely abolished by 10 mg IV propranolol. The adequacy of the cholinergic blockade was checked in two subjects. An R_L increase of 400 and 275 per cent of control respectively with inhaled methacholine was completely abolished by atropine 0.6 mg IV and 80 μg IV of inhaled ipratropium bromide. In two subjects, the bronchodilatation was abolished by a block of the superior laryngeal nerves and direct applications of local anaesthesia of the vocal cords with a mixture of lidocaine one per cent and bupivacaine 0.5 per cent. These results suggest that the bronchodilatation is neither cholinergic nor adrenergic in nature but reflex in origin. The afferent pathway of this reflex is the superior laryngeal nerve.

The importance of this reflex bronchodilatation during intubation remains to be established.

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Usefulness of the oxygen cost of breathing as an index of weaning ability from mechanical ventilation

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The spontaneous ventilatory measurements used to determine the ability of a patient to wean from mechanical ventilation do not aid in predicting its duration and eventual outcome.[1]

In this study we explore the relationship between the oxygen cost of breathing (OCB) and the derived variable the oxygen cost of breathing as a percentage of total oxygen consumption during spontaneous ventilation (OCB/VO_2 SV per cent) and weaning ability.

Methods

Thirty patients (14 males and 16 females) recovering from a critical illness who had required mechanical ventilation for at least 24 hours were studied. All patients were awake, haemodynamically stable and well oxygenated with an FiO_2 of less than 50 per cent.

At the start of weaning forced vital capacity (FVC), negative inspiratory force (NIF) and PaO_2/FiO_2 ratio were measured. Using indirect calorimetry, oxygen consumption was measured during controlled ventilation and again during spontaneous ventilation, the difference between the two values is the OCB. Two measurements of OCB were made within four hours of each other and the results averaged.

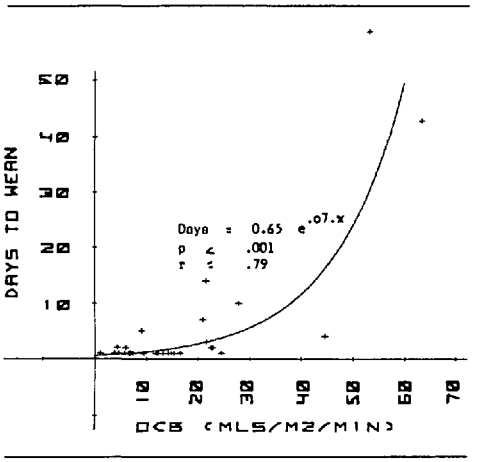

FIGURE 1 Correlation between OCB and duration of weaning.

Results

Two patients failed weaning; a 69-year-old COPD man with an OCB of 33.4 per cent died 43 days after the start of weaning from a cardiac arrest. A 52-year-old respiratory cripple with an OCB of 27.5 per cent remains ventilator dependent 240 days after the commencement of weaning.

Two patients required reintubation within 48 hours of extubation – one because of severe cardiogenic shock secondary to myocardial infarction and the other because of congestive cardiac failure. The latter patient died three days later. One patient died two days after extubation, from a cardiac arrest.

There was a significant exponential correlation between the OCB and the OCB/VO_2 SV per cent and the duration of weaning (Figures 1 and 2). FVC, NIF, PaO_2/FiO_2 did not correlate with the duration of weaning.

Discussion

Many criteria incorporating tests of mechanical capability and tests of oxygenating capability have been proposed as indices of weaning ability[2] but these have not been found useful in judging the ability of patients to wean from prolonged mechanical ventilation.[1]

The explanation for the usefulness of the OCB as an index of weaning ability may be in the fact that many factors both ventilatory and non-ventilatory can increase the OCB in critically ill patients. We have shown in our

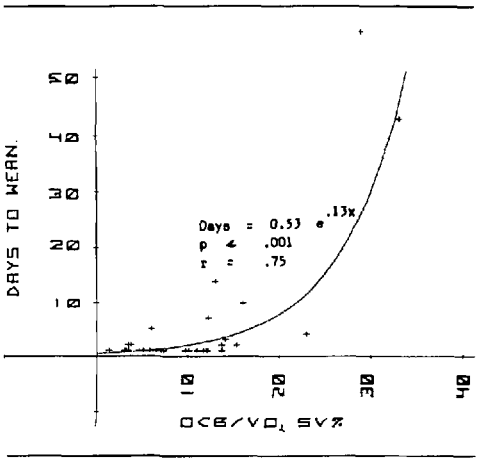

FIGURE 2 Correlation between OCB/VO_2 SV per cent and duration of weaning.

study that OCB correlated closely with the duration of weaning.

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Effects of succinylcholine on residual non-depolarizing neuromuscular blockade

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A small dose of a non-depolarizing muscle relaxant is commonly used to prevent succinylcholine (Sch) induced fasciculations. However, this drug interaction delays the onset of action and decreases the potency and duration of action of Sch.[1] A similar interaction may occur during the recovery phase of neuromuscular block induced by a non-depolarizing muscle relaxant when giving Sch to facilitate abdominal closure towards the end of a surgical procedure. This drug combination is controversial because of its unpredictable effects.[2] This study was undertaken to observe the effect of Sch when administered during partial recovery of neuromuscular blockade induced with atracurium.

Methods

After approval by the hospital research committee and with informed consent, 20 ASA physical status class I and II patients undergoing elective surgery, with the exception of eye surgery, were randomly assigned to one of two groups. Group I served as the control while group II represented the study group. Premedication with morphine 0.15 $mg \cdot kg^{-1}$ IM was given one hour prior to surgery. Atracurium 0.05 $mg \cdot kg^{-1}$ was given to prevent fasciculations. Anaesthesia was induced with thiopentone 3–7 $mg \cdot kg^{-1}$ and Sch 1–1.5 $mg \cdot kg^{-1}$ was given to facilitate endotracheal intubation. Anaesthesia was maintained with O_2 40 per cent in N_2O and isoflurane 0.7 per cent end-tidal concentration, as measured by a Datex Anesthetic Gas Monitor, and supplemented with fentanyl as required. Temperature was monitored and ventilation was controlled to maintain end-tidal CO_2 concentration between 35 and 40 mmHg. Neuromuscular blockade was monitored using integrated evoked electromyographic (IEEMG) response with the Datex monitor.

Once steady state anaesthesia was attained and the single twitch (T1) completely recovered from the effects of Sch used at induction (minimum of twenty minutes), the IEEMG was calibrated at 100 per cent. Thereafter, the T1 response to supramaximal stimulation of the ulnar nerve was monitored at 20-second intervals. A non-depolarizing neuromuscular block was established with atracurium 0.15 $mg \cdot kg^{-1}$. Once T1 recovered spontaneously to 25 per cent of its initial value, patients in group II were given Sch 0.5 $mg \cdot kg^{-1}$ while those in group I received normal saline. Changes in T1 were compared between the two groups as was the time for recovery of T1 to 75 per cent (T25–75 per cent) of its initial value.

The data were analysed using the Behrens-Fisher distribution of the "t" test. A p value <0.05 was considered significant.

Results

A summary of results is shown in the Table. After administration of Sch, the T1 recovered rapidly, reaching its maximum change from 25 per cent to a mean of 55.8 per cent within 160 seconds. The control group recovered to a mean of 33.8 per cent in the same time interval. This difference was statistically significant with a p value less than 0.005. The recovery time of T1 to 75 per cent of its

TABLE Results (mean ± SD)

	Change in T1 (%) at 160 secs	*Time for recovery (s) (T25%–75%)*
Group I	8.8 ± 2.29	748 ± 114
Group II	30.8 + 8.87†	610 + 190*

*$p < 0.05$ when compared to control.
†$p < 0.005$ when compared to control.

initial value was also shorter ($p < 0.05$) in group II (610 seconds) compared to the control group (748 seconds).

Discussion

This study demonstrates a consistent paradoxical effect of Sch when administered to patients in whom a depression of the T1 to 25 per cent of its initial value is induced with atracurium. Although the time to recovery of the single twitch to 75 per cent was also shortened, we cannot conclude this effect to be the result of steeper recovery slope as has been suggested.[3]

The precise mechanism of action for this paradoxical effect is unknown but may be speculated upon based on current theories of neuromuscular junction physiology. Sch may bind to the post-junctional receptor causing transient opening of the channel, or may bind to and stimulate the pre-junctional receptor causing increased mobilization and release of acetylcholine, or it may even occupy the acetylcholinesterase receptor in a manner similar to an anticholinesterase.

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Single breath end-tidal PCO_2 approximates arterial PCO_2 in infants and children

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End-tidal gas sampling is used to assess the adequacy of alveolar ventilation and anaesthetic gas concentrations in paediatric anaesthesia. However, end-tidal gas sampling is useful only if it approximates the arterial values.[1-3] To determine if end-tidal gas sampling is useful in paediatrics, end-tidal and arterial values for PCO_2 were compared in infants and children during general anaesthesia.

Methods

With approval from the Human Review Committee, 68 healthy infants and children scheduled for surgery requiring tracheal intubation were studied. All infants and children were mechanically ventilated through an Ayre's t-piece. The total fresh gas flow was 2.5 to 3.0 times the alveolar ventilation. Positive end-expiratory pressure was avoided. After ventilation was controlled for 15 minutes, a single breath end-tidal gas sample was obtained as follows: a #23 gauge needle was inserted through the wall of the endotracheal tube immediately below the connector. During the next tidal volume, the fresh gas line was disconnected from the anaesthetic machine at peak inspiration. During the same breath, 3–4 ml of expiratory gas were aspirated through the needle into a 5 ml plastic syringe at end-expiration. An arterial blood sample was then obtained from an in-dwelling arterial cannula or through a percutaneous arterial puncture. Both end-tidal gas and arterial blood samples were analyzed in a Corning® blood/gas analyzer (Model 175). After inserting the end-tidal gas sample into the Corning® analyzer, the "reset" button was pushed twice to flush the sample chamber. The blood/gas analyzer was calibrated daily with standard solutions. The end-tidal and arterial PCO_2 values were plotted on a linear scale. Least squares linear regression analysis (and the coefficient of determination, r^2) were used to correlate end-tidal and arterial PCO_2 values.

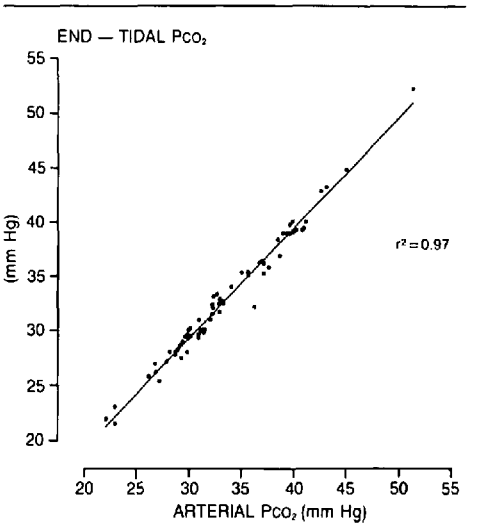

FIGURE Correlation of arterial PCO_2 with end-tidal PCO_2.

Results

The mean (± SD) age and weight for the 68 children were 6.4 ± 5.1 years and 18.4 ± 16.3 kg. The mean (± SD) end-tidal and arterial PCO_2 values were 33.6 ± 6.9 mmHg and 33.6 ± 5.6, respectively. The end-tidal PCO_2 correlated very closely with the arterial PCO_2 ($r^2 = 0.97$) (Figure).

Discussion

Single breath end-tidal PCO_2 measurements accurately approximate the arterial PCO_2 values in infants and children who are mechanically ventilated with a partial rebreathing circuit. Previous studies have suggested that continuous gas sampling in paediatric patients may not accurately approximate the arterial gas tensions.[3] To minimize inaccuracies in continuous end-tidal gas sampling, we recommend the use of single breath end-tidal gas sampling for easy, accurate, and non-invasive PCO_2 monitoring in infants and children.

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Increasing carbon dioxide tension during emergence – how safe is your approach?

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A mild degree of hypocapnia is usually induced during the maintenance phase of anaesthesia, when controlled ventilation is used in conjunction with a muscle relaxant. During emergence it is often necessary to increase the patient's arterial CO_2 tension to a level compatible with the return of spontaneous respiration. A survey done locally revealed that there are at least four approaches to this practice: (1) by flushing the circuit with a large fresh gas flow of O_2 but leaving the patient apnoeic, (2) by flushing the circuit with a large fresh gas flow of O_2 and ventilating the lungs for a few breaths before leaving the patient apnoeic, (3) by leaving the inflow of O_2/N_2O mixture used during the anaesthetic unchanged with the patient apnoeic and ventilating the lungs manually on occasion only, and (4) by flushing the circuit with a small fresh gas flow of O_2 only but ventilating the lungs continuously. This study was carried out to determine if there are any differences in the state of oxygenation of the patients and to follow the rise in end-tidal CO_2 tension during these procedures.

Methods

Twenty ASA physical status class I patients were randomly divided into four equal groups at the end of an O_2/N_2O/relaxant/controlled ventilation anaesthetic using the Bain circuit, during which the end-tidal CO_2 tension was reduced to about 30 mmHg. The fresh gas used was 66 per cent N_2O in O_2 flowing at approximately 70 $ml \cdot kg^{-1} \cdot min^{-1}$; the tidal volume and rate were set at 10 to 12 $ml \cdot kg^{-1}$ and 10 to 12 breaths/min respectively; anaesthesia was supplemented with a volatile agent and a narcotic analgesic as necessary. During emergence those in group I were allowed to remain apnoeic with O_2 only flowing into the circuit at 6 $L \cdot min^{-1}$; those in group II were ventilated for 30 sec with O_2 only flowing into the circuit at 6 $L \cdot min^{-1}$ and then allowed to remain apnoeic; those in group III were allowed to remain apnoeic with the fresh gas flow of N_2O in O_2 unchanged; those in group IV were ventilated but the fresh gas was changed to O_2 only flowing at 15 $ml \cdot kg^{-1} \cdot min^{-1}$. All patients were monitored by ear oximeter (Biox III) and end-tidal capnography (Hewlett-Packard 47210A). Oxygen saturation was recorded at 30 sec intervals for ten minutes before the lungs were ventilated again with O_2 if O_2 saturation remained above 90 per cent; but the lungs were ventilated immediately with pure O_2 if O_2 saturation fell to 90 per cent. In the first three groups of patients, end-tidal CO_2 tensions were noted immediately before and immediately after the apnoeic period; in the fourth group of patients, end-tidal CO_2 tensons were recorded at 30-sec intervals.

Results

Mean ($\pm$SD) oxygen saturation readings of the four groups of patients at the beginning of emergence were 98.6($\pm$2.1), 98.4($\pm$1.3), 97.6($\pm$0.6), and 98.0($\pm$1.9) per cent respectively. Among group I patients, O_2 saturation remained at pre-apnoeic levels in four but fell from 99 to 94 per cent by the end of the apnoeic period in one. Among group II patients it remained at pre-apnoeic levels in three, fell by one per cent by the end of the apnoeic period in one, and fell from 98 to 94 per cent in another. Among group III patients O_2 saturation fell to 90 per cent within 2.5 to 6.5 min after the onset of apnoea in all five. Among group IV patients O_2 saturation did not decline in four and fell by only one per cent in one. Mean ($\pm$SD) end-tidal CO_2 tensions of the four groups were 30.4($\pm$1.1), 30.4($\pm$0.9), 30.6($\pm$0.9), and 29.8($\pm$0.5) mmHg respectively at the start of the study. They were 58.0($\pm$5.0), 52.0($\pm$2.5), and 50.6($\pm$0.9) mmHg respectively in groups, I, II, and IV at the end of the 10 min period. In group III patients, apnoea was interrupted at various intervals after its onset and mean end-tidal CO_2 tension of the group at the end of apnoea was not calculated.

Discussion

Although the number in each group is small, our results

have shown that certain methods of increasing arterial CO_2 tension are potentially unsafe and further investigation is warranted. Leaving the fresh gas flow of O_2/N_2O unchanged and the patient apnoeic at the same time has the smallest margin of safety; large falls in O_2 saturation can occur early on without observable cyanosis. Occasional manual ventilation will slow this fall, but reliance should not be placed upon it because the anaesthetist can easily be distracted by other chores. Flushing the circuit with a large fresh gas flow of O_2 and allowing the patient to be apnoeic at the same time, carried out either with or without first ventilating the lungs with O_2, also cannot be condoned because one of five patients in each of groups I and II still had a four to five per cent fall in O_2 saturation by 10 min after the onset of apnoea. The only safe approach is to continue ventilation of the lungs but maximize rebreathing by using a low fresh gas flow of O_2 only. This method guarantees optimum oxygenation and allows the end-tidal CO_2 tension to rise at a rate comparable to apnoea. We have shown that an O_2 fresh gas flow of 15 $ml \cdot kg^{-1} \cdot min^{-1}$ will allow the end-tidal CO_2 tension to rise to a level compatible with return of spontaneous respiration during emergence.

Decreasing the toxic potential of intravenous regional anaesthesia: Bier's block revisited

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The main complications associated with intravenous regional anaesthesia result from the sudden introduction of a toxic amount of local anaesthetic (LA) into the systemic circulation. To minimize the impact of such occurrence one must use a LA of low toxicity.[1] This paper focuses on another approach: reducing the amount of LA required to perform the block either by reducing the volume (e.g. *forearm* tourniquet) or by decreasing the concentration of LA. We attempted to answer the following: (1) What is the volume required to fill the forearm venous system without causing any leakage? Despite mention of possible difficulties related to interosseous arterial configuration,[2] a forearm tourniquet has been used successfully.[3] (2) Using the above volume, what is the minimal effective concentration of lidocaine? While a 0.5 per cent solution provides reliable anaesthesia[2,3] and a 0.25 per cent solution does not,[4] a 0.375 per cent solution has not been evaluated.

Methods

Informed consent was obtained from all subjects.

Volume determination

Twelve healthy volunteers (members of our department, 6M, 6F) participated. A 20 g teflon catheter was inserted in a dorsal vein of the hand and used for injection of contrast material (Hexadrix™). A similar canula was inserted in the ipsilateral radial vein for pressure recording during the injection. After placement of an 8 cm surgical cuff 1 cm below the elbow, the forearm was exsanguinated with an Esmarch bandage and the cuff inflated 100 mmHg above systolic blood pressure. The injection of contrast medium was then started at a rate not exceeding 0.5 $ml \cdot sec^{-1}$, under *constant* fluoroscopic control and videotaped. The injection was stopped when the radiologist judged the venous system full.

Concentration determination

Twelve healthy volunteers (6M, 6F, 9 of whom were enrolled in the first study) participated. A venous block was performed, using the technique above, except that (1) only one canula was inserted, on the dorsum of the hand; (2) the volume injected was based on angiographic findings (see results); (3) the solution injected consisted of lidocaine 0.5, 0.375 or 0.25 per cent administered in a double-blind, pseudo-randomized order, such that each concentration was used twice for each sex. Neurologic assessments[4] were carried out at 2, 5, 10, 15 and 20 minutes after the end of injection.

Results

Volume determination

(1) Volume. Final filling volumes were determined by independent review of videotapes by two investigators using standardized criteria. These volumes (mean = 17.67 mL SD = 4.29) correlated significantly ($p < 0.01$) with body weight ($r = 0.71$), height ($r = 0.73$), volume of forearm ($r = 0.79$) and length of forearm ($r = 0.81$). Since weight is most convenient, the following equation (linear regression) was used to compute the volume of LA solution: vol = 0.281 × weight + 3.31 (in ml and kg). (2) Filling pattern. A fairly constant pattern emerged. The veins immediately below the cuff were the first to be filled, followed by the palmar arcade and digital veins. Veins of the distal forearm and proximal hand filled last. We observed no leak of contrast medium nor congestion of the limb. Pressure recordings showed a poor correlation with the volume injected.

Concentration determination

Satisfactory analgesia, based on subjective evaluation at 15 minutes by the same investigator, was attained in all patients of the 0.5 per cent group but in only two of the four patients of the 0.375 per cent group and in only two of the four patients receiving the 0.25 per cent solution. All patients with satisfactory analgesia had complete loss of pinprick sensation at 15 min or less. Congestion of the

forearm was noted in two (male) patients immediately following forearm movments requested for motor testing.

Conclusions

(1) For a venous block with a forearm tourniquet, the volume required to fill the venous system is vol = 0.281 × weight + 3.31 (in ml and kg), or approximately 15 to 20 ml for an adult. (2) This volume of lidocaine 0.5 per cent provides satisfactory analgesia. More dilute solutions are inadequate. (3) The amount of lidocaine thus administered does not exceed the IV toxic dose, minimizing the danger secondary to premature cuff deflation. (4) Filling of the venous system is segmental and discontinuous because fluid progression requires pressure induced venous valves dysfunction. Accordingly, pressure recording does not reflect whole limb filling. Finally, the risk of limb congestion appears to be significant with forearm tourniquet, especially if there is movement of the limb.

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The effects of isoflurane or nitrous oxide on cerebral blood volume in the dog

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A current controversy in neuroanaesthesia concerns the safety with which nitrous oxide (N_2O) and isoflurane (ISO), alone or in combination may be administered to patients with intracranial hypertension. Some authors assert that the vasodilation produced by these drugs is minimal,[1] while others feel that the vasodilating effects are important, producing dangerous increases in ICP,[2] particularly when these agents are used together.[3]

The present experiments were undertaken to study the effects of clinically relevant concentrations of N_2O and ISO, alone or in combination, on cerebral blood volume (CBV) in the dog. In addition, we sought to determine whether hypocapnia produced after the introduction of 1.0 MAC ISO + 0.5 MAC N_2O would significantly decrease CBV.

Methods

Eight unmedicated, fasted mongrel dogs (18–22 kg) were studied. Induction of anaesthesia was performed with intravenous thiopentone 7 $mg \cdot kg^{-1}$ and fentanyl 12 $\mu g \cdot kg^{-1}$. Following endotracheal intubation, a fentanyl infusion (2.4 $\mu g \cdot kg^{-1} \cdot hr^{-1}$) was maintained. Controlled ventilation with 100 per cent O_2 at normocarbia was facilitated with pancuronium as required. All skin wounds were carefully infiltrated with 0.25 per cent bupivacaine prior to closure.

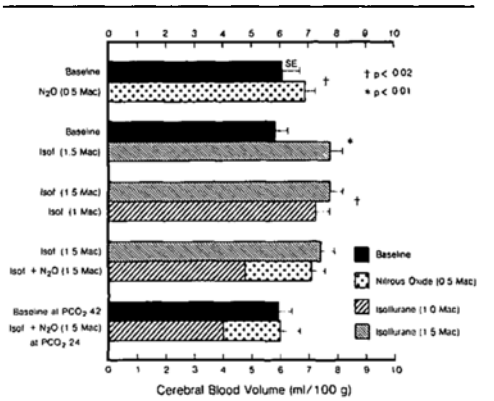

FIGURE Cerebral blood volume with isoflurane and/or nitrous oxide.

Following *in vivo* labelling of red cells by inhalation of ^{11}CO, CBV was measured by positron emission tomography using the method validated by Phelps *et al.*[4]

CBV, mean arterial pressure, end-tidal ISO, and $PaCO_2$ were measured serially under anaesthesia conditions in the following sequence: Baseline 1 (90 min after induction of anaesthesia), N_2O 50 per cent (after 15 min exposure), Baseline 2 (after 15 min washout N_2O), ISO 2 per cent (1.5 MAC), ISO 1.3 per cent (1.0 MAC), ISO 1.3 per cent + N_2O 50 per cent (1.5 MAC total), ISO + N_2O (1.5 MAC total) with $PaCO_2$ reduced to 24 mmHg. Blood pressure was maintained within ten per cent of control levels with a phenylephrine infusion. Control and experimental measurements of CBV were compared using a paired t-test with Bonferroni's modification for multiple comparisons where appropriate.

Results

Technical difficulties precluded the use of CBV values from all eight dogs under each anaesthetic condition. CBV under Baseline 1 conditions was 6.1 ml/100 g brain tissue. (Figure). N_2O 50 per cent caused a 13 per cent increase ($p < 0.02$, $n = 6$) in CBV which was reversed when the N_2O was washed out (Baseline 2). Administration of ISO 2 per cent caused a 32 per cent increase in CBV ($p < 0.01$, $n = 7$), which decreased ($p < 0.02$, $n = 7$) when ISO was reduced to 1.3 per cent. At an anaesthetic level of 1.5 MAC, CBV with the combination

of ISO and N_2O was not statistically different from values obtained with ISO alone (n = 6). Acute hyperventilation caused an immediate decrease in CBV ($p < 0.01$, n = 6) down to levels similar to control.

Discussion

The absolute values for CBV obtained in this study are similar to those obtained by previous workers.[4] This study demonstrates that for the sequence used, administration of N_2O, ISO (1.0 and 1.5 MAC), and ISO + N_2O (1.5 MAC total) all result in increases in CBV. If these results apply to man, two per cent ISO would be associated with a 22 ml increase in CBV. There was no evidence to suggest that the combination of ISO + N_2O produced a greater increase in CBV than ISO alone at equianaesthetic levels.

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Monitoring of somatosensory-evoked potentials in man during isoflurane and isoflurane-nitrous oxide anaesthesia

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Intraoperative monitoring of evoked responses may prevent neurological injury during certain neurosurgical procedures. To allow intelligent interpretation of changes in evoked responses, the influence of nonpathological factors must be delineated and taken into account. To date, the influence of isoflurane anaesthesia on somatosensory evoked potentials (SSEP) has not been studied in a dose-related manner under controlled conditions. Accordingly, we have examined the influence of isoflurane and isoflurane-nitrous oxide anaesthesia on SSEP in eight healthy human volunteers.

Methods

The study was approved by the Institutional Ethics Committee. Eight healthy male subjects aged 19–38 admitted for minor orthopaedic procedures were studied. SSEP was recorded from the scalp over the sensory cortex (C3′ or C4′, international 10–20 system), C_7 spine and the Erb's point contralateral to the cortex but ipsilateral to the median nerve that was stimulated with a square wave at an intensity of 2 MA above the motor threshold. All recordings were replicated. Following recording of baseline awake SSEP, anaesthesia was induced with tubocurarine 3 mg, thiopentone 5–6 $mg \cdot kg^{-1}$, and succinylcholine 1.5 $mg \cdot kg^{-1}$. During maintenance isoflurane-oxygen anaesthesia, the end-tidal CO_2 was controlled between 32–38 mmHg. Temperature was kept near normal with a heating blanket and warm intravenous fluid. SSEP was then recorded at two steady end-tidal concentrations of isoflurane, one and two per cent as monitored by mass spectrometry. The sequence of study was randomized among the eight subjects. In five subjects, the additional influence of nitrous oxide was examined during one per cent isoflurane anaesthesia. Surgery was only allowed to proceed after completion of all recordings. Change in latency and amplitude of the peaks – N20 (cortex), N13 (C7), and N10 (Erb's) were analyzed using ANOVA for repeated measures, Dunnett's test and Scheffe's test.

Results

SSEP was successfully recorded from all subjects. With the exception of amplitude of N10, isoflurane reduced the amplitude as well as increased the latency of all peaks. The influence was maximal at the cortex, and decreased towards the periphery. (Table I). Although the further decrease in the mean amplitude of N20 from one to two per cent isoflurane was not statistically significant, in three of the eight subjects the peak was totally abolished.

TABLE I Results. Isoflurane 1% and 2%

	Amplitude (μV ± SEM)		
	N20	*N13*	*N10*
Awake	1.24 ± 0.18	2.77 ± 0.25	2.50 ± 0.41
1% Isoflurane	0.55 ± 0.11*	2.23 ± 0.29*	2.77 ± 0.48
2% Isoflurane	0.24 ± 0.09*	1.79 ± 0.23*†	2.74 ± 0.48

	Latency (msec ± SEM)		
	N20	*N13*	*N10*
Awake	20.2 ± 0.1	14.2 ± 0.2	10.6 ± 0.1
1% Isoflurane	23.8 ± 0.4*	14.8 ± 0.3*	10.8 ± 0.1*
2% Isoflurane	25.0 ± 0.4*‡	15.0 ± 0.3*	10.8 ± 0.1*

*Significantly different from awake control $p < 0.05$.
†Significantly different from 1%, $p < 0.05$.
‡n = 5 because 3 subjects had no identifiable peak.

TABLE II Results. Isoflurane 1% and isoflurane 1% + 50% N20

	Amplitude ($\mu V \pm SEM$)		
	N20	*N13*	*N10*
1% Isoflurane	0.52 ± 0.10	2.62 ± 0.47	3.14 ± 0.51
1% + 50% N_2O	0.17 ± 0.10*	2.12 ± 0.29	3.00 ± 0.48
	Latency (msec ± SEM)		
	N20	*N3*	*N10*
1% Isoflurane	23.6 ± 0.5	14.7 ± 0.4	10.8 ± 0.2
1% + 50% N20	23.6†	14.8 ± 0.4	10.7 ± 0.2

*Significantly different from 1%, $p < 0.05$.
‡n = 2 because 3 subjects had no identifiable peak.

The addition of nitrous oxide to one per cent isoflurane anaesthesia in five subjects had a similar effect, abolishing the N20 peak in three out of five subjects (Table II).

Discussion

In this study we have identified the influence of isoflurane on SSEP in a dose-related manner. Isoflurane up to an end-tidal concentration of one per cent decreases the amplitude and increases the latency of the cortical peak but nevertheless allows the recording and evaluation of SSEP. Nitrous oxide, on the other hand, profoundly affects the recording of the cortical peak, and should be avoided during intraoperative recording of SSEP. This observation on nitrous oxide is consistent with previous reports.[1,2]

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Do mannitol-induced haemodynamic responses influence its effect on intracranial pressure? A study in the dog with and without induced intracranial hypertension

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Caution has been urged regarding the use of mannitol during states of raised intracranial pressure (ICP) and lost autoregulation.[1] Recent studies, however, confirmed the safety of rapid infusion of mannitol in settings of raised ICP in dogs and suggested an important role of haemodynamics.[2] The present study was therefore undertaken to compare the haemodynamic responses to mannitol in two groups of dogs: those with induced intracranial hypertension and those without.

Methods

Sixteen unmedicated dogs, weighing 18–22 kg, were studied. Anaesthesia was induced with a single IV dose of thiopentone. The dogs were intubated and ventilated using compressed air. $PaCO_2$ was adjusted to 40 ± 2 mmHg. Anaesthesia was maintained with fentanyl and metocurine. The dogs were randomly divided into 3 groups. *In group A* (six dogs): after a stabilization period of 30 minutes, baseline measurements of ICP, heart rate (HR), mean arterial pressure (MAP), central venous pressure (CVP), mean pulmonary artery pressure ($\overline{PAP}$), pulmonary capillary wedge pressure (PCWP), and cardiac output (CO) were obtained and a 20 per cent solution of mannitol: 2 $g \cdot kg^{-1}$, was rapidly infused over a three-minute period. Data were collected at the end of the infusion and at two, five and ten minutes post-infusion. *In group B (six dogs)*: an epidural balloon was inserted and gradually inflated with 3 ml of air. Once a sustained elevation of ICP was secured, mannitol was infused following the same protocol as in group A. *Group C*: Consisted of four control dogs that received no mannitol despite the inflation of the epidural balloon. Total peripheral resistance (TPR) and pulmonary vascular resistance (PVR) were derived from appropriate formulae. Data were analysed using analysis of variance and Dunnett's modified t-test. P values <0.05 were considered significant.

Results

Results are detailed in Tables I and II. Data are expressed as the mean ± SEM. *In group A dogs*, mannitol caused a

TABLE I Results: mean ± SEM group A (n = 6)

	Baseline	*End of infusion*	*Ten-minutes post-infusion*
ICP	8.2 ± 0.5	12.3 ± 0.7*	8.0 ± 0.7
HR	60.0 ± 3.8	112.7 ± 4.9*	87.8 ± 3.9*
MAP	75.1 ± 2.3	114.2 ± 4.3*	92.6 ± 4.3*
CVP	4.8 ± 0.5	8.3 ± 0.3*	6.7 ± 0.6†
$\overline{PAP}$	13.4 ± 0.3	21.7 ± 0.8*	16.3 ± 0.3*
PCWP	6.3 ± 0.3	10.0 ± 0.7*	7.8 ± 0.4*
CO	2.0 ± 0.1	5.1 ± 0.2*	2.4 ± 0.1†
TPR	2796 ± 84	1674 ± 37*	2806 ± 118
PVR	266 ± 8	183 ± 10*	279 ± 23

*$p < 0.01$.
†$p < 0.05$.

TABLE II Results: mean ± SEM group B (n = 6)

	Baseline	*End of infusion*	*Ten-minutes post-infusion*
ICP	24.5 ± 2.5	20.0 ± 1.8†	15.6 ± 2.1*
HR	80.0 ± 8.3	124.5 ± 12.2*	110.0 ± 11.3*
MAP	111.5 ± 2.4	83.2 ± 2.0*	114.7 ± 2.7
CVP	6.1 ± 0.3	11.2 ± 0.8*	7.5 ± 0.4†
$\overline{PAP}$	16.2 ± 0.7	27.7 ± 1.5*	21.0 ± 1.3*
PCWP	8.3 ± 0.3*	14.0 ± 1.2*	11.0 ± 0.9*
CO	2.4 ± 0.1	6.1 ± 0.4*	4.1 ± 0.3*
TPR	3530 ± 141	966 ± 87*	2213 ± 223*
PVR	263 ± 23	177 ± 10*	203 ± 21

*$p < 0.01$.
†$p < 0.05$.

significant initial rise in ICP (4.7 ± 0.6 mmHg), and in HR (52 ± 4 beats/minute), MAP (39.1 ± 3.2 mmHg), CVP (4.5 ± 0.4 mmHg), $\overline{PAP}$ (8.3 ± 0.6 mmHg), PCWP (3.7 ± 0.5 mmHg), and CO (3.2 ± 0.2 $L \cdot min^{-1}$). In contrast, TPR dropped by 1,121.9 ± 41.3 dynes·sec·cm^{-5} and PVR decreased by 82.2 ± 9.2 dynes·sec·cm^{-5}. ICP, HR, MAP, CVP, $\overline{PAP}$, PCWP and CO gradually decreased over the following ten minutes, and TPR and PVR gradually returned to pre-infusion values. *In group B dogs*, mannitol caused an immediate decline in ICP, MAP, TPR and PVR. ICP decreased by 4.5 ± 2.1 mmHg, MAP decreased by 28.3 ± 2.2 mmHg, TPR decreased by 2.563.4 ± 114.2 dynes·sec·cm^{-5}, and PVR decreased by 86.4 ± 11.2 dynes·sec·cm^{-5}. Initial changes in HR, CVP, PAP, PCWP, and CO closely correlated with group A results. Thus, at the end of the infusion: HR rose by 45 ± 10 beats/minute, CVP increased by 5.0 ± 0.6 mmHg, $\overline{PAP}$ increased by 11.5 ± 1.2 mmHg, PCWP increased by 5.7 ± 0.9 mmHg and CO increased by 3.7 ± 0.3 $L \cdot min^{-1}$. ICP continued to decrease over the following ten minutes, while MAP, TPR, and PVR gradually increased and HR, CVP, $\overline{PAP}$, PCWP, and CO gradually decreased.

Discussion

In dogs with no mass lesion, mannitol in addition to its direct cerebral vasodilating properties, augmented plasma volume, increased CO, and raised MAP. A transient increase in cerebral blood flow and volume may have caused the initial rise in ICP. In group B dogs, the induction of intracranial hypertension eliminated the capacity of the cerebral vasculature to autoregulate and caused large surges in MAP and TPR. As MAP is determined by changes in CO and TPR, we therefore speculate that in this group mannitol's effect on TPR overrode its effect on CO and consequently lowered MAP and hence ICP.

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Isoflurane augments the hypothermia-induced reduction of cerebral metabolic rate during cardiopulmonary bypass

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It has been shown that isoflurane reduces the cerebral metabolic rate for oxygen ($CMRO_2$) in surgical patients.[1] Hypothermia during cardiopulmonary bypass (CPB) induces a marked reduction in $CMRO_2$[2] and the purpose of this study was to ascertain whether further reductions in $CMRO_2$ during hypothermic CPB for coronary artery bypass surgery were attainable with the use of isoflurane.

Methods

The study was approved by the Institutional Committee on Human Research, and written informed consent was obtained from patients scheduled for coronary artery bypass surgery who were then randomly allocated to control group (CG) or isoflurane treated group (IG). After premedication with lorazepam 0.06 $mg \cdot kg^{-1}$ and morphine 0.15 $mg \cdot kg^{-1}$ all patients were anaesthetised with fentanyl 0.1 $mg \cdot kg^{-1}$ and ventilated with oxygen. IG patients were given isoflurane, in air and oxygen, via the pump oxygenator in a concentration sufficient to produce a predominantly isoelectric EEG for the duration of CPB. CG patients were given air and oxygen during CPB with no additional anaesthetic agents.

Cerebral venous blood was sampled from a catheter which had been threaded percutaneously to the bulb of the internal jugular vein, and arterial blood from a radial artery line or the arterial port of the pump oxygenator. Blood gases were measured at 37° C and corrected to nasopharyngeal temperature for determination of oxygen content. Cerebral washout of ^{133}Xe was measured with five scintillation counters over each hemisphere, following injection of 5 mCi of the isotope into a peripheral vein or the arterial port of the pump oxygenator, and used to

determine regional cerebral blood flow. The mean cerebral blood flow (CBF) from all ten detectors was applied to the Fick equation to calculate the cerebral metabolic rate for oxygen ($CMRO_2$). A ten lead EEG using a standard parasagittal bipolar block montage with a sensitivity of 7 μV and a passband of 0.5–70 Hz was continuously monitored throughout surgery.

Pump flows of 2.0–2.5 $L \cdot m^2 \cdot min$ were used during CPB. Arterial PCO_2 was maintained at about 40 mmHg, measured at 37° C and uncorrected for patient temperature.

Results

One per cent isoflurane added to the fresh gas supply of the pump oxygenator induced a predominantly isoelectric EEG during hypothermic CPB (25.5–29.7° C) in the six IG patients. During normothermic CPB (37–38° C) 2.5 per cent isoflurane was required to maintain the predominantly isoelectric EEG in five out of six patients. The five CG patients had continuous low-frequency EEG activity throughout CPB.

Following induction of anaesthesia and prior to CPB, mean $CMRO_2$ for all patients was 1.65 ml/100 g/min. Mean $CMRO_2$ values during hypothermic CPB in CG patients were 0.45 and 0.49 ml/100 g/min at 15 minutes and 30 minutes. During normothermic CPB $CMRO_2$ in CG was 1.08 ml/100 g/min. Use of isoflurane during CPB resulted in a 35–40 per cent reduction of $CMRO_2$ from control values at each stage of CPB (Table). CBF tended to be lower in isoflurane-treated patients compared to controls during CPB. Under anaesthesia post CPB (and after discontinuation of isoflurane in IG) $CMRO_2$ approached pre-CPB values in both groups. At each measurement arterial PCO_2 and nasopharyngeal temperature were comparable between groups.

TABLE Results mean ± standard deviation.

Groups		*Pre-CPB*	*15 min cold CPB*	*30 min cold CPB*
Control	CBF	25.9 ± 9.6	20.8 ± 5.1	17.2 ± 8.6
5 patients	$CMRO_2$	1.53 ± 0.38	0.45 ± 0.12	0.49 ± 0.09
	n =	4	4	3
Isoflurane	CBF	28.1 ± 8.5	15.4 ± 6.4	13.2 ± 7.3
6 patients	$CMRO_2$	1.77 ± 0.51	0.29 ± 0.04	0.29 ± 0.08
	n =	3	6	4

Groups		*Warm CPB*	*Post-CPB*
Control	CBF	23.4 ± 2.3	28.6 ± 5.2
5 patients	$CMRO_2$	1.08 ± 0.17	1.32 ± 0.27
	n =	4	5
Isoflurane	CBF	16.8 ± 2.6	25.2 ± 3.3
6 patients	$CMRO_2$	0.63 ± 0.1	1.10 ± 0.21
	n =	4	6

CBF = ml/100 g/min; $CMRO_2$ = ml/100 g/min.

Discussion

Experimental studies have shown that isoflurane has similar cerebral metabolic and cerebro-protective properties to the barbiturates, and that maximal effect is achieved when EEG suppression occurs.[3,4] Reduction of $CMRO_2$ during hypothermic and normothermic CPB has been previously documented[2] and this study shows that further reductions in $CMRO_2$ even during hypothermia are attainable with the use of isoflurane during CPB in sufficient concentration to induce a predominantly isoelectric EEG. In a recent clinical study a reduced incidence of persistent neuropsychiatric sequelae of CPB was demonstrated in patients undergoing open-heart surgery when thiopentone was used to suppress the EEG during CPB.[5] Isoflurane has the advantage of being rapidly and completely eliminated upon discontinuation and therefore the results of this study are compatible with our hypothesis that isoflurane has the potential to afford cerebral protection during CPB without the side effects of myocardial depression and prolonged anaesthesia which occur with the use of thiopentone.[5]

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Divided doses of thiopentone attenuate heart rate changes after intubation

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Laryngoscopy and tracheal intubation are associated with a rise in heart rate and blood pressure following thiopentone induction.[1] Pharmacologic interventions with fentanyl,[2] lidocaine[3] and propranolol[4] attenuate this re-

sponse. The haemodynamic effects of a thiopentone dose given prior to thiopentone induction has not been reported. A prospective randomized clinical trial was conducted to compare the effects of a single bolus administration of thiopentone with thiopentone administration in two divided doses.

Methods

Fifty patients were studied. The protocol was approved by the Human Research Ethics Committee of the Hospital and informed written consent was obtained. Patients selected were unpremedicated females, ASA physical status 1, undergoing outpatient procedures requiring intubation. They were randomly assigned to two groups: the control group and the thiopentone group. Four minutes before intubation, patients were preoxygenated and curare 3 mg was injected intravenously. Three minutes before intubation the control group received 3 ml of normal saline and the thiopentone group a preinduction dose of thiopentone 1.0 $mg \cdot kg^{-1}$. The patients were induced 1.5 minutes before intubation with thiopentone 5.0 $mg \cdot kg^{-1}$ in the control group and 4.0 $mg \cdot kg^{-1}$ in the thiopentone group. Both groups received succinylcholine 2.0 $mg \cdot kg^{-1}$. Cricoid pressure and apnoeic oxygenation were used in order to standardize airway manipulation. Orotracheal intubation was accomplished in less than 20 seconds. The post-intubation anaesthetic consisted of O_2 30 per cent, N_2O and isoflurane one per cent. Ventilation was controlled at a rate of 10/min with a tidal volume of 10 $ml \cdot kg^{-1}$. Patients were not stimulated for a period of five minutes. Heart rate and blood pressure were measured and recorded using an automatic blood pressure monitor with printer (Dinamap vital signs monitor 1846P), every minute from an initial value, four minutes prior to intubation until five minutes after intubation. Statistical analysis was performed with the Student's t-test and the one way analysis of variance, using a multiple range test. A $p < 0.05$ was considered statistically significant.

Results

There were 24 patients in the control group and 25 patients in the thiopentone group. One patient was excluded because of a difficult intubation. Age, weight, height and initial values for heart rate and systolic blood pressure were similar in both groups. Compared to the initial values, both groups had a significant rise in heart rate from one minute before intubation until three minutes after in the thiopentone group and until five minues after intubation in the control group (Figure 1). Heart rate was significantly different between the groups at 2, 3, 4 and 5 minutes after intubation, with a 15 per cent increase in the thiopentone group compared to a 26 per cent increase in the control group at two minutes post-intubation. Systolic

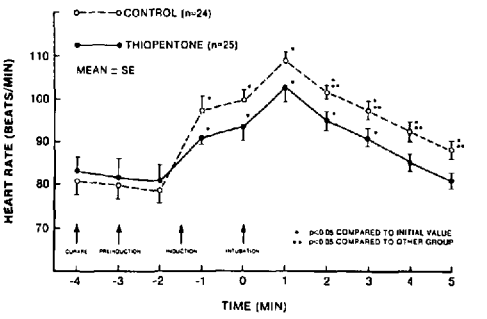

FIGURE 1 Heart rate during induction of anaesthesia and tracheal intubation.

blood pressure was significantly increased compared to the initial values at one and two minutes after intubation in the control group and at one minute in the thiopentone group (Figure 2). Blood pressure was significantly lower than the initial values at four and five minutes post-intubation in both groups. There were no statistical differences regarding blood pressure recorded between the groups.

Discussion

In healthy patients, thiopentone administration in a dose of 1.0 $mg \cdot kg^{-1}$ prior to an induction with thiopentone 4.0 $mg \cdot kg^{-1}$ produces less variation in heart rate than thiopentone 5.0 $mg \cdot kg^{-1}$ administered as a single bolus. Although statistically significant, these results are not important clinically in the healthy population studied. More haemodynamic stability could possibly be reached by finding the ideal preinduction dosage and the optimal time of administration. Further investigation in patients with impaired cardiovascular reserve may elicit a more

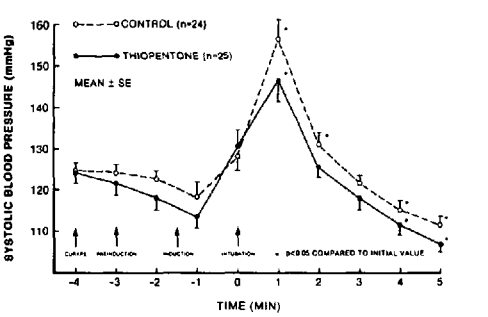

FIGURE 2 Systolic blood pressure during induction and tracheal intubation.

stable alternative method of administration of thiopentone to the standard single bolus technique.

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Dose–response relationship of clonidine in tetracaine spinal anaesthesia

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Clonidine is a centrally acting antihypertensive agent with α_1 and α_2 adrenergic agonist activity. It has been demonstrated to produce peripheral vasoconstriction, and is known to be analgetic when given by the intrathecal or epidural route in animals and humans.[1] Previous work in animals has shown that in tetracaine spinal anaesthesia, intrathecal clonidine (150 μg) is equally effective to epinephrine (200 μg) in prolonging motor blockade, but significantly more efficacious in prolonging sensory blockade.[2] The present study was undertaken to define a dose–response relationship of clonidine in prolonging tetracaine spinal anaesthesia in dogs.

Methods

Six mongrel dogs weighing 16–21 kg were studied using a randomized blind crossover design. Under thiopentone-N_2O-O_2-isoflurane anaesthesia a lumbar puncture was performed at either L_5L_6 or L_6L_7 interspace with a #22 gauge spinal needle. Solutions of tetracaine (4 mg in 1 ml D5/W) with incremental doses of clonidine (0, 10, 25, 50, 100, 150, 200 and 300 μg) were given to each dog intrathecally, over an eight-week period. Following intrathecal injection N_2O-isoflurane anaesthesia was discontinued and time to arousal was recorded. Sensory and motor reponses were evaluated at 20-minute intervals for one hour and every 15 minutes thereafter. Duration of motor block was defined as time from intrathecal injection to time of standing unsupported. Sensory block was evaluated using a 25 cm rubber-shod haemostat applied to the proximal third of the tail for a 30-second application or until an avoidance response was elicited.

Dose–response curves were plotted using first and second order polynomial regression analysis.

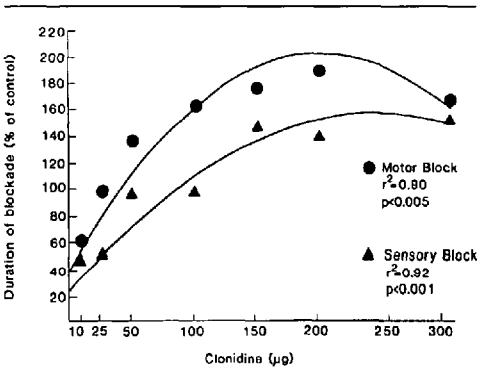

FIGURE Effects of clonidine on tetracaine spinal anesthesia

Results

Introduction of clonidine into the C.S.F. increased time to arousal from 22.8 ± 5.9 min (mean ± SEM) with tetracaine, to 40.7 ± 1.9 min with tetracaine in combination with 300 μg of clonidine. Linear regression analysis followed the equation $y = 0.07 \times +23$, with $r^2 = 0.801$ and $p < 0.01$.

The duration of motor and sensory blockade were analyzed as a percentage of control (i.e.: observed time – control time/control time × 100). The results are expressed in the Figure. With increasing doses of clonidine, the average duration of sensory blockade was prolonged, with a plateau being reached at a dose of clonidine of 150 μg. Polynomial regression analysis produced $r^2 = 0.92$, $p < 0.001$. Similarly the average motor block was prolonged with increasing doses of clonidine. However, the plateau for maximal prolongation of motor blackade was reached at a dose of 100–150 μg. Polynomial regression analysis showed $r^2 = 0.90$, $p < 0.001$. Increasing the dose of clonidine above 150 μg did not prolong the duration of sensory or motor blockade. All dogs had full neurologic recovery following each intrathecal injection and were neurologically intact at the conclusion of the study.

Discussion

The results indicate that clonidine effectively prolongs tetracaine spinal anaesthesia and that a dose response relationship exists. The study suggests that, in the dog, a dose of 150 μg of clonidine provides maximum benefit in prolonging motor and sensory blockade. It would appear

that clinical trials are indicated with clonidine in spinal and epidural anaesthesia.

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The influence of patient's sex, age and weight on pancuronium onset time

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A rapid onset of action is a desirable feature of muscle relaxants. Although alterations in the mode of administration (e.g., priming) have been proposed in an attempt to shorten the onset time, little attention has been brought to the patient characteritics which may alter onset. This study was designed to study the effect of sex, age and weight on the onset of neuromuscular blockade produced by pancuronium.

Methods

One hundred and fourteen ASA physical status I and II adults of both sexes, aged 18–75 years and 45–100 kg in weight were studied during elective procedures. Anaesthesia was induced with thiopentone, 3–5 $mg \cdot kg^{-1}$, and maintained with nitrous oxide (70 per cent), and enflurane (0.5–1.5 per cent) in oxygen. Train-of-four stimulation was applied to the ulnar nerve every 12 seconds, and the force of contraction of the adductor pollicis muscle was measured. Pancuronium, 0.06 $mg \cdot kg^{-1}$ was given into a rapidly running intravenous line. The percentage blockade of first twitch tension was measured two minutes after the injection of pancuronium, and the time to reach 90 per cent maximum blockade was also noted. For each sex, the relationship of blockade at two minutes and age and weight was calculated by multiple linear regression analysis.

Results

For the same dose of pancuronium, expressed in $mg \cdot kg^{-1}$, the onset was more rapid in women than in men. Mean ($\pm$ SEM) neuromuscular blockade after two minutes was 45.4 $\pm$ 3.5 per cent in men and 69.1 $\pm$ 3.4 per cent in women ($p < 0.0001$). Time to 90 per cent maximum blockade was 203 $\pm$ 13 and 154 $\pm$ 8 seconds in men and women respectively ($p < 0.002$). In both sexes, blockade after two minutes decreased with increasing age, and increased with increasing weight. Multiple regression equations for block at two minutes were, for men:

$$\text{Block}(\%) = 52 - 0.93 \times \text{age (yrs)} + 0.50 \times \text{weight (kg)} \quad (r = 0.546;\ p = 0.00024),$$

and for women:

$$\text{Block}(\%) = -2 - 0.53 \times \text{age (yrs)} + 1.56 \times \text{weight (kg)} \quad (r = 0.436;\ p = 0.004).$$

For example, a 20-year-old woman weighing 70 kg is expected to exhibit 97 per cent block after two minutes, whilst the same dose (0.06 $mg \cdot kg^{-1}$) will most likely produce only a 12 per cent block in a 75-year-old weighing 60 kg.

Discussion

This study identified three characteristics most likely associated with slow onset of pancuronium blockade: male sex, old age and lean stature. However, large inter-individual variability still exists in patients who are comparable with respect to sex, age and weight. Onset time presumably depends on three factors: the volume of distribution of the drug, its rate of delivery to the receptor, and the concentration required to produce the desired effect. Pancuronium is an ionized drug which has a volume of distribution approximately equal to that of extra-cellular fluid. Thus, the volume of distribution, in $mg \cdot kg^{-1}$, is most likely decreased by the presence of more adipose tissue in women and in heavy individuals. This increases the drug concentration at the receptor, and favours a more rapid onset. Neuromuscular blockade occurs more rapidly in young individuals probably because of their greater cardiac output, which promotes delivery of the drug to the tissues. However, the possibility that the sensitivity to relaxants depends on sex, weight and age cannot be ruled out. Finally, this study suggests that values of onset times determined for certain groups of adults might not be applicable to all patients.

d-Tubocurarine priming in children

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The onset of non-depolarizing neuromuscular blockade can be accelerated by the administration of a subparalyzing dose of a relaxant before a paralyzing dose is given (priming). This mode of administration has been studied in adults, but onset times and the effect of priming might be different in children. The purpose of this study was to measure the onset time of d-tubocurarine in children of

TABLE I First twitch height (%) (mean ± SEM) versus time (s) after paralyzing dose

	Without priming		
Age group	*30 s*	*60 s*	*90 s*
0–1 yr	62 ± 12*	20 ± 6	10 ± 3
1–3 yr	84 ± 6*	33 ± 6	15 ± 4
3–10 yr	92 ± 6*	56 ± 9	40 ± 10
	With priming		
Age group	*30 s*	*60 s*	*90 s*
0–1 yr	32 ± 7*	10 ± 3	5 ± 2
1–3 yr	58 ± 10*	23 ± 6	12 ± 4
3–10 yr	57 ± 6*	20 ± 5*	12 ± 3*

*$p < 0.05$ between with and without priming.

different ages, and to evaluate the effect of priming, with the same methodology which has been used in adults.[1]

Methods

After institutional approval, 60 ASA physical status I or II children undergoing elective procedures were studied under thiopentone-nitrous oxide-halothane anaesthesia. There were 20 patients in each of the following groups: 0–1 yr, 1–3 yrs, and 3–10 yrs. The force of contraction of the adductor pollicis muscle was measured following train-of-four stimulation of the ulnar nerve every 12 sec. After induction of anaesthesia and stabilization of twitch recording, normal saline or d-tubocurarine, 0.04 $mg \cdot kg^{-1}$, was administered into a rapidly running intravenous line. Three minutes later, a paralyzing dose of d-tubocurarine was given, such that the total dose was 0.4 $mg \cdot kg^{-1}$. The patients were monitored until first twitch height recovered to at least ten per cent. The results were analyzed using Student's t test, and differences were considered statistically significant when $p < 0.05$.

Results

In all three age groups, the patients who received a priming dose showed a faster onset of neuromuscular blockade (Table I). Priming did not affect significantly the time to spontaneous recovery of ten cent twitch height (Table II). The onset of neuromuscular blockade tended to be faster in younger subjects. A linear regression analysis between time to 90 per cent block and age showed a positive correlation both with ($r = 0.681$; $p = 0.00012$) and without ($r = 0.316$; $p = 0.09$) priming.

TABLE II Duration of action (time to 10% recovery) (minutes, mean ± SEM)

Age group	*Without priming*	*With priming*
0–1 yr	36 ± 5	44 ± 9
1–3 yr	30 ± 5	33 ± 3
3–10 yr	24 ± 3	35 ± 6

Discussion

The onset of d-tubocurarine neuromuscular blockade is more rapid than with other long-acting non-depolarizing blockers.[1,2] This study demonstrated a generally more rapid onset of neuromuscular blockade than found in a similar study in adults.[1] Then, the use of priming doses in children, which produces a small acceleration of the onset of neuromuscular blockade, is relatively more important. This is accomplished without prolongation of the duration of action. The rapid onset observed in young patients might be due to their relatively larger tissue perfusion.

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Dose–response relationships for edrophonium, pyridostigmine and neostigmine as antagonists of pancuronium and d-tubocurarine

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The potencies of edrophonium, pyridostigmine, and neostigmine may depend on several factors, such as the relaxant used, its mode of administration, and the degree of spontaneous recovery when administered. The purpose of this study was to obtain dose–response relationships for all three antagonists, when used to antagonize the block produced by single doses of pancuronium or d-tubocurarine, at the same degree of spontaneous recovery.

Methods

The study was conducted on 120 ASA physical status I and II adults. Anaesthesia was induced with thiopentone, 3–5 $mg \cdot kg^{-1}$, and maintained with nitrous oxide (70 per cent), and enflurane (0.5–1.5 per cent) in oxygen. Train-of-four stimulation was applied to the ulnar nerve every 12 seconds, and the force of contraction of the adductor pollicis muscle was measured. Patients were

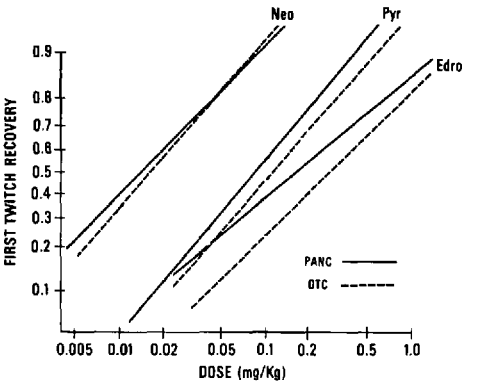

FIGURE 1

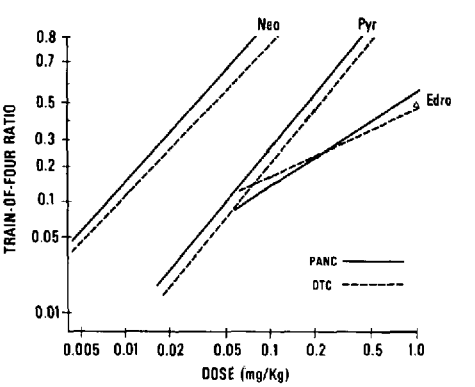

FIGURE 2

given either pancuronium, 0.06 mg·kg^{-1}, or d-tubocurarine, 0.36 mg·kg^{-1}. When first twitch tension had recovered to ten per cent of its initial height, edrophonium, 0.1, 0.2, 0.4 or 1 mg·kg^{-1}, or pyridostigmine, 0.02, 0.04, 0.1 or 0.2 mg·kg^{-1}, or neostigmine, 0.005, 0.01, 0.02 or 0.05 mg·kg^{-1} were given by random allocation. The first twitch tension and train-of-four ratio were measured ten minutes after the antagonist was given. Dose–response curves were obtained by linear regression of the logit transformation of first twitch recovery or train-of-four ratio versus the logarithm of the dose of the antagonist.

Results

The dose–response curves for first twitch tension did not deviate significantly from parallelism (Figure 1). The ED50's for d-tubocurarine were greater for all three antagonists, and this difference reached statistical significance ($p < 0.05$) for pyridostigmine and endrophonium (Table). The dose–response curves for train-of-four ratio were flatter for edrophonium (Figure 2), and the ED50 of edrophonium was greater when used with d-tubocurarine.

TABLE Results. Mean ± SE

	Pancuronium	*d-Tubocurarine*	*p*
ED50 – mg·kg^{-1}			
Neostigmine	0.013 ± 0.0015	0.017 ± 0.0012	NS
Pyridostigmine	0.085 ± 0.0054	0.11 ± 0.005	0.001
Edrophonium	0.17 ± 0.024	0.27 ± 0.027	0.006
Train-of-four ratio			
Neostigmine	0.031 ± 0.004	0.043 ± 0.006	NS
Pyridostigmine	0.18 ± 0.017	0.23 ± 0.023	NS
Edrophonium	0.77 ± 0.11	1.23 ± 0.16	0.025

Discussion

This study demonstrated that the dose–response relationship of relaxant antagonists may depend on which relaxant has been used, which may be a consequence of the relaxant's different mechanisms of action. Compared with the other antagonists, edrophonium reversed train-of-four fade well at low doses but not at higher doses as indicated by a flatter train-of-four ratio–dose relationship. This might be a reflexion of a different mechanism of action of edrophonium compared with the other antagonists. In clinical practice, the dose of antagonist required to reverse neuromuscular blockade completely might be smaller than in this study because the antagonists are commonly given when spontaneous recovery is greater than ten per cent.

Neostigmine, edrophonium and pyridostigmine as antagonists of deep pancuronium blockade

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It has been suggested that neostigmine was superior to edrophonium as an antagonist of deep blockade[1,2] using doses based on potency ratios determined in a different setting. This study was designed to establish equipotent doses of neostigmine, edrophonium and pyridostigmine when given at 90 per cent pancuronium blockade, and compare them when administered at 99 per cent blockade.

Methods

In 120 ASA physical status I or II adults, anaesthesia was induced with thiopentone 3–5 mg·kg^{-1} and maintained with nitrous oxide 70 per cent and enflurane 0.5–1.5 per

cent in oxygen. Train-of-four stimulation was applied to the ulnar nerve and the force of contraction of the adductor pollicis muscle was recorded. Pancuronium 0.06 $mg \cdot kg^{-1}$ was given, and increments of 0.5 mg were added, if needed, until 100 per cent blockade was achieved. In 60 patients, neostigmine (0.005, 0.01, 0.02, or 0.05 $mg \cdot kg^{-1}$), or edrophonium (0.1, 0.2, 0.4 or 1 $mg \cdot kg^{-1}$), or pyridostigmine (0.02, 0.04, 0.1 or 0.2 $mg \cdot kg^{-1}$) were given by random allocation when first twitch tension had recovered to ten per cent of control. Ten minutes after administration of the antagonist, first twitch recovery was measured and the doses expected to produce 80 per cent (ED80) and 90 per cent (ED90) recovery were determined. The next 60 patients received either the ED80 or the ED90 of each drug, administered at one per cent first twitch height recovery (or 99 per cent blockade). First twitch tension (T1) and train-of-four ratio (T4/T1) were measured ten minutes after the antagonist was given. The groups were compared using analysis of variance.

Results

The ED80's and ED90's for the antagonists when administered at 90 per cent blockade are shown in the Table. For both doses used, neostigmine was a better antagonist of 99 per cent blockade than edrophonium or pyridostigmine (Table). However, no agent produced a mean train-of-four ratio greater than 0.5.

Discussion

The doses of antagonist used in this study were comparable to the doses used clinically. The neuromuscular recovery indicates that deep block is difficult to antagonize. However, neostigmine appeared superior to the other two agents, when given in doses expected to be equipotent at a lesser degree of blockade. Clinically, it appears preferable to avoid producing deep neuromuscular blockade because of its poor reversibility.

TABLE Dose-effect relationship of antagonists after 10 minutes

	Dose given $mg \cdot kg^{-1}$	*Effect at 99% block (mean ± SEM)* *T1*	*T4/T1*
	ED80 at 90% block		
Neostigmine	0.04	0.78 ± 0.030	0.43 ± 0.028
Edrophonium	0.54	0.56 ± 0.023	0.19 ± 0.023
Pyridostigmine	0.2	0.57 ± 0.058	0.28 ± 0.028
		p = 0.0006	p = 0.00001
	ED90 at 90% block		
Neostigmine	0.08	0.84 ± 0.030	0.45 ± 0.030
Edrophonium	1.15	0.73 ± 0.035	0.32 ± 0.027
Pyridostigmine	0.38	0.74 ± 0.032	0.38 ± 0.040
		p = 0.035	p = 0.038

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The effect of pre-existing beta blockade on potassium flux in patients receiving succinylcholine

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There is evidence that the beta-adrenoreceptor is involved in the acute regulation of serum potassium (K^+). McCammon and Stoelting have shown that in dogs pre-treated with propranolol, succinylcholine, (SCh) leads to an exaggerated and prolonged rise in serum K^+ with delayed peak levels occurring at 60–90 min.[1] The purpose of this study was to determine whether similar effects occurred in man undergoing anaesthesia.

Methods

Patients who were taking propranolol (120–160 $mg \cdot day^{-1}$) or atenolol (50–100 $mg \cdot day^{-1}$), and a control group, were studied (Table). All patients underwent peripheral surgery. Those receiving concurrent diuretics or calcium channel blockers were excluded.

Anaesthesia was induced with thiopentone 4–5 $mg \cdot kg^{-1}$. Tracheal intubation was facilitated with SCh 1 $mg \cdot kg^{-1}$, without pre-treatment. The lungs were mechanically ventilated with nitrous oxide and 40 per cent oxygen to achieve an end-tidal CO_2 of 36 mmHg. Anaesthesia was maintained with enflurane (0.5–1.0 per cent inspired) and fentanyl.

Venous blood samples were obtained for serum K^+ analysis, pre-induction, and at 1, 3, 5, 10, 20, 30, 45, 60 and 120 min after SCh.

TABLE Patients studied

Group	*Number*	*Age*	*Weight (kg)*	*Sex M/F*	*Heart rate (resting)*
Control	11	43 ± 46.8	71 ± 24.9	7/4	76 ± 11.7
Propranolol	5	57 ± 7.8	67 ± 26.5	3/2	56 ± 5.1
Atenolol	7	55 ± 11.6	70 ± 36.2	4/3	54 ± 5.4

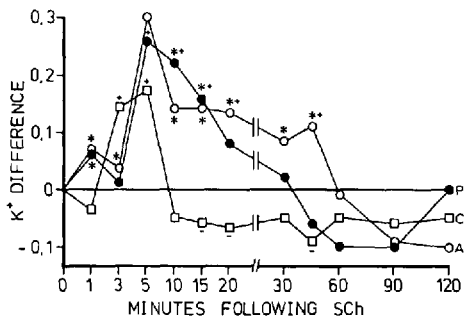

FIGURE K^+ differences (mmol·L^-) from time zero for the three groups, control (C), propranolol (P) and atenolol (A). Values depicted are mean. *P < 0.05 groups P and A versus control C. + and − denote significant (p < 0.05) increases and decreases from initial levels within individual groups.

Results

In all three groups serum K^+ peaked at the 5 min period in response to the SCh. In the control group the serum K^+ returned to resting levels by 10 min, whereas in beta-blocked patients, the K^+ remained elevated and did not reach control levels until 30 min (propranolol) to 60 min (atenolol) (Figure).

Kruskal-Wallis analysis showed statistically significant differences ($p < 0.05$) between the control and the beta-blocked groups following SCh, however there was no significant difference between the atenolol and propranolol groups. Wilcoxon analysis showed a significant increase in both beta-blocked groups with respect to resting levels.

Discussion

In this study, serum K^+ peaked in all groups within 5 min of the administration of SCh and in beta-blocked patients the return of serum K^+ to pre-induction levels was delayed in comparison with the control group. These findings support the postulate that beta-adrenoreceptor blockade impairs the intracellular uptake of the SCh-induced acute K^+ load. The time course of this response which was observed is more understandable than that seen in the study by McCammon and Stoelting, where the peak elevation in serum K^+ did not occur until 60–90 min following SCh and where K^+ remained elevated even at 180 min.

At the level of beta-blockade which was present in the patients who were studied, the increase in serum K^+ following SCh is probably not clinically significant. However, these findings emphasise the importance of careful monitoring of beta-blocked patients in situations where an acute elevation of serum K^+ is likely to occur.

Reference

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Atracurium to prevent succinylcholine fasciculations and myalgias

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Although a multitude of agents have been shown to be useful in the prevention of succinylcholine fasciculations and myalgias, the standard agent for this purpose remains d-tubocurarine.

Atracurium is a new non-depolarizing muscle relaxant with minimal histamine releasing properties, marked cardiovascular stability and metabolism and excretion that is independent of renal and hepatic function. Atracurium is rapidly replacing d-tubocurarine as an intermediate duration non-depolarizing muscle relaxant, especially in patients with renal insufficiency or patients where tachycardia and hypertension wish to be avoided.

Methods

We studied 45 patients aged 18 to 45 years who underwent elective dental, otolaryngeal or urological procedures and were mobile the day of surgery. The study protocol was approved by the hospital Ethics Committee and informed consent was obtained from each patient. The patients were randomly divided into three groups of 15. All patients received a standard anaesthetic consisting of morphine 0.1–0.2 mg·kg^{-1} and promethazine 0.3–0.5 mg·kg^{-1} intramuscularly one hour prior to induction. The patients were induced with thiopentone 5 mg·kg^{-1} followed by succinylcholine 1.5 mg·kg^{-1} intravenously. The patients were observed for fasciculations and intubated 90 seconds after administration of succinylcholine. Anaesthesia was maintained with 70 per cent nitrous oxide in oxygen and isoflurane. Ventilation was controlled to maintain end-tidal CO_2 between 35 and 40 mmHg. Patients in Group A received d-tubocurarine 50 μg·kg^{-1}, Group B received atracurium 30 μg·kg^{-1} and Group C received atracurium 60 μg·kg^{-1} three minutes prior to succinylcholine. Serum potassium and creatine phosphokinase levels were measured prior to induction and five minutes after succinylcholine administration.

Results

Demographic and biochemical information is summarized in Table I. There was no statistically significant difference in sex distribution, patient age or patient weight amongst the three groups. There was no statistically significant change in serum potassium or creatine

TABLE I Patient demographics and biochemistry

	Group A	*Group B*	*Group C*
Sex distribution	10 Male 5 Female	8 Male 7 Female	7 Male 8 Female
Age (years)	24.3 ± 3.1	27.9 ± 7.0	24.4 ± 4.7
Weight (kg)	69.1 ± 15.7	69.6 ± 11.6	63.5 ± 9.4
Change in potassium $mEq \cdot L^{-1}$	−0.04 ± 0.20	−0.06 ± 0.45	−0.09 ± 0.42
Change in creatine $units \cdot L^{-1}$	8.6 ± 35.1	15.3 ± 54.6	9.7 ± 30.6

TABLE II Incidence of fasciculations

	Group A	*Group B*	*Group C*
Nil	47%	20%	53%
1+	20%	13%	13%
2+	33%	27%	20%
3+	0%	40%	13%

TABLE III Incidence of myalgias

	Group A	Group B	Group C
Nil	27%	53%	40%
Mild	33%	33%	27%
Moderate	33%	13%	27%
Severe	7%	0%	7%

phosphokinase levels prior to succinylcholine administration as compared to five minutes after succinylcholine administration in any of the three groups.

Intubating conditions were ideal in 44 patients and adequate in one patient (Group B). There were no statistically significant differences amongst the three groups in incidence or severity of fasciculations or postoperative myalgias; however, a trend towards more severe fasciculations was present in Group B (Tables II and III). A p level ≤ 0.05 was considered to be statistically significant in all cases.

We recommend the administration of atracurium 60 $\mu g \cdot kg^{-1}$ three minutes prior to succinylcholine as a method as efficacious as d-tubocurarine 50 $\mu g \cdot kg^{-1}$ in reducing fasciculations and post-operative myalgias due to succinylcholine. Atracurium offers many benefits over d-tubocurarine with regards to cardiovascular and respiratory stability as well as "auto-degradation."

The effect of high-dose mannitol on serum and urine electrolytes and osmolality in neurosurgical patients

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High-dose mannitol (2 $g \cdot kg^{-1}$) has been shown to have a protective effect in acute focal cerebral ischaemia.[1] Clinically, we use high-dose mannitol as a protective measure during temporary or permanent cerebral arterial occlusion. The influence of low-dose mannitol on blood chemistry is known, but the intra-operative effects of high-dose mannitol in man have not been fully investigated. The purpose of this study was to compare the effects of 1 $g \cdot kg^{-1}$ versus 2 $g \cdot kg^{-1}$ of 20 per cent mannitol in man.

Methods

Informed consent was obtained from each subject. Fourteen patients scheduled for clipping of cerebral aneurysms were studied. Patients in whom temporary or permanent clipping of an artery was anticipated were given high-dose mannitol. Group A (seven patients) received 1 $g \cdot kg^{-1}$ mannitol and Group B (seven patients) received 2 $g \cdot kg^{-1}$. The patients were unpremedicated. Anaesthesia was with thiopentone 5 $mg \cdot kg^{-1}$, fentanyl 2–3 $\mu g \cdot kg^{-1}$, succinylcholine 1 $mg \cdot kg^{-1}$, nitrous oxide, oxygen, isoflurane and pancuronium. $PaCO_2$ was maintained at 30–32 mmHg. After positioning and during steady state anaesthesia, mannitol was infused rapidly through a large-bore intravenous cannula. Blood was obtained for serum osmolality, electrolytes, bun, creatinine, glucose, haemoglobin and haematocrit. Urine was obtained for osmolality and electrolytes. All samples were obtained at the following times: (1) preoperative, (2) after induction of anaesthesia, (3) after 1/3 of mannitol infused, (4) after 2/3 mannitol infused, (5) completion of mannitol, (6) 15 min postinfusion, (7) 30 min postinfusion (8) 60 min postinfusion, (9) recovery room, (10) postoperative (day 1). Statistical analysis within each group was performed with one-way analysis of variance for repeated measures and where significant Dunnet's test was used. Results between Group A and B were analyzed with two-way analysis of variance.

Results

Eleven females and three males (mean age 42.4 ± 13 years) were studied. The rate of infusion of mannitol for Group A was 3.4 $g \cdot min^{-1}$ and Group B was 3.6 $g \cdot min^{-1}$. Serum Na^+ decreased in both groups during mannitol infusion with a greater decrease in Group B. Serum K^+ decreased in Group A but there was a significant increase in Group B. The increase in serum osmolality was greater in Group B. The other results were not significantly different. Urine output was greater in Group B as

TABLE Serum Na^+, K^+, bicarbonate and osmolality (mean ± SD) Group A (1 g·kg$^-$), Group B (2 g·kg^{-1})

Time of sampling	Na^+		K^+	
	A	B†	A	B†
1	139 ± 1.5	140 ± 2.7	4.2 ± 0.30	4.0 ± 0.45
2	137 ± 2.2	138 ± 2.9	3.8 ± 0.44	4.4 ± 0.22
3	131 ± 2.2*	129 ± 3.6*	3.6 ± 0.46	4.2 ± 0.32
4	129 ± 2.8*	125 ± 3.6*	3.6 ± 0.39	4.3 ± 0.60
5	130 ± 4.3*	120 ± 2.0*	3.8 ± 0.50	4.7 ± 0.86
6	132 ± 3.4*	124 ± 2.0*	3.8 ± 0.50	5.1 ± 0.83*
7	133 ± 3.4*	126 ± 2.3*	3.9 ± 0.60	5.1 ± 0.81*
8	131 ± 1.3*	129 ± 1.7*	4.0 ± 0.44	4.8 ± 0.70
9	137 ± 3.4	135 ± 5.0*	3.8 ± 0.45	4.0 ± 0.35
10	139 ± 2.9	140 ± 4.3	3.6 ± 0.27	3.7 ± 0.18

Time of sampling	Bicarbonate		Osmolality	
	A	B	A	B†
1	24 ± 4	27 ± 2		
2	21 ± 2	23 ± 3*	285 ± 10	285 ± 7
3	20 ± 2*	20 ± 1*	299 ± 5*	300 ± 6*
4	19 ± 2*	20 ± 1*	301 ± 5*	307 ± 8*
5	19 ± 2*	20 ± 1*	298 ± 4*	314 ± 10*
6	20 ± 2*	20 ± 1*	295 ± 3*	307 ± 10*
7	20 ± 2*	20 ± 1*	293 ± 3	304 ± 10*
8	21 ± 1	21 ± 1*	290 ± 3	300 ± 10*
9	22 ± 2	21 ± 1*	292 ± 4	295 ± 10
10	25 ± 1	24 ± 1*	282 ± 7	282 ± 12

*$p \leq 0.05$ within each group.
†$p \leq 0.05$ between Group A and Group B.

compared to Group A (1527 ± 477 ml vs 748 ± 353 ml). Urine electrolytes and osmolality showed no significant difference.

Discussion

We found that high dose mannitol (2 g·kg^{-1}) given rapidly significantly decreased serum Na^+ and increased osmolality in comparison to low dose mannitol. The most striking finding was the increase in serum K^+. An explanation for this is the dilution of plasma bicarbonate producing an "expansion acidosis."[2] Intracellular K^+ is then exchanged for extracellular H^+. However, our study does not support this explanation as the changes in serum bicarbonate were not different between the groups. We conclude that the rapid infusion of high dose mannitol changes serum electrolytes. This may have important clinical implications for patients with underlying medical disorders and should, therefore, be given cautiously.

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Haemodynamic effects of high-dose mannitol in man

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Low-dose mannitol (0.125–0.25 mg·kg^{-1}) can cause transient hypotension by decreasing systemic vascular resistance.[1] In neurosurgical practice it is not uncommon to administer high-dose mannitol (2 g·kg^{-1}) for its potential cerebral protective effect, yet the haemodynamic consequence of such a large dose of mannitol is unknown. The present study is undertaken to evaluate the haemodynamic effect of high-dose mannitol under clinical conditions.

Methods

The study was approved by the Institutional Ethics Committee. Seven patients, aged 22 to 63 scheduled for cerebral aneurysm surgery, whose surgical condition necessitates high-dose mannitol were studied. Anaesthesia was induced in a standardized manner, with fentanyl 2–3 μg·kg^{-1}, thiopentone 5–6 mg·kg^{-1}, lidocaine 1.5 mg·kg^{-1} and succinylcholine 1 mg·kg^{-1}. Maintenance anaesthesia consisted of isoflurane 0.5–1.0 per cent, N_2O/O_2 (66/33 per cent), and pancuronium as required. End-tidal CO_3 was maintained between 30–35 mmHg. Mannitol infusion began after the bone flap was raised, and haemodynamic measurements including heart rate (HR), systemic blood pressure (BP), pulmonary artery pressure, central venous pressure (CVP), and pulmonary wedge pressure (PCWP) were taken during five measurement periods; (I) before infusion of mannitol, (II) after 1/3 infusion of mannitol, (III) after 2/3 infusion, (IV) after completion of infusion and (V) 15 min after completion of infusion. Cardiac output (CO) by thermodilution performed in at least duplicates were measured only during measurement periods I, IV and V. All measurements were recorded during as near steady state as possible; inspired isoflurane concentration was maintained constant throughout the study periods, and stages of intense surgical stimulation such as raising the bone flap were avoided. The study was to be discarded if other drugs had to be administered to control unacceptable haemodynamic values. For statistical analysis, one-way ANOVA for repeated measures was employed, and where significance was observed ($p < 0.05$), Dunnett's test was used for comparison with control values.

TABLE Results

	I	II	III
Mean BP (mmHg ± SEM)	114 ± 6	108 ± 6	109 ± 6
CVP (mmHg ± SEM)	4 ± 1	6 ± 1*	7 ± 1*
PCWP (mmHg ± SEM)	8 ± 1	10 ± 2	14 ± 2*
C.O. ($L \cdot min^{-1}$)†	5.75 ± 0.40		
SVR ($dyne \cdot s \cdot cm^{-5}$)†	11115.1 ± 139.2		

	IV	V
Mean BP (mmHg ± SEM)	112 ± 8	115 ± 6
CVP (mmHg ± SEM)	7 ± 2*	3 ± 1
PCWP (mmHg ± SEM)	12 ± 2*	6 ± 1
C.O. ($L \cdot min^{-1}$)†	7.28 ± 0.42*	6.13 ± 0.22
SVR ($dyne \cdot s \cdot cm^{-5}$)†	773.9 ± 95.2*	989.9 ± 95.2

*Significantly different from control $p < 0.05$.
†n = 6.

Results

All patients were successfully studied and there were no complications. With the exception of cardiac output, which was not determined in one patient, all other haemodynamic data were collected as planned. Infusion of mannitol was completed within 30 min in all patients. The transient decrease in systemic blood pressure was small and not statistically significant. Increases in CVP and PCWP were significant and lasted until completion of the infusion, but returned to control values after 15 min. The most striking observation was the increase in cardiac output and the decrease in systemic vascular resistance (SVR). The decrease in vascular resistance masked the increase in cardiac output, accounting for the nearly unchanged systemic blood pressure. By 15 min post-infusion the cardiac output as well as the vascular resistances had returned to normal values (Table).

Discussion

Our study showed that high-dose mannitol infusion is accompanied by increases in filling pressures, decrease in systemic vscular resistance and increase in cardiac output. Transient hypotension may or may not occur, depending on the balance between the resistance and cardiac output. The previous study on low-dose mannitol reporting significant transient hypotension was carried out in patients with coronary artery disease undergoing cardiopulmonary bypass. Since none of our patients had known cardiovascular disease, it is conceivable that more severe and potentially dangerous haemodynamic consequences could occur when high-dose mannitol is administered to patients with limited cardiac reserves. Should this be necessary because of surgical requirement, benefits must be balanced against the risks.

Reference

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Dose low-dose lidocaine have a protective effect in focal cerebral ischaemia?

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It has been suggested that lidocaine has a protective effect on cerebral ischaemia. However, a recent study using high-dose lidocaine failed to demonstrate this.[1] It is possible that the haemodynamic consequences of high-dose lidocaine outweighed any protective effect. Indeed, lidocaine in low doses has been shown to be beneficial in focal cerebral ischaemia created by air embolism.[2] However, these animals were only studied for two hours. We have therefore monitored somatosensory evoked potentials (SEP) during and for six hours after permanent unilateral middle cerebral artery occlusion in cats to assess the influence of lidocaine compared to saline on focal cerebral ischaemia.

Methods

Twenty cats had tourniquets implanted around their left middle cerebral artery using a transorbital approach under halothane anaesthesia at least one week prior to the actual occlusion. All animals were allowed to recover following the implant and were judged neurologically normal before occlusion. On the day of occlusion, under halothane anaesthesia (1.0 per cent inspired) the cats were randomly assigned to receive either intravenous lidocaine 5 $mg \cdot kg^{-}$ or an equivalent volume of saline ten minutes before occlusion of the middle cerebral artery. SEP were recorded from silver/silver chloride electrodes placed 1 cm lateral to the midline on the coronal suture. Stimuli were delivered to the median nerves using needle electrodes and the intensity was adjusted to produce visible twitches of the paw. Bandpass filter was set between 5 to 3000 Hz. At least 256 sweeps of 20 msec were averaged. The SEP was evaluated according to the amplitude of the primary positive and negative peaks. We have previously determined that low-dose lidocaine does not influence the recording of the evoked responses. SEP were recorded prior to occlusion, every five minutes for the first 30 minutes, and then evey 30 minutes until the end of six hours from the time of occlusion. For comparison between the two groups, both the presence of the SEP and the amplitude of the peaks were assessed.

TABLE Number of animals with preserved SEP

Time after occlusion	*15 min*	*30 min*	*60 min*	*120 min*	*240 min*
Lidocaine (N = 10)	4*	3	3	5	5
Saline (N = 9)	0	1	2	2	4

*$p < 0.05$

Results

Ten cats in the lidocaine and nine cats in the saline group were successfully studied. There was no difference in blood pressure, heart rate or anaesthetic depth between the two groups during the course of the study. In the lidocaine group, SEP persisted in 40 per cent of the cats immediately following occlusion of the artery vs. 0 per cent in the saline group ($p < 0.05$ by Chi Square). However, gradual recovery occurred subsequently in both groups and differences did not exist at the end of the experiment (Table). Similarly in the animals that recovered the SEP, no differences in amplitude could be demonstrated between the two groups.

Discussion

A transient protective effect of lidocaine was demonstrated based on an electrophysiological evaluation using the SEP which provides a functional assessment of cerebral integrity. As the lidocaine was given as a bolus, its effect may have dissipated during the course of the experiment. Our results probably differ from Evans[2] because air embolism produces a less severe ischaemic injury than complete vessel occlusion.

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Effects of high frequency vs. conventional mechanical ventilation on intracranial and cerebral perfusion pressures

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When brain injury is combined with a lung injury that requires the use of positive end-expiratory pressure (PEEP), high frequency jet ventilation (HFJV) may be preferable to conventional mechanical ventilation (CMV), because the lower peak inspiratory (PIP) and mean airway ($\overline{Paw}$) pressures that may be associated with HFJV[1] are postulated to result in lower intracranial pressure (ICP).[2] We compared the effects of the two modes of ventilation on ICP and cerebral perfusion pressure (CPP) in a combined brain/lung-injury model. Unlike previous studies,[3,4] barbiturates were not used; ICP was specifically elevated to the steep portion of the cerebral compliance curve; and PEEP was used concomitantly with HFJV.

Methods

Six mongrel dogs (16–22 kg) were studied. They were paralysed throughout the experiment with succinylcholine. Anaesthesia was induced and maintained with N_2O/O_2 and isoflurane. An endotracheal tube, subarachnoid bolt, and venous, arterial, and flow-directed pulmonary arterial catheters were placed. A Fogarty balloon catheter was placed intradurally contralateral to the subarachnoid bolt and inflated until an increase in volume of 0.5 ml increased ICP by $\geq$ 5 mmHg. Lung injury was effected with oleic acid, 0.075 $ml \cdot kg^{-1}$, infused into a central vein 1.5 hr before data collection. Isoflurane was then discontinued and anaesthesia was maintained with 70 per cent N_2O and O_2. After analysis of exhaled gases showed no isoflurane, data were collected during alternating periods of CMV and HFJV, each at 0, 10, and 15 cm H_2O of PEEP. CMV was applied with a tidal volume of 15 $ml \cdot kg^{-1}$ and a rate appropriate to keep $PaCO_2$ at 35–40 mmHg. HFJV was applied at a rate of 100 breaths/min, an inspiratory time of 30 per cent of the respiratory cycle, and a drive pressure appropriate to keep $PaCO_2$ at 35–40 mmHg. Metabolic acidosis and systemic hypotension were treated with sodium bicarbonate and intravenous fluids; temperature was maintained at 37°C. $\overline{ICP}$, PIP, blood pressure (BP), cardiac output (CO), pulmonary artery (PAP) and capillary wedge (PCWP) pressures, and arterial blood gas values were measuring 20 min after HFJV or CMV was adjusted. $\overline{Paw}$ was calculated by planimetry. Data were evaluted with analysis of variance and Duncan's multiple range test; values are means ± SD.

Results

pH (7.39 ± 0.03), $PaCO_2$ (37 ± 2 mmHg), BP (121 ± 15 mmHg) PAP (17 ± 5 mmHg), and CO (1.3 ± 0.6 $L \cdot min^{-1}$) did not differ significantly among the six conditions (pooled data). $\overline{PCWP}$ ranged between 1–14 mmHg and tended to be higher with CMV than HFJV at PEEP > 0 cm H_2O. PaO_2 was > 50 mmHg in all cases. PIP and $\overline{Paw}$ correlated positively with the level of PEEP for HFJV and CMV and were consistently lower with HFJV than with CMV at each level of PEEP ($p < 0.05$;

TABLE Effects of CMV and HFVJ on ventilatory and cerebral pressures

	0 cm H_2O PEEP	
	CMV	*HFJV*
PIP (cm H_2O)	17.2 ± 1.6	12.8 ± 3.1*
$\overline{Paw}$ (cm H_2O)	5.8 ± 0.5	3.0 ± 0.5*
$\overline{ICP}$ (mmHg)	33.2 ± 4.1	34.3 ± 4.1
CPP (mmHg)	87.7 ± 5.6	89.8 ± 4.8
	10 cm H_2O PEEP	
	CMV	*HFJV*
PIP (cm H_2O)	24.3 ± 1.1	18.0 ± 1.8†
$\overline{Paw}$ (cm H_2O)	13.2 ± 1.0	11.3 ± 0.4
$\overline{ICP}$ (mmHg)	33.5 ± 3.7	33.8 ± 4.1
CPP (mmHg)	87.3 ± 5.7	90.3 ± 6.5
	15 cm H_2O PEEP	
	CMV	*HFJV*
PIP (cm H_2O)	31.8 ± 2.2	24.7 ± 2.1†
$\overline{Paw}$ (cm H_2O)	19.2 ± 1.2	16.7 ± 0.9*
$\overline{ICP}$ (mmHg)	34.3 ± 4.7	35.2 ± 3.9
CPP (mmHg)	82.3 ± 5.7	86.5 ± 6.7

Values are means ± SD. Abbreviations are defined in the text. *$p < 0.05$ or †$p < 0.01$ compared with CMV.

Table). $\overline{ICP}$ and CPP did not differ significantly between HFJV and CMV at any level of PEEP. Correlation analysis confirmed that ICP and airway pressures were not correlated.

Discussion

The two modes of ventilation affected airway pressures in the expected manner, HFJV producing lower values of PIP and $\overline{Paw}$ at each level of PEEP. However, these differences were not reflected intracranially, despite measuring ICP at values along the steep portion of the cerebral compliance curve. These findings may be explained by the normalization of BP at higher levels of PEEP, and by less transmission of airway pressures to the intracranial compartment because of decreased lung compliance.

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The effects of thoracic aortic occlusion on the canine cerebral circulation

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Occlusion of the thoracic aorta is associated with marked alterations in systemic haemodynamics.[1] The effects of the acute haemodynamic changes on the cerebral circulation are unclear.[2] The present study was undertaken to determine the effects of thoracic aortic occlusion and subsequent clamp release on cerebral blood flow (CBF) and cerebral spinal fluid (CSF) pressure in dogs.

Methods

Six mongrel dogs weighing 15–24 kg were anaesthetized with pentobarbitone and paralyzed with pancuronium. Their tracheas were intubated, and the animals were ventilated (FiO_2 1.0) to maintain a $PaCO_2$ of 35–42 mmHg. Three cerebral blood flow measurements were made in each dog using 15 ± 0.05 μm microspheres labelled with Cerium[141], Chromium[51] or Strontium[85]. The microspheres were injected through a left atrial catheter and sampled from a brachial arterial line. Haemodynamic measurements were made using a femoral arterial line, a brachial arterial line and a pulmonary artery thermodilution catheter. Cerebral spinal fluid (CSF) pressure was measured using a left parietal subarachnoid bolt and a lumbar subarachnoid catheter. Following the surgical preparation, end tidal CO_2, PaO_2, pH and MABP were stabilized. A control CBF measurement was made and the thoracic aorta was cross-clamped immediately distal to the left subclavian artery and a distal clamp was placed just beyond the origins of the last pair of intercostal arteries. Ten minutes following aortic occlusion a second CBF measurement was made. The thoracic aorta was occluded for one hour, following which the clamps were removed. Ten minutes following clamp-release, a third CBF measurement was made. The dogs were exsanguinated, the brain removed, and scintillation counting of tissue from 12 cerebral regions was performed. The data were analyzed using Tukey's Test or Bartlett's Test, followed by a repeated measures ANOVA or completely randomized ANOVA and Duncan's Test.

Results

The results are summarized in the Table. Following thoracic aortic occlusion, a significant proximal hyper-

TABLE Results

	Control	*Following occlusion*	*Following release*
CBF ($ml \cdot 100\,g^{-1} \cdot min^{-1}$)	61 ± 7	56 ± 4	123 ± 22†
CO ($ml \cdot kg^{-1} \cdot min^{-1}$)	144 ± 7	159 ± 36	140 ± 17
MABP (mmHg) – Brachial	102 ± 4	133 ± 6*	104 ± 5
– Femoral		11 ± 1†	
CVP (mmHg) (n = 5)	3 ± 1	5 ± 1†	2 ± 1*
ICP (mmHg)	6 ± 1	11 ± 1*	11 ± 1*
Lumbar CSF pressure (mmHg)	6 ± 1	10 ± 1*	10 ± 1*
$PaCO_2$ (mmHg)	39 ± 1	36 ± 1	62 ± 3†
PaO_2 (mmHg)	325 ± 54	296 ± 51	155 ± 34†
pH	7.33 ± 0.01	7.32 ± 0.02	7.01 ± 0.04†

n = 6 in each group unless otherwise indicated, values expressed as mean ± SEM.
*$p < 0.05$.
†$p < 0.01$ compared to control.

tension and distal hypotension were observed. Aortic occlusion produced similar significant increases in both ICP and lumbar CSF pressure. The increased CSF pressure following aortic occlusion was associated with an increased CVP, but no change in CBF. Following clamp release a significant increase in $PaCO_2$ was observed, while pH and PaO_2 significantly decreased. The increased $PaCO_2$ was associated with a marked rise in CBF. Both ICP and lumbar CSF pressure remained unchanged from post aortic occlusion values following clamp release.

Discussion

Under pentobarbitone anaesthesia, thoracic aortic occlusion produces a significant increase in CSF pressure without significantly altering CBF, providing MABP does not exceed the upper pressure limit of CBF autoregulation. The observed increases in ICP and lumbar CSF pressure following aortic occlusion may be secondary to an increase in cerebral blood volume. Release of the aortic clamps results in a significant hypercarbia which is associated with a marked increase in CBF. These physiological alterations should be considered in patients undergoing thoracic aortic occlusion without the use of shunting or partial bypass.

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Visual evoked potential changes following transurethral prostatectomy – correlation with glycine absorption and ammonia metabolism

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Intravascular absorption of irrigating fluid during transurethral prostatic resection (TURP) depends on the number and size of open venous sinuses, the duration of resection and the hydrostatic pressure employed. Glycine 1.5 per cent, a non-essential amino acid, is a popular irrigation fluid because of its low cost, non-electrolytic and good optical properties. Glycine functions as an inhibitory neurotransmitter at synapses in the retina, pons and medulla. Neurotoxicity from systemic glycine absorption or its metabolites have been implicated in reports of blurred vision, transient blindness and pupillary dilatation.[1]

Intermediate latency, cortical, far-field, visual evoked potentials (VEPs) may be employed to monitor visual pathways.[2] The objectives of this study were to assess the systemic absorption and hepatic metabolism of glycine during TURP and the correlation with changes noted in VEPS.

Methods

Ten unpremedicated, ASA physical status I-II, patients undergoing elective TURP with 1.5 per cent glycine irrigation were studied. Standard subarachnoid anaesthesia with bupivacaine was employed. Crystalloid 500 ml was infused prior to subarachnoid block. Five patients having surgery with subarachnoid block, without glycine administration, served as controls. Electrocardiographic, blood pressure and temperature monitoring was employed. Blood samples were withdrawn from an arterial line before resection and every 15 minutes thereafter for 120 minutes to measure serum sodium, potassium, chloride, glucose, osmolarity, glycine and ammonia levels. VEPs were elicited with biocular flashes (rate 1.1-s) by means of a photic stimulator. Bipolar evoked potentials were recorded from scalp electrodes Oz and Cz with right frontal ground. Electrical activity was amplified × 4 and evoked responses were recorded after 128 computer averages. A cursor measured the major positive (P_2) peak latency. VEPs were recorded prior to resection 15 minutes after resection ended and 120 minutes following resection. Data were analysed by Student's t-test for paired date, analysis of variance and linear regression coefficients $p < 0.05$ was considered significant.

Results and discussion

Significant rises in serum glycine and ammonia were

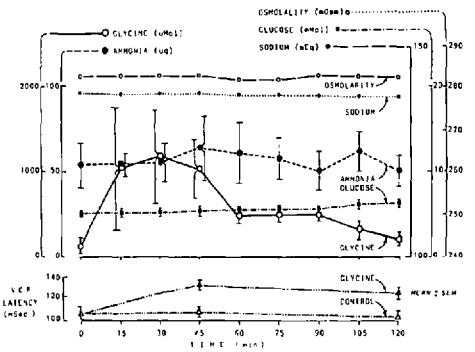

FIGURE Results.

noted within the first 60 minutes following resection in the glycine irrigation group, coupled with prolongation of the latency of the dominant positive peak of the VEP (Figure). No alteration in VEP latency was noted in the control group. The correlation in this study between elevated serum glycine/ammonia and prolonged VEP latency suggests that visual disturbances following TURP may more likely result from glycine's role as inhibitory retinal neurotransmitter or hyperammonia's role in reducing central neurotransmitters rather than the commonly postulated occipital cortical oedema aetiology.

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Incidence of pre-bypass ischaemia during sufentanil/O_2/pancuronium anaesthesia in patients undergoing coronary artery surgery

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Sufentanil has been suggested as a better anaesthetic for patients undergoing coronary artery bypass grafting (CABG).[1] Investigators have found sufentanil to provide more stable haemodynamics at times of stimulation in the pre-bypass period. This increased stability might lead to a decreased incidence of intraoperative myocardial ischaemia, which previous studies using varying anaesthetic techniques, have shown to range between 37 and 50 per cent.[2,3]

The aim of this study was to detect the incidence of pre bypass ischaemia by Holter monitoring while recording haemodynamic parameters in an attempt to assess the value of moderately high dose sufentanil (20 $\mu g \cdot kg^{-1}$) in patients undergoing CABG surgery.

Methods

With institutional approval, written consents were obtained from twenty patients with ejection fractions ≥ 0.40 scheduled for elective CABG surgery. All patients were receiving beta blockers, with 9/20 and 16/20 receiving organic nitrates and calcium channel blockers, respectively. These medications were continued until the time of premedication which consisted of diazepam 0.15 $mg \cdot kg^{-1}$ PO, morphine 0.15 $mg \cdot kg^{-1}$ IM and scopolamine 0.4 mg IM. A Holter monitor recording modified V_6 and V_9 leads was applied prior to entry into the OR. Intravenous, radial artery and thermodilution pulmonary artery catheters were inserted (under local anaesthesia). Haemodynamic profiles were recorded during the pre-bypass period at the following intervals: (A) before induction (baseline); one minute after (B) induction, (C) intubation, (D) skin incision, (E) sternotomy and at (F) aortic dissection. Sufentanil 10 $\mu g \cdot kg^{-1}$ at a rate of 175 $\mu g \cdot min^{-1}$ with pancuronium (PCB) 0.1 $mg \cdot kg^{-1}$ at 2 $mg \cdot min^{-1}$ were given for induction. Additional sufentanil 5 $\mu g \cdot kg^{-1}$ was given at one minute before skin incision and sternotomy. Heart rate (HR) and blood pressure (BP) were maintained within 20 per cent of the averaged ward values (control). For elevated HR and/or BP incremental doses of sufentanil (25 to 50 μg) followed when necessary by infusion of nitroglycerin or the addition of an inhalational anesthetic. For lowered BP volume and when necessary infusion of phenylephrine were given. Holter tapes were examined retrospectively by an independent cardiologist for evidence of ischaemia defined as depression or elevation of ST segment ≥ 0.01 mV in either lead. Student's "t" test was used to compare differences in averaged haemodynamic variables where appropriate. $p < 0.5$ was considered statistically significant.

Results

Four patients, at the times indicated by the numbers in parentheses in the Table, developed myocardial ischaemia during the pre-bypass period. Hypotension occurred in 11 patients; appeared most often after induction; was accompanied by a decrease in systemic vascular resistance and an increase in cardiac index and required phenylephrine to correct in the majority of cases. Hypertension occurred in eight patients and was corrected in the majority of cases with additional sufentanil. The HR increased significantly from baseline recordings but was not increased when compared to those of ward controls.

TABLE Numbers of patients with changes in parameters occurring at the time studied. Numbers in parentheses are those patients who were ischaemic at the time indicated. N = 20

	Time					
	B	*C*	*D*	*E*	*F*	*Total*
Ischaemic ECG	2	3	1	1	0	4
Hypotension	7(2)	5(2)	2	2	1	11(3)
Hypertension	0	3(1)	1	4	3	8(1)
HR-increased	0	1(1)	0	0	0	1(1)
PCWP-elevated	1(1)	2(2)	0	0	0	3(3)

*Continuous Holter monitor.

Ischaemia was most frequently associated with hypotension and elevated pulmonary capillary wedge pressures (PCWP).

Discussion

Myocardial ischaemia occurred in 20 per cent of patients anaesthetized with 20 $\mu g \cdot kg^{-1}$ of sufentanil. This incidence of ischaemia is similar to that obtained with fentanyl O_2/PCB technique in this institution and compares favourably with that reported elsewhere in the literature. Myocardial ischaemia as related to changes in BP, HR, contractility and filling pressures appeared to occur most often in patients developing hypotension and elevated PCWP's.

We were unable to achieve the degree of stability reported by others using sufentanil in patients undergoing CABG surgery. We believe the dose and rate of administration of sufentanil contributed to the incidence of hypotension and ischaemia. Pre-induction fluid loading and titration of the drug to the desired haemodynamic effects may be a more effective method of administration.

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The role of an ultra-short-acting beta blocker (esmolol) in patients undergoing coronary artery surgery

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The incidence of pre-bypass ischaemia still remains significant[1,2] despite advances in anaesthetic techniques aimed at avoiding haemodynamic instability at this time. Undesirable events such as tachycardia and hypertension may be due to inadequate beta blockade during narcotic-O_2 anaesthesia. We wished to assess the effect of esmolol, an ultra-short-acting beta blocker, on pre-bypass ischaemia arrhythmias and anaesthetic requirements.

Methods

Thirty patients scheduled for elective myocardial revascularization were studied using a randomized, double-blinded technique. A high-dose fentanyl-O_2 anaesthetic technique was used for all patients. Group I received an infusion of esmolol, initially at 500 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 4 min, followed by a maintenance infusion of 300 $\mu g \cdot kg^{-1} \cdot min^{-1}$ until the start of CPB. Group II received an infusion of five per cent dextrose. All patients were fitted with a Holter monitor, from arrival in the OR until the start of CPB. Modified V_6 and V_9 leads were observed to detect left ventricular ischaemia. Haemodynamic profiles were recorded at specific intervals in the pre-bypass period. The incidence, in each group, of pre-bypass ischaemia and significant arrhythmias was compared using Chi-squared analysis with Yates correction for continuity. The total time at MAC concentration of isoflurane was recorded in each patient and the differences compared using Student's t test. The null hypothesis was rejected when $p < 0.05$.

Results

Four patients developed ischaemia during the pre-bypass period (ranging from 5 sec–5 min), giving an overall incidence of 13.3 per cent. Three patients were in the control group and one in the esmolol group (Table). In all patients these episodes occurred at the time of aortic dissection or cannulation. The incidence of "complex ventricular arrhythmias" that occurred at this time was reduced from 73.3 per cent in the control group to 26.7 per cent in the esmolol group. Additional volatile anaesthetic requirements was reduced by up to 75 per cent in the esmolol group.

Discussion

Recent studies still show the incidence of pre-bypass ischaemia to range from 37–50 per cent.[1,2] We believe

TABLE Incidence of pre-bypass ischaemia and arrhythmias

	Ischaemia	*Arrhythmias*
Esmolol	1/15 (6.7%)	4/15 (26.7%)
Control	3/15 (20%)	11/15 (73.3%)
X^2	NS	0.05 p 0.02

that the degree of beta blockade was a major contributing factor to our lower incidence of 13.3 per cent. Sill *et al.* concluded that the plasma propranolol concentration was a major factor influencing haemodynamic responsiveness to stressful stimuli during CABG surgery.[4] In all four patients the ischaemic episode occurred during a period often associated with haemodynamic instability. Three of the four patients were in the control group. This may be related to the loss of the therapeutic effect of the preoperative beta blockade during the pre-bypass period, compared to the effective therapeutic plasma levels maintained by the esmolol infusion. It might also be speculated that these therapeutic plasma levels also attenuated the ventricular response to catecholamines, so significantly reducing the incidence of arrhythmias at this time. Narcotic requirements have been shown to be reduced in patients on chronic beta-blocker therapy.[5] With the growing concern of the detrimental effect of the volatile agents on the myocardial vasculature, the reduction in isoflurane requirement seen in the esmolol group may be of some clinical relevance. Esmolol offers a unique advantage of rapid, controllable levels of beta-blockade, which may reduce the haemodynamic instability due to noxious stimulation in the pre-bypass period, and in turn help reduce the incidence of pre-bypass ischaemia and arrhythmias. In addition it favourably reduces the requirements for additional volatile anaesthesia.

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Nitrous oxide causes deterioration of myocardial function and blood flow during ischaemia

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This study compared two equipotent anaesthetic regimens to test if nitrous oxide, without changing the level of anaesthesia, can affect myocardial function and blood flow in an ischaemic region of the heart.

Methods

Eight dogs were induced with thiopentone, intubated, and ventilated with isoflurane in oxygen during instrumentation. The left anterior descending coronary artery was cannulated and blood flow through it controlled using an autoperfusion circuit and screw clamp. Myocardial function was measured in the anterior wall of the left ventricle by implanting two piezo-electric crystals in the subendocardium and recording segment length changes with a sonomicrometer. Regional myocardial blood flow was measured with left atrial injections of 15 micron microspheres labelled with ^{141}Ce, ^{85}Sr, or ^{95}Nb.

Blood flow to the anterior left ventricular wall was diminished by tightening the screw clamp until segment shortening was decreased by 20 to 50 per cent. A parallel bypass shunt was then opened to restore coronary blood flow and allow recovery. The identical stenosis was re-applied by clamping the bypass shunt during two anaesthetic treatments with a 45-minute recovery period between. Ischaemic measurements were made after imposing the flow restriction, when myocardial function and haemodynamics were stable. This required less than ten minutes of ischaemia.

The treatments were 1.8 per cent (end–tidal) isoflurane in 50 per cent N_2 and O_2 and 1.4 per cent isoflurane in 50 per cent N_2O and O_2. Both were estimated to be 1.3 MAC for the dog. Myocardial function is reported as per cent systolic segment shortening and equals 100× (end diastolic length–end systolic length)/(end diastolic length). Myocardial perfusion is reported as endo/epi ratio, the ratio of blood flow in the inner third of the myocardium (subendocordium)/blood flow in the outer third (subepicardium). The order of treatment was randomized and balanced (i.e., four received N_2O first and four received N_2 first).

Results

Seven of the eight animals showed diminished shortening and decreased endo/epi blood flow ratio while receiving nitrous oxide. There was no effect of treatment sequence. The Table shows that heart rate and mean arterial pressure did not change significantly while shortening was dimin-

TABLE Effect of N_2O during myocardial ischaemia

Anaesthetic	*Heart rate (bpm)*	*Mean arterial pressure (mmHg)*	*Systolic segment shortening %*	*Endo/epi blood flow ratio*
Isoflurane 1.8% in 50% N_2/O_2	121 ± 9.5	91.6 ± 16	15.1 ± 4.8	0.56 ± 0.17
Isoflurane 1.4% in 50% N_2O/O_2	125 ± 10.7	99.4 ± 15.7	12.1 ± 4.6	0.43 ± 0.15
Mean difference	−4.1	−7.8	3.0	0.14
SEM difference	1.8	3.9	0.88	0.05
P	NS	NS	<0.05	<0.05

First two rows are mean ± SD.
P is probability that the difference is due to chance as calculated by a 2-tailed paired T-test.

ished by 20 per cent and the endo/epi blood flow ratio fell by 25 per cent.

Discussion

Nitrous oxide caused a deterioration in myocardial function and myocardial blood flow distribution in an ischaemic region of the heart. This effect was demonstrated using equipotent anaesthetic techniques with and without nitrous oxide and this result is therefore unlikely to be due to a change in depth of anaesthesia.

Segment length changes measured by the sonomicrometer reflect regional myocardial function. The changes reported here likely indicate subendocardial but not transmural ischaemia. The low endo/epi blood flow ratio indicates loss of coronary vasodilator reserve and an adverse myocardial energy supply/demand ratio.

The combined findings in this study of diminished shortening and diminished endo/epi ratio together suggest that the use of nitrous oxide exacerbated the ischaemic process. Whether this effect was due to an increase in myocardial energy demand or due to a direct action of nitrous oxide on the coronary vessels causing a maldistribution of blood flow will require further studies.

Global and regional myocardial effect of verapamil when added to fentanyl

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Intravenous verapamil during isoflurane anaesthesia results in depression of global cardiac performance[1] and regional contraction abnormalities in the dog.[2] As large doses of opiates are commonly employed in cardiac anaesthesia, we assessed the effect of intravenous verapamil in the presence of fentanyl.

Method

Under halothane anaesthesia seven dogs were instrumented to measure global left ventricular (LV) performance, and wall motion in the apical and basal regions (sonomicrometry). Halothane was then replaced by fentanyl, 100 $\mu g \cdot kg^{-1}$ (loading dose) plus 3 $\mu g \cdot kg^{-1}$ (maintenance dose). After control measurements, verapamil 0.25 $mg \cdot kg^{-1}$ was administered over 30 min followed by 3 $\mu g \cdot kg^{-1}$, and measurements were repeated 30 min after the start of the loading dose.

Results

Verapamil caused an increase in PR interval, and modest reductions in mean arterial pressure (MAP) and indices of contractility (LV dP/dt max., LV peak power; Table). No other indices of global cardiac function were significantly altered, although there was a trend to reduced heart rate (HR), cardiac output (CO), and systemic vascular resistance (SVR). End diastolic length (EDL) and per cent systolic shortening (%SS) were maintained in both segments (Table). The increase in post-systolic shortening (PSS) in the apical segment although significant, was of small magnitude (six per cent of total shortening).

Discussion

The results demonstrate mild depression of contractility when verapamil is added to fentanyl; however, pump function (expressed as stroke volume (SV)) is maintained because of vasodilation. At variance with the effect of verapamil in the presence of isoflurane, where marked

TABLE Effect of verapamil on global and regional function. Mean data for 7 dogs (± SEM)

	Fentanyl	*Fentanyl-verapamil*
HR ($\cdot min^{-1}$)	120 ± 7.6	109 ± 6.7*
PR (msec)	100 ± 4	146 ± 9*
MAP (mmHg)	121 ± 3.4	96 ± 3.7*
LV dP/dt ($mmHg \cdot s^{-1}$)	2399 ± 129	2050 ± 141*
LV Peak Power (mW)	6126 ± 581	5065 ± 721*
SV (ml)	31 ± 2.7	31 ± 3.1
CO ($ml \cdot min^{-1}$)	3714 ± 310	3329 ± 278
SVR ($dyne \cdot s \cdot cm^{-5}$)	2710 ± 210	2427 ± 256
Apical segment:		
EDL (mm)	13.2 ± 1	13.2 ± 1
%SS	24.8 ± 1.9	24 ± 1.7
%PSS	1.1 ± 0.9	6 ± 1.7*
Basal segment:		
EDL (mm)	12 ± 0.5	12.1 ± 0.6
%SS	14.3 ± 1.9	15.1 ± 1.7
%PSS	10.0 ± 2.7	8.7 ± 3.9

*Indicates $p < 0.05$.

depression and apical segment dysfunction were observed,[2] the effect of verapamil on regional wall motion in the presence of fentanyl was very small. This suggests that with isoflurane there is a drug interaction, possibly mediated via Ca^{++} channels, where as with fentanyl the effect is only that of verapamil. The association verapamil-fentanyl may be better tolerated than verapamil-isoflurane.

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Myocardial metabolism and haemodynamic responses with fentanyl-halothane anaesthesia in hypertensive patients undergoing coronary arterial surgery

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It has previously been shown that fentanyl-halothane anaesthesia effectively maintained haemodynamic depression and myocardial oxygen balance in normotensive patients receiving fentanyl-halothane.[1] We have now studied this same drug combination in long-term, treated hypertensive patients undergoing coronary artery bypass grafting (CABG). Coronary sinus blood flow (CSBF), MVO_2, and myocardial lactate extraction (MLE) were correlated with haemodynamics before, during and after anaesthesia.

Methods

Ten patients, seven male and three female, gave informed consent to participate in the study which had institutional approval. All were treated hypertensives with preserved ventricular function. Means ($\bar{x}$) were age = 65.7 years, weight = 73.4 kg, ejection fraction = 0.71, cardiac index (CI) = 2.32 $L \cdot min^{-1} \cdot m^2$, LVEDP = 12 mmHg. Nine patients had NYHA disability Class III or IV. All patients were taking beta-adrenoceptor blocking agents and calcium channel antagonists continued to the day of operation. Six were also taking other antihypertensive medication.

After diazepam and morphine premedication ($\bar{x}$ = 11 and 12 mgs), a radial artery cannula and two thermodilution catheters (right internal jugular) were inserted, one a pulmonary artery (PA) catheter, the other a Ganz catheter guided into mid-coronary sinus by fluoroscopy. Sequential studies were done – before induction, six times during anaesthesia, and at 1 and 24 hours postoperatively. Each study measured central and arterial presures, CI, CSBF, plus arterial and CS sampling for Hb, O_2 saturation and lactate content. Lead V5 of the EKG was recorded.

Induction began with 30 $\mu g \cdot kg^{-1}$ of fentanyl IV with pancuronium 0.1 $mg \cdot kg^{-1}$ with halothane (mean end-tidal = 0.51 per cent) and oxygen to reduce systolic arterial pressure by 25 per cent for 10 minutes before intubation. Maintenance was with halothane-O_2 in concentrations to keep mean arterial pressure (MAP) below awake levels.

Results

Mean anaesthesia time was 326 minutes, mean bypass time was 125 minutes, and mean aortic cross-clamp time was 47 minutes. Heart rate decreased on induction and remained so up to bypass. MAP was reduced 30 per cent at induction and was maintained below that awake throughout anaesthesia. CI remained depressed from induction through to the one hour study. Stroke work index (SWI) fell during and after anaesthesia. Systemic vascular resistance (SVR) was unchanged apart from a

TABLE Results

Means ± SD n = 10	*Awake control*	*Post-induction*	*Post-intubation*	*Post-sternotomy*
Heart rate beats/min	65 ± 14	58 ± 14*	60 ± 13	60 ± 9
MAP mmHg	96 ± 11	67 ± 5*	73 ± 6*	79 ± 7*
PC Wedge mmHg	11 ± 5	8 ± 4	7 ± 2*	8 ± 4*
CI $L \cdot min^{-1} \cdot m^2$	2.8 ± 0.4	2.1 ± 0.4*	2.2 ± 0.6*	1.9 ± 0.4*
SWI $gM \cdot m^2$	76 ± 19	45 ± 12*	48 ± 11*	45 ± 10*
SVR dynes·sec·cm^{-5}	1417 ± 225	1324 ± 222	1394 ± 310	1688 ± 322*
CSBF $ml \cdot min^{-1}$	128 ± 44	86 ± 30*	87 ± 39*	88 ± 37*
CSO_2 Saturation %	37 ± 7	55 ± 8*	51 ± 9*	50 ± 8*
MVO_2 $ml \cdot min^{-1}$	14 ± 5	7 ± 3*	7 ± 4*	7 ± 4*
MLE%	3 ± 64.5	24 ± 31	27 ± 15	24 ± 37
Hearts producing lactate	3	2	0	2

Means ± SD n = 10	*Post-pump*	*ICU 1 hour*	*ICU 24 hours*
Heart rate beats/min	77 ± 12*	84 ± 9*	87 ± 7*
MAP mmHg	68 ± 7*	91 ± 14*	83 ± 14*
PC Wedge mmHg	9 ± 6	10 ± 6	13 ± 5
CI $L \cdot min^{-1} \cdot m^2$	2.4 ± 0.7	2.2 ± 0.6*	2.9 ± 0.3
SWI $gM \cdot m^2$	35 ± 8*	38 ± 12*	48 ± 15*
SVR dynes·sec·cm^{-5}	1288 ± 451	1723 ± 631*	1113 ± 245*
CSBF $ml \cdot min^{-1}$	146 ± 85	172 ± 86*	191 ± 64*
CSO_2 Saturation %	55 ± 12*	49 ± 8*	49 ± 13*
MVO_2 $ml \cdot min^{-1}$	5 ± 3*	11 ± 6*	12 ± 3*
MLE%	−0.7 ± 34	23 ± 15	23 ± 12
Hearts producing lactate	3	0	0

*$p < 0.05$. Statistics included analysis of variance and paired t-test.

rise post-sternotomy. CSBF decreased from induction through to bypass, but was increased at the 1 and 24 hour studies. CSO_2 content increased on induction and remained so until bypass. MVO_2 fell during and after anaesthesia. MLE increased after induction and continued throughout the study except for the post-bypass series. Three hearts produced lactate during the awake control period, with two hearts continuing lactate production at all but one of the pre-pump series. In the ICU none of the nine patients studied produced lactate. The tenth patient whose coronary sinus catheter was displaced during bypass produced lactate consistently pre-bypass and a myocardial infarction was evident postoperatively. The pre-bypass course was haemodynamically stable with no ST depression evident. She died on the tenth postop day. Seven patients required nitroglycerine (NTG) to control hypertension during bypass and four patients required nitroprusside to control blood pressure in the first 24 hours (mean duration of treatment = 3.8 hours).

Discussion

These hypertensive patients, maintained on beta and calcium channel blockade until operation, were normotensive during the awake study. With a fentanyl-oxygen-halothane induction heart rate, MAP, CI, SWI and MVO_2 were all reduced, thus providing smooth controlled depression of the circulation. Haemodynamically these hypertensive patients behaved similarly to normotensive patients who received fentanyl-oxygen-halothane using the same protocol.[1] However, in contrast to the normotensive group, three myocardia were producing lactate when studied awake breathing air. After induction, two myocardia produced lactate at all but one study before bypass. Thus controlled haemodynamic depression failed to reverse the global left ventricular lactate production present when awake in two of the three patients, with one showing acute infarction postoperatively.

Reference

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Electrocardiographic ST-segment elevation following myocardial reperfusion

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We have frequently observed electrocardiographic (ECG) ST-segment elevation at the time of myocardial reperfusion following aortocoronary bypass grafting (ACBG). Such injury currents may indicate transmural myocardial ischaemia. We undertook this prospective study to document the incidence, duration, and associated morbidity of ST-segment elevation following reperfusion in patients undergoing ACBG.

Methods

Institutional approval was obtained and the requirement for informed consent waived. Thirty patients (24 male, 6 female) undergoing elective ACBG were studied. Patients with preoperative ST-segment elevation or conduction abnormalities were excluded. In the operating room, ECG leads II and CS5 were attached and continuously recorded for the next 24 hours by a Holter monitor. Under fentanyl-oxygen anaesthesia, hypothermic cardiopulmonary bypass (CPB) was initiated and the distal coronary anastomoses performed with cold potassium cardioplegia. The aortic anastomoses were completed during rewarming and reperfusion. Postoperatively, 12 lead ECGs and creatine kinase MB (CK-MB) determinations were performed daily for three days. The Holter ECG tapes were later reviewed for ST-segment changes. ST-segment elevation ≥ 0.1 MV was considered positive. The data were analyzed by analysis of variance (ANOVA) or Fischers' Exact Test. A p-value ≤ 0.05 was regarded as significant.

Results

During the 24-hour ECG recording, thirteen patients (10 M, 3 F) had 18 separate episodes of ST-segment elevation lasting 29.0 ± 25 min (range 2–60 min). In 12 of 13 patients, ST-elevation was first apparent during CPB upon resumption of supraventricular rhythm after aortic unclamping. ST-elevation first occurred after CPB in the other patient. Six patients had ST-elevation in lead II only, six had elevation in leads II and CS5, while one had elevation in CS5 only. One patient with ST-elevation in lead II had a non-diseased, non-grafted right coronary artery. Patients with and without ST-elevation did not differ with respect to age, sex, antianginal medication, ejection fraction, number of grafts, bypass time, cross-clamp time, or need for pharmacologic or mechanical support. There were no deaths. Historically, angina at rest was more frequent in patients with ST-elevation (5/13 vs. 2–17, p = 0.10). Postoperative CK-MB levels were significantly higher in patients with ST-segment elevation

TABLE Post-operative CK-MB (units)

	1	*2*	*3*
ST-elevation	157 ± 236	71 ± 82	37 ± 33
No ST-elevation	68 ± 39	38 ± 21	23 ± 12

$P \leq 0.05$ ANOVA.

(Table). Only two patients had postoperative ECG evidence of transmural infarction, and both had ST-elevation after reperfusion.

Discussion

In this study, ST-segment elevation was very frequent (43 per cent) after reperfusion during ACBG. Elevation was most common in lead II (12/13) and usually became evident with resumption of supraventricular rhythm after aortic unclamping. Although transient, such changes often recurred later in the postoperative period (5/13). Significantly, ST-elevation was associated with higher postoperative CK-MB levels, indicating myocardial damage. The etiology of the ECG changes is not clear, but the differential diagnosis includes inadequate myocardial protection, or transient coronary artery or graft occlusion by spasm, embolism or thrombosis. However, the tendency for ST-elevation to occur in patients with rest pain, to be recurrent and to occur most commonly in lead II, suggests coronary spasm as an important mechanism.[1] Further studies are needed to confirm these observations and to clarify the aetiology of the observed changes. Meanwhile, transient ST-elevation following reperfusion should be viewed with concern by clinicians and postoperative recurrence anticipated.

Reference

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Altered pharmacokinetics of alfentanil

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The pharmacokinetics of alfentanil (A) make it theoretically suitable for use as a constant infusion during coronary artery surgery (CAS).[1] In this study we examine the clinical characteristics and pharmacokinetics of A during and after CAS.

Methods

With approval of the Hospital Ethics Committee three groups of eight (G1), ten (G2) and ten (G3) patients were studied. Except for coronary artery disease all patients were well. All were maintained on regular medications preoperatively and premedicated with morphine, hyoscine and diazepam. Intravenous, intra-arterial and thermodilution pulmonary artery catheters were inserted and a control haemodynamic profile obtained pre-induction. Anaesthesia was induced with 250, 300 and 350 $\mu g \cdot kg^{-1} \cdot hr^{-1}$ of A for one hour in groups 1, 2 and 3 respectively. Simultaneously an infusion of 2.5, 3.0 and 3.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ was started and continued to the end of surgery. Pancuronium was given in 1.5 mg increments (first dose pre-induction) every 30 seconds to 0.1 $mg \cdot kg^{-1}$. All patients were intubated after 60 $\mu g \cdot kg^{-1}$ of the induction dose. Haemodynamic profiles were repeated following intubation, incision, sternotomy and aortic dissection. An adrenergic response was defined as a 20 per cent increase from control in heart rate and/or systolic pressure and treated with isoflurane 1-2 MAC inspired until abolished. Samples for plasma A conc. were taken at 5, 10, 15, 30 and 60 minutes following induction, then half hourly for three hours and hourly for a further five to ten hours. Plasma A conc. was measured by radioimmunoassay. Postoperative time to return of consciousness and extubation ($PECO_2 < 6.6$ kPa) were documented. Data were analysed using Student's "t" test with Bonferroni correction and Chi squared test where appropriate. All results are expressed as mean ± SE. The elimination half-time of A was calculated as

$$T_{\frac{1}{2}}\beta = \frac{0.693}{K}$$

with K values determined by fitting an exponential curve using the least squares method to the terminal portion of the plasma A conc. curve. Linear regression analysis was used to plot $T_{\frac{1}{2}}\beta$ versus A conc. at end surgery.

Results

17/28 patients had adrenergic responses to intubation (mean A conc. 479 ± 54, 510 ± 68 and 610 ± 119 $ng \cdot ml^{-1}$) but none responded to aortic dissection (mean A conc. 826 ± 71, 1001 ± 104 and 1166 ± 113 $ng \cdot ml^{-1}$) in groups 1, 2 and 3. There was no difference in response rates among groups. There was no difference in time to return of consciousness (3.2 ± 0.6 hrs) or extubation (8.8 ± 1.2 hrs). $T_{\frac{1}{2}}\beta$ increased with increasing plasma A conc. ($p = 0.04$) and was 3.8 ± 0.5, 4.8 ± 0.5 and 6.3 ± 0.8 hrs in groups 1, 2 and 3.

Discussion

The absence of responses to aortic dissection suggest that plasma A conc. achieved by that time were adequate to suppress adrenergic responses to surgical stimuli. Induction dose and infusion rates of A should be designed to achieve plasma A conc. greater than 800 $ng \cdot ml^{-1}$ before surgical stimuli occur. The lack of difference among groups in time to return of consciousness and extubation suggests that relatively high plasma A conc. might be achieved, with concomitant adrenergic suppression intraoperatively, without necessarily incurring delayed awakening or prolonged ventilatory support postoperatively.

The $T_{\frac{1}{2}}\beta$ of A in this study is much longer than previously reported,[1] but similar prolongation of $T_{\frac{1}{2}}\beta$ of fentanyl following cardiopulmonary bypass has been reported.[2] However, dose dependent increases in $T_{\frac{1}{2}}\beta$ could be due to increasing depression of elimination mechanisms (cardiac output, hepatic blood flow, hepatic enzymatic activity) with increasing plasma A conc. or to saturation of enzyme systems that metabolize A.

In summary, alfentanil can provide adequate anaesthesia for CAS without prolonged postoperative depression but $T_{\frac{1}{2}}\beta$ increases with increasing dose.

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Fentanyl and responsiveness of canine coronary arterial smooth muscle

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Increased tone (coronary vasospasm) in large coronary arteries is a feature of both Prinzmetal's angina and atherosclerotic coronary artery disease. We have previously shown that isoflurane attenuates contraction of canine coronary arteries induced by serotonin and prostaglandin F2α and that this effect is endothelium-mediated. Controversy exists regarding the effects of fentanyl on coronary smooth muscle. The present study was designed to determine the effects of the drug on isolated coronary arteries.

Methods

Rings (approximately 4 mm in length) were prepared from the circumflex and the left anterior descending coronary arteries of anaesthetized dogs. In some rings, the endothelium was mechanically removed. The rings were placed in organ chambers filled with 25 ml modified Krebs-Ringer bicarbonate solution (37° C) and aerated with a 95 per cent oxygen–5 per cent CO_2 gas mixture (pH 7.45–7.49). The rings were connected to a strain gauge for measurement of isometric force. Fentanyl was added to half the chambers 30 minutes before the experiment to a final concentration of 100 $ng \cdot ml^{-1}$.[1] Both control and fentanyl-treated rings were then exposed to increasing concentrations of phenylephrine or serotonin and the tension generated was recorded. The same experiment was repeated with vessels without endothelium. Data are expressed as per cent of maximal response to previous stimulation with 40 mEq KCl. Student's t test for paired observations was used to analyze the data.

Figure 1

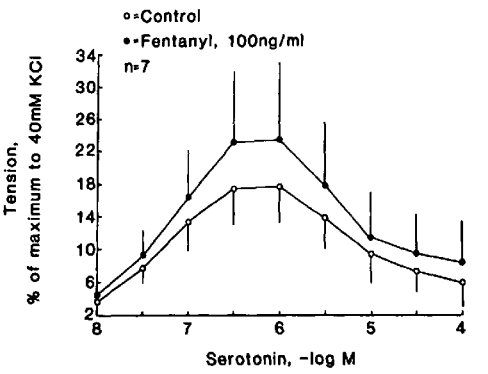
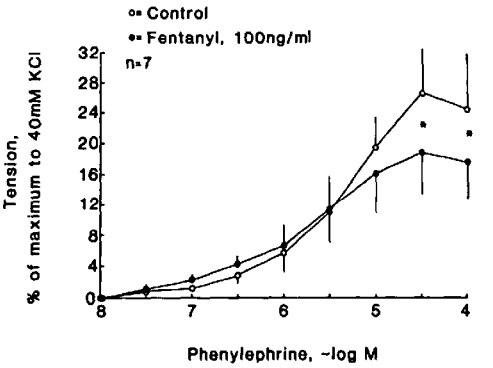


Figure 2



FIGURES 1 and 2 Isometric tension developed by intact coronary rings (mean ± SEM) following exposure to serotonin (Fig. 1) and phenylephrine (Fig. 2) during control and following fentanyl administration. The difference between treated and untreated rings is statistically significant ($p < 0.05$) at high concentrations of phenylephrine.

Results

Fentanyl had no effect on basal tone of coronary rings with or without endothelium. In rings with endothelium, it did not affect the concentration–response curve to increasing concentration of serotonin (Figure 1), but caused a small but significant depression of the response to high concentrations of phenylephrine (Figure 2). Fentanyl did not significantly alter the concentration–response curve to serotonin or phenylephrine in vessels without endothelium.

Discussion

This study shows that fentanyl has no *in vitro* effect on relaxed canine coronary arteries, and has only a minimal effect on response of coronary rings to putative mediators of coronary vasospasm. The modest inhibition of the response to high concentrations of phenylephrine probably reflects facilitation of beta-adrenergically mediated relaxation, which is more pronounced in the presence of endothelium.[2] We suggest that fentanyl does not disturb to a major extent the balance between constrictor and dilator responses of large coronary arteries.

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Profound disruption of sleep in the first week after upper abdominal surgery

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In a previous study we observed that isoflurane anaesthesia alone caused only a minor alteration of physiological sleep.[1] The purpose of this study was to describe sleep before and after isoflurane anaesthesia accompanied by major upper abdominal surgery.

Methods

Five obese patients were studied from approximately 2300 hrs to 0900 hrs for seven consecutive nights, two nights before and five nights after anaesthesia and abdominal surgery. None were known to have sleep apnoea. Anaesthesia was induced with thiopentone, and maintained with nitrous oxide and isoflurane supplemented with fentanyl and neuromuscular blocking agents. The surgical procedure was gastric stapling through an upper mid-line abdominal incision. Postoperative pain was treated with morphine. The first preoperative night was allowed for adaptation to the sleep lab. On each night of study, continuous polysomnographic recordings were made of EEG, EOG and EMG. Sleep stages were scored for each 30 sec epoch of the night according to standard criteria.[2] Total sleep time and sleep stages as a per cent of total sleep time were determined. The statistical assessment was by analysis of variance.

Results

The subjects were three females and two males, whose ages were 32 ± 3 yrs, hts 173 ± 3 cm and wts 151 ± 5 kg. Sleep data are presented in the Table. Anaesthesia with surgery did not detectably affect the total quantity of sleep but markedly disrupted sleep architecture. On the night of operation, sleep was highly fragmented. Slow wave sleep (stages 3 and 4) was severely depressed, REM sleep completely abolished and stage 2 sleep reciprocally increased. Similar but less marked changes were present during the subsequent two nights. After three nights of REM sleep suppression, there was an increase and then a rebound of REM sleep above control associated with frequent "bad dreams."

TABLE Results

	Night					
		Postoperative				
	Control	*1*	*2*	*3*	*4*	*5*
Total sleep time (min)	353 ± 31	358 ± 18	313 ± 21	331 ± 24	309 ± 38	346 ± 35
Stage 2 (%)	48 ± 4	84 ± 4*	77 ± 6*	71 ± 5*	50 ± 5	36 ± 4
Slow wave (%)	30 ± 5	7 ± 4*	10 ± 5*	15 ± 5*	25 ± 2	33 ± 3
REM (%)	17 ± 4	0 ± 0*	1 ± 1*	2 ± 1*	16 ± 3	26 ± 2*

All values mean ± SEM; sleep unaccounted for in percentage values was stage 1.
*Significantly different from control $p < 0.05$.

Discussion

We conclude that major abdominal surgery causes severe disruptions of nocturnal sleep through the first postoperative week. A comparison with our previous study of the effects of isoflurane anaesthesia alone[1] suggests that anaesthesia plays only a minor role in these changes. The relative importance of various surgical factors – such as the metabolic response to surgery stress, postoperative pain and narcotics – remains to be determined.

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Severe sleep-related hypoxaemia after abdominal surgery in the morbidly obese

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Both sleep-related hypoxaemia and hypoxaemia in the first week after abdominal surgery may be more pronounced in the obese.[1,2] The purpose of this study was to define the adequacy of arterial oxygenation during postoperative sleep in a group of morbidly obese patients.

TABLE Arterial oxygen saturation (%)

	Nights					
		Postoperative				
	Control	*1*	*2*	*3*	*4*	*5*
Wakefulness	94 ± 1 (5)	93 ± 1 (4)	91 ± 1* (5)	92 ± 1* (4)	92 ± 1* (5)	94 ± 1 (4)
Sleep						
Stage 2	94 ± 1 (5)	93 ± 1 (4)	90 ± 1* (3)	90 ± 2*† (4)	91 ± 1* (5)	94 ± 1 (4)
Slow wave	94 ± 1 (5)	93 ± 1 (3)	91 ± 1* (3)	90 ± 2*† (3)	91 ± 1* (5)	93 ± 1 (4)
REM	93 ± 2 (5)	— (0)	89 (1)	88 (1)	88 ± 3*† (5)	89 ± 3*† (4)

All values mean ± SEM; n = ( ); (n < 5 when sleep stage absent or supplemental oxygen given).
*Significantly different from control, same state ($p < 0.05$).
†Significantly different from wakefulness, same night ($p < 0.05$).

Methods

Five obese patients were studied during both wakefulness and sleep in the two nights before and five nights after surgery for gastric stapling. The investigation was conducted in conjunction with a study of sleep described in an accompanying abstract. In addition to electrophysiological variables of sleep, we monitored arterial oxygen saturation (SaO_2) continuously with an ear oximeter (Biox II) while the patients inhaled air. We also assessed ventilation with a nasal thermistor probe and a respiratory inductive plethysmograph (Respitrace). Mean SaO_2 values were computed for each 30 sec interval of each night and considered in relation to wakefulness or stage of sleep. Statistical assessment was by a two-way analysis of variance.

Results

SaO_2 values are presented in the Table. Surgery was followed by modest reductions of SaO_2 during periods of wakefulness of postoperative nights 2, 3 and 4. Sleep after surgery caused greater reductions of SaO_2 during stage 2 and slow wave sleep of postoperative night 2 and during REM sleep of nights 4 and 5. REM sleep after surgery was associated with marked variability of SaO_2 and episodic reductions to values as low as 50 per cent (PaO_2 26 mmHg). These arterial desaturations after surgery were not related to apnoea.

Discussion

We conclude that physiological sleep after upper abdominal surgery in the morbidly obese causes marked hypoxaemia during the third through fifth postoperative nights. This impairment of oxygenation may represent the most severe disturbance of respiratory function associated with uncomplicated anaesthesia and surgery.

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Diprivan versus thiopentone for outpatient surgery

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Diprivan (di-isopropylphenol) is a sterically-hindered phenol which has been reported to provide good surgical anaesthesia and quick awakening.[1] It has been recently reformulated in a lipid emulsion, thereby eliminating the hazard of allergic reactions to Cremophor EL. This study compares the new formulation of Diprivan with thiopentone. The haemodynamic and respiratory effects of both agents were evaluated in outpatients. Time elapsed to awakening and returning to orientation in three spheres was compared.

Methods

Informed consent was obtained from 90 outpatient females undergoing uterine dilatation and curettage (D&C). All subjects were ASA physical status Class I or II with an age range of 18–65 yr. The subjects were divided into thiopentone (n = 30) and Diprivan (n = 60) groups using a method of restriction randomization. Both groups were comparable with respect to age, race, smoking history and baseline heart rate (HR), blood pressure (BP) and respiratory rate (RR). The patients were unaware of which drug was used until recovery from anaesthesia. No premedication was used. The induction dose of thiopentone (4 $mg \cdot kg^{-1}$) or Diprivan (2.5 $mg \cdot kg^{-1}$) was given over 20 sec and any adverse effects noted. Patients were asked to count coincident with beginning the injection. The onset of anaesthesia was taken as the time when they stopped counting. Increments of 25 per cent of the induction dose were administered as required, to maintain anaesthesia for the remainder of the procedure. For the first 3 min after induction the patients were given supplementary O_2 and were left undisturbed. The HR, BP and RR were recorded each minute. Following this stabilization period, inhalation anaesthesia with 70 per cent nitrous oxide (N_2O) in O_2 was added and the D&C performed. During this maintenance phase HR, BP, RR and end-tidal CO_2 ($EtCO_2$) concentration were recorded each minute. Upon completion of the procedure, the N_2O was discontinued and time elapsed until eye opening and return to orientation to person,

place and time were measured. Each patient was questioned about subjective impressions and adverse reactions. Data analysis was done using Student's t test or Chi-square, as appropriate.

Results

All patients in both groups lost consciousness with the induction dose and no patient had recall of the procedure. The quality of anaesthesia was judged to be adequate to excellent by the attending anaesthetists. There were no statistical differences in HR, BP, or $EtCO_2$ concentration at any time during the study period for the two groups. Time to awakening was 569 ± 555 (SD) sec in the thiopentone group versus 331 ± 151 sec in the Diprivan group ($p < 0.05$). Time to orientation was 685 ± 453 in the thiopentone group versus 460 ± 184 sec in the Diprivan group ($p < 0.05$). Preliminary analysis suggests that, as total drug dosage increases, the difference in the times to awakening and orientation increases between both groups, favouring Diprivan. There was no significant difference between the groups for hiccoughs, apnoea, electrocardiographic changes or pain with injection. Patients in the Diprivan group perceived a difference in mental function postoperatively. Subjectively they felt more awake and able to think clearly.

Discussion

(1) Diprivan with 70 per cent N_2O and O_2 provides good surgical anaesthesia for D&C. (2) Orientation occurs sooner after Diprivan than after thiopentone. As total dosage increases, the difference becomes more pronounced. (3) The haemodynamic and respiratory effects of Diprivan and thiopental are indistinguishable at comparable doseages.

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Plasma levels and mucosal damage following rectal administration of 2% or 10% methohexitone in rats

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Methohexitone is an ultrashort-acting barbiturate that, when administered rectally, is a safe, effective method of inducing anaesthesia in young children. Damage to the rectal mucosa[1,2] has been reported following administration of rectal methohexitone; however, it remains unclear whether the damage was due to the high osmolality and pH of the solution or resulted from a direct effect of methohexitone on the bowel mucosa.

The purpose of this study was to compare the effects of pH and osmolality and differing concentrations of methohexitone on the rectal mucosa of the rat and to compare plasma levels of methohexitone achieved when two and ten per cent solutions of methohexitone are administered rectally.

Methods

Sixty-seven male Sprague Dawley rats were studied. Each was randomly assigned to one of seven groups:

Group 1 – Control, no rectal catheter or injection (n = 7)
Group 2 – Control, intraperitoneal two per cent methohexitone (n = 6)
Group 3 – Isotonic-neutral pH saline 290 mOsm; pH 7.1 (n = 6)
Group 4 – Hypertonic-neutral pH saline 850 mOsm; pH 7.3 (n = 12)
Group 5 – Isotonic-alkaline saline 290 mOsm; pH 10.7 (n = 12)
Group 6 – Rectal methohexitone two per cent 290 mOsm; pH 10.7 (n = 12)
Group 7 – Rectal methohexitone 10 per cent 850 mOsm; pH 11.4 (n = 12)

Osmolality of some solutions was adjusted using polyethylene glycol 400.

Under Innovar anaesthesia the femoral artery and vein of each animal was cannulated. An endotracheal tube was placed and ventilation controlled to maintain a constant $PaCO_2$ (38 ± 3 mmHg) and PaO_2 (94 ± 7 mmHg). A control saline solution (Groups 3–5) or methohexitone two or ten per cent was instilled rectally 2.5 cm from the anal sphincter using a soft, rubber catheter. Animals in Group 2 received two per cent methohexitone into the peritoneal cavity.

Blood pressure and heart rate were monitored continually and blood samples collected intermittently for determination of plasma methohexital levels. At four hours following administration of the test solutions one half the animals in each group were sacrificed and rectal specimens were excised. The remainder of the animals were sacrificed at 24 hours. Rectal specimens were fixed in ten per cent formalin and stained with hematoxylin-eosin for histologic examination.

Results

Mucosal histology

Mild to moderate focal mucosal erosions and/or oedema were present in 3/24 rats that received rectal methohexitone. Evidence of mucosal damage was absent in all other groups.

Cardiovascular effects
Five minutes following administration of two or ten per cent methohexitone there was a significant fall in systolic and diastolic blood pressure. However, blood pressure returned to control levels by ten minutes and remained there throughout the experimental period.

Plasma methohexitone concentrations
Five minutes after administration of ten per cent methohexitone, the mean plasma level was 19.07 ± 16.09 $\mu g \cdot ml^{-1}$. This was significantly higher than the level following two per cent methohexitone rectally, 4.71 ± 2.23 $\mu m \cdot ml^{-1}$, or intraperitoneal, 8.55 ± 4.03 $\mu g \cdot ml^{-1}$. There was no statistical difference in the plasma methohexitone concentrations at any other time interval.

Discussion
The only animals that showed evidence of mucosal damage were those that received rectal methohexitone. Unlike earlier reports,[1,2] the mucosal damage seen in this study was infrequent and mild to moderate in severity. This difference may have occurred because previous investigators did not control blood pressure or ventilation. The mucosal damage in those studies may have been exacerbated by hypoxia, hypercarbia or hypotension.

We conclude that the mucosal damage seen following the rectal administration of methohexitone was due to a direct action of the drug on the bowel mucosa. Further investigation will be required to determine the incidence and extent of mucosal damage that may occur in humans.

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Combinations of volatile anaesthetics do not produce simple additive effects on a single isolated neuron

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The precise mechanism(s) or site(s) of action of general anaesthetics have yet to be defined. Early theories of anaesthesia emphasised a single site and mechanism predicting simple additivity with combinations of two agents. Recent literature suggests that general anaesthesia is a more complex phenomenon which involves multiple sites and mechanisms.[1] Previous studies of combinations of general anaesthetic agents[2,3] have also suggested multiple sites and mechanisms. This *in vivo* data is, however, difficult to interpret due to respiratory and other physiological changes produced by the anaesthetics. To avoid these complications the effects of combinations of volatile anaesthetics were studied at a cellular level, using an isolated neuron preparation. This model permitted application of controlled concentrations of anaesthetic and measurement of a relatively simple response.[4]

Methods
Crayfish (Procambarus clarkii) stretch receptor neurons were mounted in a tissue chamber and continuously perfused with Van-Harraveld's solution (3 $ml \cdot min^{-1}$: 10° C).[1] Discharge activity was recorded from the stimulated (stretched) neuron. The preparation was enclosed in a "tent" of polyvinylchloride film to control the ambient environment. Oxygen was administered at a rate of 3 $L \cdot min^{-1}$ from two gas sources each of 1.5 $L \cdot min^{-1}$. The vapours of halothane, enflurane and isoflurane were administered either singly or in binary combination from standard (Ohmeda Tec IV®) anaesthesia vapourisers. Combinations were 0.5 per cent vol/vol increments of the first anaesthetic applied simultaneously with a constant concentration of the second. Each combined or single concentration was administered for ten minutes to achieve a stable effect, followed by a ten-minute washout to return to control level. At equilibrium, aliquots of bathing solution were sampled and aqueous anaesthetic concentrations quantified. Dose response curves of the neuron's discharge activity versus concentration of single and combined anaesthetics were constructed.

Results
The vapour of a single volatile anaesthetic produced alterations of both the rate and pattern of firing of the neuron, and the dominant effect was a concentration-dependent depression of firing frequency.[4] Binary combinations of halothane, enflurane and isoflurane interacted in a complex fashion to produce a range of effects from antagonism to synergism. Additivity was rarely a major feature. Low concentrations of a second anaesthetic partially antagonised the effects of a first anaesthetic. Increasing the concentration of the second anaesthetic resulted in greater antagonism, followed by a synergistic response at a critical combined dose. These opposing effects resulted, on occasion, in a biphasic dose response curve. Regular firing frequencies, sustained slightly above control levels, were observed with some combinations; none of the volatile anaesthetics alone produced this phenomenon.

Discussion
We have demonstrated that combinations of volatile anaesthetics do not produce simple additive effects on a single isolated neuron. The major finding was that combinations resulted in antagonism; however, other

results including synergism were observed. These data do not support a unitary theory of mechanism for all anaesthetics, but provide confirmation for a hypothesis involving multiple sites and/or mechanisms. We propose that non-additive neurophysiological changes may also occur *in vivo* when two different volatile agents are employed in the course of an anaesthetic procedure.

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Isoflurane-induced hypotension does not cause an increase in catecholamines

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Induced hypotension is frequently employed during cerebral aneurysm surgery. However, there is no concensus on the ideal hypotensive agent for this purpose. The use of sodium nitroprusside (SNP) is associated with rebound hypertension due to increased catecholamine and renin release during and after induced hypotension. Deep isoflurane anaesthesia has been employed successfully as a hypotensive agent. In this study we examined the effect of isoflurane-induced hypotension on catecholamine and renin release.

Methods

Written informed consent was obtained from eight patients aged 35–69 years presenting for cerebral aneurysm surgery. Patients receiving β-blockers were excluded. Anaesthesia was induced in a standardized manner with fentanyl 2–3 $\mu g \cdot kg^{-1}$, thiopentone 5–6 $mg \cdot kg^{-1}$, lidocaine 1.5 $mg \cdot kg^{-1}$ and succinylcholine 1 $mg \cdot kg^{-1}$. Maintenance anaesthesia consisted of pancuronium, nitrous oxide/oxygen (66/33 per cent) and 0.5–1 per cent inspired isoflurane. Mechanical ventilation was employed to maintain end-tidal carbon dioxide between 25–30 mmHg. Hypotension was induced by increasing the inspired concentration of isoflurane to three per cent until the desired level of induced hypotension was achieved, thereafter it was reduced to 2–2.5 per cent to maintain this level of blood pressure. After induced hypotension, the inspired isoflurane concentration was returned to its pre-hypotension level.

TABLE Results (Mean ± SEM)

N = 8	*Before hypotension*	*During hypotension*	*After hypotension*
PRA ($ng \cdot L^{-1} \cdot s^{-1}$)	0.97 ± 0.13	1.33 ± 0.20	0.99 ± 0.13
Plasma E ($pmol \cdot L^{-1}$)	301 ± 102	189 ± 63*	166 ± 49*
Plasma NE ($pmol \cdot L^{-1}$)	1201 ± 264	1260 ± 345	1209 ± 250
MAP (mmHg)	75 ± 2	51 ± 1*	74 ± 2
HR	80 ± 3	84 ± 3	78 ± 4

*$p < 0.05$ compared to before hypotension value.

Blood samples for plasma epinephrine (E), norepinephrine (NE) and renin activity (PRA) were drawn from a peripheral artery after dural opening but pre-induced hypotension, 15 minutes into induced hypotension and 30 minutes after termination of induced hypotension. No narcotics were given during the period of sampling. Mean arterial pressures (MAP) and heart rates (HR) were recorded at the time of sampling. The results were analyzed for statistical significance using the Friedman analysis of variance.

Results

Duration of induced hypotension ranged from 15–75 minutes. Plasma E decreased significantly during the period of hypotension and remained significantly lower following recovery of blood pressure. Plasma NE did not change during the period of sampling. PRA increased in some patients during hypotension but this did not reach statistical significance. Rebound hypertension after induced hypotension did not occur.

Discussion

In two previous studies[1,2] Khambatta *et al.* showed that mean PRA, plasma E and NE levels rose significantly during SNP-induced hypotension and remained elevated after induced hypotension. Rebound hypertension occurred on stopping the SNP. In contrast, we did not find similar changes and therefore conclude that during isoflurane-induced hypotension renin release is attenuated and catecholamine release suppressed.

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The influence of halothane and Innovar on brain oedema formation

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Patients at risk of developing brain oedema frequently require anaesthesia. Such patients include those having cerebral angiography or neurosurgical procedures. The interaction between anaesthetic agents and the development of brain oedema has not been extensively investigated and the available literature is conflicting.[1] Our study was designed to further explore this issue.

Methods

Nineteen female New Zealand white rabbits weighing approximately 3 kg were studied. The agents used were halothane (one per cent inspired) and Innovar-Vet (fentanyl 400 $\mu g \cdot ml^{-1}$ and droperidol 20 $mg \cdot ml^{-1}$) 0.5 $ml \cdot kg^{-1}$ IM in divided doses.

Anaesthesia was induced with the agent being studied. Once the animals were anaesthetized, a tracheostomy was performed and ventilation was controlled to maintain $P_{ET}CO_2$ at 35 mmHg. An intravenous infusion was started in the marginal ear vein and an arterial line was inserted in the central artery of the left ear. The right internal carotid artery was cannulated and isolated by ligation of the other arterial branches. A vasogenic brain lesion was produced by injection of 1 $mg \cdot kg^{-1}$ of 2M NaCl via the right internal carotid artery at a pressure 15–20 mmHg above systemic systolic blood pressure, as described by Durward.[2] Blood pressure was kept within 20 per cent of the pre-injection value. The anaesthetic was then continued for a further ten minutes to allow oedema formation while BP and stump BP were recorded every minute.

The animal was then rapidly sacrificed by exsanguination and the brain carefully removed. Each brain was divided into 18 sections for assessment. All pieces were assessed by *in vitro* NMR proton relaxation times (T_1 and T_2) and wet to dry weight ratios (W:D).

Six animals received Innovar-Vet and seven halothane. As controls, three animals received halothane and a sham operation, and three received Innovar and a sham operation.

Results

The 2M NaCl injection produced statistically significant oedema in four of seven halothane and three of six Innovar anaesthetized animals. There was no statistically significant difference in the amount of oedema between the anaesthetic groups. Similarly, comparing sections containing predominantly white brain matter failed to show a difference.

TABLE Results

	T_1	T_2	*W:D ratio*
Halothane control	539 ± 9	74 ± 1	5.1 ± 0.1
Halothane	586 ± 10†	78 ± 0.9†	5.6 ± 0.1*
Fentanyl	601 ± 12†	79 ± 0.8*	5.9 ± 0.1*
Fentanyl control	551 ± 9	73 ± 0.9	5.3 ± 0.1

*$p < 0.001$ compared to control.
†$p < 0.005$ compared to control.

Discussion

T_1 has been shown to correlate more closely with free tissue water and T_2 to relate to bound water. Changes in these two parameters would reflect changes in the quality of the oedema fluid (e.g., protein binding). However, this study does not reveal any differences in either T_1 and T_2 between the investigated drugs. We conclude from this study that there is no difference between halothane and Innovar in terms of the quality or quantity of cerebral oedema as assessed by magnetic resonance spectroscopy and wet to dry weight ratios.

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A double-blind comparison of cimetidine and ranitidine with or without metoclopramide for acid aspiration prophylaxis in morbidly obese patients

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Morbidly obese patients are known to be at risk of acid aspiration during induction of anaesthesia.[1] Previous studies have demonstrated that this risk can be reduced with the preoperative administration of cimetidine and that the intravenous route is superior to the oral route.[2] More recent studies in non-obese patients suggest that its effectiveness can be further improved with the addition of metoclopramide, and that the newer H_2 antagonist ranitidine may be superior, but neither the combination nor ranitidine has been studied in obese patients. Accordingly, the present study is undertaken to evaluate prospectively in a double-blind manner the relative effectiveness of cimetidine and ranitidine with and without metoclo-

pramide for the purpose of acid aspiration prophylaxis in morbidly obese patients.

Methods

The study protocol was approved by the Institutional Ethics Committee and a written consent was obtained from each patient. All patients fasted a minimum of 8 hrs prior to induction of anaesthesia. Sixty patients scheduled to undergo gastroplasty for morbid obesity were randomly assigned into four groups; (1) cimetidine 300 mg + saline, (2) cimetidine 300 mg + metoclopramide 10 mg, (3) ranitidine 100 mg + saline, and (4) ranitidine 100 mg + metoclopramide 10 mg. All combinations were administered intravenously in a double-blind manner 60–90 minutes preoperatively. No other premedication was given. Anaesthesia was induced in a standard manner using a rapid sequence technique. Following stabilization of the patient's condition, a modified #18 nasogastric tube with extra orifices was inserted into the stomach and all gastric content aspirated for analysis of volume and acidity. To ensure complete aspiration of gastric fluid, the stomach was manually compressed by the surgeon upon entry into the peritoneal cavity. The volume and pH were measured respectively with a graduated cylinder and a Corning pH meter immediately following collection of the specimens. For comparison between groups, one-way analysis of variance was used. Because of the concern that pH may not be normally distributed in obese patients, Kruskall-Wallis rank-sum test was also used for analysis of pH.

Results

The four groups were similar in age and weight. In all patients the gastric volume was reduced compared to expected values. pH was similarly elevated. One patient in each of the cimetidine groups (Groups 1 and 2) remained at risk with volume exceeding 25 ml and pH less than 2.5, whereas no patient in the ranitidine groups were at risk. However, no statistically significant differences could be demonstrated between the groups with any parameters (Table). Combining the cimetidine groups to compare with the ranitidine groups yielded no differences, and similarly no difference could be demonstrated between the metoclopramide groups (Groups 2 and 4) versus the saline goups (Groups 1 and 3).

TABLE Results

	Group 1	*Group 2*	*Group 3*	*Group 4*
Age (±SD)	39 ± 9	44 ± 10	38 ± 11	37 ± 9
Weight (±SD)	138 ± 23	137 ± 27	134 ± 21	121 ± 18
Volume of gastric fluid (ml ± SEM)	11.4 ± 2.9	17.1 ± 4.5	14.2 ± 2.1	13.5 ± 3.2
pH of gastric fluid (SEM)	6.84 ± 0.43*	6.51 ± 0.52	6.76 ± 0.31	6.72 ± 0.48*
No. of patients with vol > 25 ml and pH < 2.5	1	1	0	0

*n = 12 because in one patient there was no gastric fluid aspirated.

Discussion

A control group was not included in the study design because the risk was deemed not justified. In comparison to expected values, it appears that cimetidine and ranitidine are equally effective in reducing the risk of acid aspiration pneumonitis and that adding metoclopramide does not afford further protection. Although not statistically significant, one patient in each of the cimetidine groups remained at risk while none of the patients in the ranitidine groups belonged to this category. The fact that ranitidine has a longer duration of action and less potential for drug interaction suggests that it may be the premedicant of choice in morbidly obese patients for the purpose of acid aspiration prophylaxis.

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The need for oxygen following anaesthesia in children: correlation with recovery scores

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It has been recently suggested that most children recovering from general anaesthesia are likely to become hypoxic, and therefore should receive supplemental oxygen until they are awake and active in the postanaesthesia recovery room (PARR).[1] The exact time, however, when a child is considered to be awake enough not to require supplemental oxygen in PARR has not been established. The purpose of this study was to: (1) correlate oxygen saturation measurements (SaO_2) in healthy children recovering from anaesthesia with the degree of recovery as indicated by the Aldrete postanaesthetic recovery score,[2] (2) document the stage of recovery at which oxygen therapy is no longer indicated, and (3) identify preoperative factors which might suggest an increased need for oxygen during the recovery period, specifically a history of an upper respiratory infection (URI).

Methods

The study was approved by the institutional research committee, and an information sheet explaining the protocol was made available to parents of the 81 children who were studied. All were ASA physical status I unpremedicated children who underwent elective surgical procedures under general inhalation anaesthesia (halothane or isoflurane). Patients who had intracranial, intrathoracic, or intra-abdominal procedures were not included. Immediately upon arrival in the PARR, the finger tip sensor of the Nelcor® pulse oximeter (model N-100) was placed for continuous monitoring of SaO_2. The Aldrete's postanaesthesia recovery score (1–10) was simultaneously computed. Patients who had $SaO_2 < 95$ per cent (estimated $PaO_2 = 75$ torr), or were clinically hypoxic, were administered oxygen via a blow-by system ($10\ L \cdot min^{-1}$). Those whose $SaO_2 \geq 95$ per cent received no supplemental oxygen. The measurements were repeated at five-minute intervals until the patient met the PARR discharge criteria (Aldrete score of 10, or 9 if due to an increase in blood pressure). Data were analyzed using the likelihood ratio test.

Results

Table I shows the mean SaO_2 value recorded upon admission to PARR compared to Aldrete's recovery scores before any patient received oxygen.

There was no statistically significant correlation between the recovery scores and SaO_2 ($p > 0.05$) nor was there a difference in the magnitude of increase in SaO_2 in patients who had high PARR scores (≥ 7) or those who had low scores (<7) when oxygen was administered (Table II).

Twelve patients still had $SaO_2 < 95$ per cent even when they were fully awake (PARR scores of 10). Four of these patients had history of a resolving URI at the time of surgery (Table III).

TABLE I SaO_2 (mean ± SEM) on admission to PARR (no O_2)

PARR Score	*n*	*SaO_2*	*SEM*	*Min*	*Max*
3	1	96.00	0	—	—
4	11	92.82	1.1	85	97
5	28	96.32	0.47	89	100
6	3	95.67	0.33	95	96
7	1	96.00	0.0	—	—
8	4	95.75	0.75	95	98
9	4	94.25	1.11	92	97
10	9	96.33	0.69	92	99

TABLE II Change in SaO_2 with O_2 administration

	Aldrete score < 7	*Aldrete score ≥ 7*
Number of patients	34	11
Mean	4.09	5.36
SEM	0.87	2.10
Maximum	18	25
Minimum	−11	0

TABLE III Patients with $SaO_2 \leq 95\%$ and PARR score of 10

	$SaO_2 \leq 95$	*$SaO_2 > 95$*
Recent URI	4	10
No URI	8	59

($0.18 > p > 0.05$)

Discussion

Our study confirms earlier findings that children recovering from general anaesthesia can become hypoxic in the PARR. We failed to show any correlation between hypoxia (as indicated by low SaO_2 values) and the degree of recovery following general anaesthesia in children. Since many patients who had low measured SaO_2 did not appear clinically hypoxic, it is recommended that, unless SaO_2 is measured, all patients should receive supplemental O_2 in the PARR. The observation that 12 of our patients had $SaO_2 < 95$ per cent when they were awake enough to leave the PARR (Aldrete score = 10) was quite disturbing. It is interesting to note that 33 per cent of those patients had a history of a resolving URI, which has been previously shown to result in perioperative atelectasis and hypoxaemia. Our sample was too small; however, to establish a clear association between preoperative URI and low SaO_2 in the PARR. A study of a larger group of children is currently underway to clarify that possible association.

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Is prophylactic dantrolene indicated for MHS patients undergoing elective surgery?

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Prophylactic dantrolene is recommended for malignant hyperthermia susceptible (MHS) patients undergoing elective surgery.[1,2] However, the incidence of MH reactions and anaesthetic complicaitons in a large population of MHS patients who receive a trigger-free anaesthetic for elective surgery without prophylactic dantrolene is not known. To determine the incidence of these complications in MHS patients, we reviewed the anaesthetic records of 956 MHS patients undergoing elective muscle biopsy.

Methods

We retrospectively reviewed the anaesthetic management and perioperative complications of 956 MHS patients undergoing elective muscle biopsy. The patients were referred for elective muscle biopsy because of a previous MH reaction, a family history of MH, or undiagnosed muscle cramps. We recorded the perioperative complications in the operating room, recovery room, and on the ward postoperatively (Table). The criteria for positive muscle biopsy included a positive response to halothane contracture (normal = 0), caffeine contracture (normal 4.1), and combined halothane and caffeine contracture (normal 1.2). Statistical significance ($p < 0.05$) was determined using the Chi-squared test with Yates correction.

Results

Of the 956 patients (mean age 31.2 yrs, range 1–95), 643 were biopsy-positive and 313 were biopsy-negative. Regional anaesthesia (spinal, epidural, and field block with tetracaine, lidocaine, and mepivacaine) was used in 6.3 per cent of the patients. Those receiving general anaesthesia (93.7 per cent) were premedicated with oral diazepam and intramuscular pantopon. General anaesthesia was induced with intravenous diazepam, droperidol, and fentanyl, and maintained with nitrous oxide and oxygen after endotracheal intubation. Muscle relaxants were not used. All patients were monitored in a routine manner for MHS. In most cases, the vastus lateralis muscle was biopsied. Six patients (ten per cent) receiving regional anaesthesia had nausea, or pain at the biopsy site, whereas 127 patients (14.2 per cent) receiving general anaesthesia had minor complications (Table). There was no significant difference in the incidence of complications between regional and general anaesthesia. Four patients who were muscle biopsy-positive (0.62 per cent) developed mild MH (14.2 per cent) receiving general anaesthesia had minor complicaitons (Table). There was no significant difference in the incidence of complications between regional and general anaesthesia. Four patients who were muscle biopsy-positive (0.62 per cent) developed mild MH reactions in the recovery room after general anaesthesia: one was treated successfully with general measures, and the other three were treated with intravenous dantrolene.

TABLE Results

	Operating room		*Recovery room*		*Ward*	
Muscle biopsy	*Pos.*	*Neg.*	*Pos.*	*Neg.*	*Pos.*	*Neg.*
Complications						
Respiratory						
difficult intubation	12	8	—	—	—	—
laryngospasm	7	3	—	—	—	—
bronchospasm	3	1	—	1	—	1
cyanosis	—	—	1	—	—	—
apnoea	—	—	1	1	—	—
Cardiovascular						
tachycardia	1	1	3	1	1	—
bradycardia	2	—	2	1	—	—
atrial fib.	—	—	1	1	1	—
PVC	5	2	7	2	1	—
hypotension	1	—	—	—	—	—
Temperature						
decrease	1	—	4	—	—	—
increase	5	1	8	2	6	1
MH reactions	—	—	4	—	—	—
Other						
nausea			4	3	3	1
vomiting			1	1	3	1
drowsiness			11	12	1	1
wound pain			5	1	—	—

Discussion

The incidence of MH reactions in a large population of biopsy-positive MHS patients who receive a trigger-free anaesthetic for minor elective surgery without prophylactic dantrolene (0.62 per cent), is extremely small. The four minor MH reactions which did occur, occurred in the recovery room and were easily reversed with intravenous dantrolene. In view of the very low incidence of MH reactions in this high-risk (biopsy-positive) group of MHS patients who received a trigger-free anaesthetic, and because intravenous dantrolene reverses MH reactions,[3] prophylactic dantrolene is not indicated for MHS patients undergoing minor elective surgery.

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Is there an optimum concentration of bupivacaine for caudal analgesia in outpatient surgery for children?

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Prior studies have demonstrated that a regional block with 0.25 per cent bupivacaine hydrochloride provided effective postoperative pain relief 80–86 per cent of the time in children who had undergone either a circumcision or an orchidopexy.[1,2] The current study examines the question of whether a more concentrated solution such as 0.30 or 0.375 per cent bupivacaine may provide more effective analgesia without delaying discharge from the hospital.

Methods

Thirty-nine unpremedicated ASA physical status 1 or 2 children, ages 4–11 years, were the subjects of this double-blind prospective study. All were having ambulatory inguinal or penile surgical procedures. Following induction with either intravenous thiamylal or with N_2O, O_2 and halothane, but prior to the onset of surgery, all children received a caudal block using bupivacaine containing epinephrine (1:200,000) in a concentration of 0.25, 0.30 or 0.375 per cent. The volume of bupivacaine injected was calculated by the formula of Takasaki[3] (0.056 ml/kg/spinal segment). A T-12 level was sought in every case. Anaesthesia was maintained with N_2O, O_2 and halothane by mask. The block was presumed to be effective if the inspired halothane concentration could be reduced to 0.5 per cent during surgery.

In the recovery room the severity of pain was equated with blood pressure elevation, crying, movement, anxiety level and verbal reports of pain using a scale of 0–2 for each of the five categories. In addition, children ages 7 to 11 years evaluated their own pain using a 0–10 linear analogue pain scale. Fentanyl (1 $\mu g \cdot kg^{-1}$ IV) was given to all children scoring six or more points on either pain scale on two consecutive five-minute observations. The time required for each patient to meet all standard discharge criteria from the hospital was noted.

Results

Thirty-seven of the 39 blocks provided satisfactory operative anaesthesia and postoperative analgesia regardless of the bupivacaine concentration used. Two caudal blocks out of 39 (five per cent) failed to meet the criteria for satisfactory intraoperative analgesia. The two blocks were repeated at the completion of surgery with 0.25 per cent bupivacaine and both provided satisfactory postoperative analgesia. None of the children required supplemental postoperative analgesia. Discharge times were 184 ± 25, 224 ± 32 and 278 ± 37 minutes for children who received 0.25, 0.30 and 0.375 per cent bupivacaine respectively. These differences were not statistically significant (analysis of variance $p > 0.1$).

Discussion

It is concluded that 0.25 per cent bupivacaine containing epinephrine 1:200,000 produces effective postoperative analgesia without delaying discharge. Increasing the bupivacaine concentration does not appear to offer any advantage. The failure rate in previous reports of 10–14 per cent is assumed to have been due to either poor technique or inadequate volume.

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Do epinephrine-containing solutions decrease the risk of using bupivacaine for caudal anaesthesia in children?

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Caudal anaesthesia may improve the management of postoperative pain after lower abdominal and limb surgery in children.[1] The long-acting amide, bupivacaine, is a popular agent for this purpose. Because of complications of epidural anaesthesia attributed to use of

*Deceased

this drug in obstetrical patients and others, bupivacaine solutions containing epinephrine have been recommended.[2] In children, it is unclear if the use of epinephrine will significantly decrease systemic absorption of bupivacaine administered for caudal block. This study was undertaken to determine peak plasma concentrations obtained with bupivacaine 0.375 per cent with and without epinephrine for caudal anaesthesia in children.

Methods

After ethical approval, consent was obtained from parents. Twelve unpremedicated ASA physical status 1 and 2 patients aged between two and five years, undergoing circumcision, received N_2O/O_2 and halothane anaesthesia. Bupivacaine 0.375 per cent with or without epinephrine (1:200,000) in a dose of 1.87 $mg \cdot kg^{-1}$ was given to two groups of six patients as a single dose including a test dose of 2 ml over two seconds. The average volume used was 23.5 (±11 ml). Patients were monitored until awake. Blood for bupivacaine assay was drawn from a 22-gauge cannula previously inserted into an antecubital vein. Samples were taken at intervals from 0–60 minutes after injection. Serum bupivacaine concentration was measured using a chromatographic method based on modification of the technique of Huy-Riem Ha *et al.*[3] Comparison by Student's t test between groups was made for serum and peak concentrations and extent of block.

Results

All patients had adequate anaesthesia, blocks reaching a mean sensory level of L3 (±2 spaces) in both groups. Duration of surgical anaesthesia was similar for the two groups, 408 (±45) min with epinephrine and 356 (±128) min without epinephrine. The mean peak serum bupivacaine concentrations with and without epinephrine were 0.48 (±0.23) $\mu g \cdot kg^{-1}$ at 30 (±16) min and 0.48 (±0.09) $\mu g \cdot kg^{-1}$ at 20 (±10) min, respectively. There was no significant difference in the peak plasma concentrations of the two groups. No systemic toxicity was observed in any patient. Heart rate and blood pressure recordings were similar in the two groups and there were no significant changes from initial recordings in any patient during the study.

Discussion

Toxicity of any local agent is related to peak plasma concentration of the drug and the rate of rise of plasma concentration. Thus, Moore and Surlock[2] recommended: the use of local anaesthetic solutions with epinephrine to delay absorption of the drug (to decrease the peak plasma concentration); to help identify accidental intravenous injection (and therefore eliminate the possibility of a rapid increase in plasma drug concentration); and to stimulate the myocardium, should systemic absorption occur. For bupivacaine, the threshold for toxic symptoms in adults has been reported as 2.3 $\mu g \cdot ml^{-1}$.[4] Plasma concentrations in our study were well below the adult toxic range, and peak concentrations were no different when using an epinephine-containing solution, although the rate of rise was slower. Also, there was no difference between groups in the level or duration of analgesia achieved. Thus in our patients, there was no advantage shown by the addition of epinephrine to bupivacaine, other than providing a slightly slower rate of rise of plasma concentration in a well-placed caudal block.

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Droperidol pretreatment in children undergoing strabismus repair: the minimal effective dose

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Intravenous droperidol 75 $\mu g \cdot kg^{-1}$ significantly reduces the incidence of vomiting after strabismus repair in children,[1] particularly when administered before manipulation of the eye.[2] It has been suggested that droperidol 50 $\mu g \cdot kg^{-1}$ does not reduce the incidence of vomiting after strabismus repair,[3] even when administered before manipulation of the eye.[4] In order to determine whether lower doses of droperidol given before manipulation of the eye reduce the incidence of vomiting to the same extent as 75 $\mu g \cdot kg^{-1}$, we determined the incidence of vomiting after strabismus repair in 60 children who were pretreated with either 50 $\mu g \cdot kg^{-1}$ or 25 $\mu g \cdot kg^{-1}$ intravenous droperidol.

Methods

With approval from the Human Review Committee, informed written consent was obtained from the parents of 60 children undergoing elective strabismus repair. Each child was randomly assigned to receive one of two doses of intravenous droperidol: 50 or 25 $\mu g \cdot kg^{-1}$. General anaesthesia was induced with intravenous thiopentone (5 $mg \cdot kg^{-1}$), atropine (0.03 $mg \cdot kg^{-1}$), and suc-

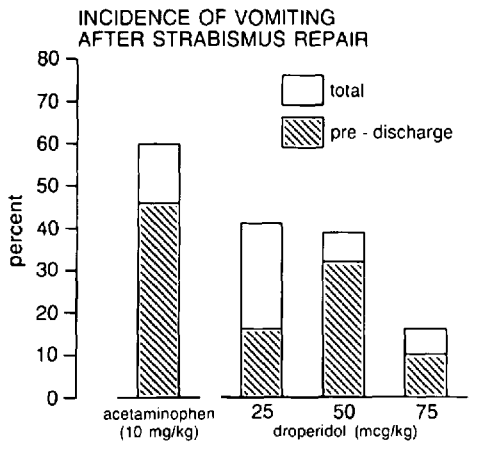

FIGURE Acetaminophen (control) and droperidol 75 $\mu g \cdot kg^{-1}$ are included for comparison.[2]

cinylcholine (1.5 $mg \cdot kg^{-1}$). Intravenous droperidol was given immediately after succinylcholine. After ventilation with 100 per cent oxygen by mask, the trachea was intubated and the lungs were ventilated with halothane (0.5–1.25 per cent), nitrous oxide (69 per cent), and oxygen (30 per cent). Care was taken to avoid gastric inflation. Intravenous fluids were administered to replace fluid deficits and provide maintenance requirements. The children were extubated when their gag reflex returned. Gastric contents were not aspirated. The children were discharged from hospital when they had stable vital signs, were awake and alert, and could retain oral fluids.

The incidence of vomiting before discharge from hospital was recorded by the nurses in the post-anaesthetic room (PAR) and on the ward, whereas the incidence of vomiting after discharge was obtained from the parents. The surgical time and time to discharge from the hospital were also compared. Statistical significance ($p < 0.05$) was determined using the Fisher exact test, ANOVA, and the Student-Newman-Keuls test.

Results

The mean ages and weights of the two groups of children were similar. The incidence of vomiting pre-discharge with droperidol 25 $\mu g \cdot kg^{-1}$ was significantly less than that with acetaminophen in a previous study[2] (Figure). The total incidence of vomiting with 50 and 25 $\mu g \cdot kg^{-1}$ droperidol did not differ significantly from acetaminophen whereas that with 75 $\mu g \cdot kg^{-1}$ was significantly less[2] (Figure). The duration of surgery and time to discharge from hospital did not differ significantly between 50 and 25 $\mu g \cdot kg^{-1}$ droperidol.

Discussion

The total incidence of vomiting in children after strabismus repair is not significantly reduced after administration of either 50 or 25 $\mu g \cdot kg^{-1}$ intravenous droperidol compared with acetaminophen. Although the pre-discharge incidence of vomiting with intravenous droperidol 25 $\mu g \cdot kg^{-1}$ is less than with acetaminophen, this dose does not prevent vomiting after discharge from hospital. We conclude that intravenous droperidol 75 $\mu g \cdot kg^{-1}$ remains the minimal effective dose of prophylactic droperidol which significantly reduces the incidence of vomiting after strabismus repair in children.

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Comparison of direct blood pressure measurements at the radial and dorsalis pedis arteries during sodium nitroprusside and isoflurane hypotension

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Various authors have commented on the differing pressure in the radial artery and the dorsalis pedis artery.[1,2] We are, however, unaware of any study that has warned of disparate measurements during controlled hypotension or compared the differences as related to various hypotensive agents. The present study was therefore designed to compare arterial blood pressure measured simultaneously from the radial (RA) and dorsalis pedis (DPA) arteries during controlled hypotension induced with either sodium nitroprusside (SNP) or high-dose isoflurane in patients undergoing surgery for clipping of intracranial aneurysms.

Methods

Twenty ASA physical status Class III patients were randomly allocated to receive either neurolept (group I,

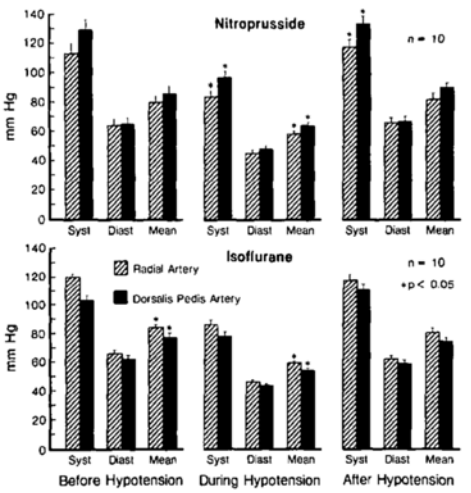

FIGURE Changes in systolic, diastolic and mean arterial pressures at radial and dorsalis pedis arteries, before, during and after nitroprusside and isoflurane-induced hypotension. Values are mean ± SEM.

n = 10) or isoflurane (group II, n = 10) anaesthesia. In group I, hypotension was induced by SNP 50 mg in 500 ml five per cent glucose, given IV as a continuous infusion. The infusion rate was adjusted to achieve a radial mean arterial pressure of 50–60 mmHg during the dissection and clipping of the aneurysmal sac. In group II, the inspired isoflurane concentration was gradually increased until the same level of hypotension had been achieved. Variables including systol (SYST) diastolic (DIAST), and mean arterial pressures (MAP) were measured and recorded from the two arteries consecutively before, during, and 20 minutes after hypotension. A minimum of five minutes of stable arterial pressure was allowed before the measurements were taken. Data were analyzed using Student's t test. $P < 0.05$ was considered significant. Results are expressed as the mean ± SEM.

Results

The results are shown in the Figure. In group I, the SYST, DIAST, and MAP were higher at the DPA than at the RA. This difference persisted during normotension, hypotension and post-hypotension. It was statistically significant during hypotension (SYST and MAP) and post-hypotension (SYST). In group II, the SYST, DIAST, and MAP were higher at the RA than at the DPA. This difference also lasted throughout the study and was statistically significant at normotension (MAP) and during hypotension (MAP).

Conclusion

Our data demonstrate that the values obtained from the DPA may be markedly different from those recorded at the RA. Furthermore DPA values are affected by the anaesthetic technique and by the hypotensive agents used. We suggest that these differences could have important clinical significance in critical situations making the DPA approach an unreliable site for monitoring arterial blood pressure.

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Réponse hémodynamique a l'intubation chez le patient éveillé

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L'hypertension et la tachycardie associées à la laryngoscopie et à l'intubation trachéale ont été attribuées à une activité sympathique accrue ayant pour origine les afférences des voies aériennes supérieures.[1] L'expérience d'Ovassapian[2] des variations de la tension artérielle et du pouls lors de 200 intubations naso-trachéales avec fibres optiques sous anesthésie locale avec cocaïne et lidocaine a démontré une hausse légère de ces variables. Il nous a semblé qu'une technique évitant la cocaïne et la voie naso-trachéale pourrait minimiser ces changements hémodynamiques. Cette étude évalue, à l'aide d'un monitoring invasif, la réponse cardio-vasculaire à l'intubation oro-trachéale sous anesthésie locale, sédation IV et laryngoscopie à fibres optiques.

Methodes

Après accord du Comité d'éthique et consentement éclairé, dix patients de classe ASA II et III, âgés de 52 à 73 ans, ont été étudiés. Tous subirent une chirurgie de l'aorte abdominale. Aucun ne présentait d'instabilité cardio-vasculaire ou pulmonaire. La médication usuelle n'introduisait pas de biais dans l'étude. Après une prémédication intramusculaire (morphine 0.15 $mg \cdot kg^{-1}$ + scopolamine 0.4 mg) un supplément intraveineux de diazépam (2.5–5 mg) et de fentanyl (50–250 μg) est administré au besoin avant la mise en place de la canule artérielle et du cathéter de Swan Ganz. L'anesthésie oro-trachéale est réalisée à l'aide de lidocaine en aérosol (maximum de 100 mg) et via l'injection transtrachéale (TT) de 160 mg de lidocaine. Le tube endo-trachéal est

TABLEAU Resultats

Moyenne ± déviation standard	T_1	T_2	T_3
Pouls·min^{-1}	72 ± 16	79 ± 16*	77 ± 16
Tension arterielle (moyenne) mmHg	96 ± 13	102 ± 10*	101 ± 15
Pression art. pulmonaire (moyenne) mmHg	21 ± 7	25 ± 6*	23 ± 6
Wedge mmHg	13 ± 5	16 ± 4*	15 ± 7*
Debit cardiaque L·min^{-1}	5.26 ± 1.6	5.57 ± 1.5	5.61 ± 2.3

*Différent de T1, $p < 0.05$ (t – test jumelé)

ensuite positionné à l'aide d'un laryngoscope à fibres optiques. Les mesures sont receuillies au repos après la mise en place des moniteurs (T1), puis immédiatement après l'anesthésie locale (T2) et l'intubation oro-trachéale (T3).

Resultats

La majorité des changements significatifs sont donc survenus suite à l'injection trans-trachéale (Table).

La mesure des PO_2 et PCO_2 n'a pas varié de façon significative aux temps 1, 2 et 3.

Conclusion

L'anesthésie topique de l'arbre bronchique par injection TT de lidocaine est une arme à double tranchant: son exécution entraîne des changements hémodynamiques significatifs mais son action protège des effets nocifs de l'intubation. Il faut noter que les variations observées, quoique significatives, demeurent minimes et se comparent favorablement à plusieurs autres méthodes de prévention de l'hypertension post-intubation.[3–5] Ces changements hémodynamiques nous apparaissent tolérables chez des patients dont la pathologie cardiovasculaire est stable et bien contrôlée.

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General or spinal anaesthesia: which is better for the elderly?

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The increase in the elderly population and advance in surgical and anaesthetic techniques have led to more operations on elderly patients. Psychological problems, in particular preoperative anxiety and postoperative confusion contribute to morbidity and mortality. The contribution of anaesthesia is difficult to assess, and review of the recovery of mental function postoperatively is inconclusive.[1,2] Tests of mental function were not performed on the day of operation, or first postoperative day nor was comparison made of recovery after general versus spinal anaesthesia in elderly patients. The purpose of this study was to compare mental recovery in elderly patients from general or spinal anaesthesia.

Methods

Following insitutional approval and after obtaining informed consent, 44 patients, aged 60 and over, scheduled for transurethral resection of the prostate or pelvic floor repair were randomized to receive either general anaesthesia or spinal anaesthesia. No premedication was given. General anaesthesia was induced with thiopentone 2–5 mg·kg^{-1} and fentanyl 1–2 μg·kg^{-1}. "Pre-curarization" with 3 mg d-tubocurarine was followed by muscle relaxation with 1.5 mg·kg^{-1} succinylcholine. The trachea was intubated. Anaesthesia was maintained with nitrous oxide, oxygen, curare, fentanyl, and isoflurane. Spinal anaesthesia was done at the L3–4 or L4–5 interspace with a 22- or 26-gauge spinal needle. Tetracaine, 10–14 mg diluted in ten per cent dextrose solution, was given. Psychological assessment included preoperative cognitive screening by the Mini Mental State test, measurement of anxiety by visual analogue scale, and standardized geriatric mental status examinaton. The Mini Mental status examination was administered six hours after surgery, and on the first, third and fifth postoperative days. Recollection of previous levels of anxiety, and anxiety on the first postoperative day were measured. Preoperative clinical data included demographic, medical and previous psychiatric information, and medication used, in addition to customary haemoglobin, electrolytes, blood sugar, urea, arterial blood gas and electrocardiogram. Postoperatively, the above laboratory investigations were repeated on the first and third postoperative days. Medications were recorded during the postoperative stay.

Data were analyzed by Students' paired and unpaired t test, Chi Square, or Fischer's Exact Test.

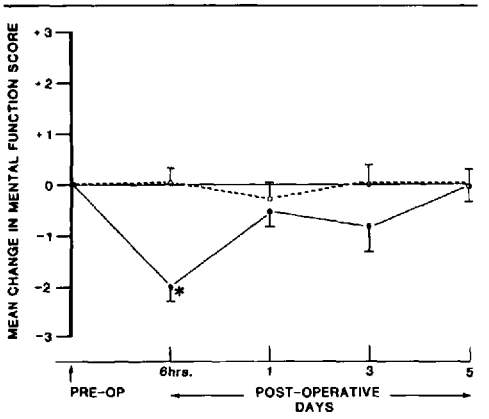

FIGURE Mean change in mental function score in patients having general anaesthesia (—) versus spinal anaesthesia (···). *$p < 0.001$.

Results

Three of the 44 patients were confused (6–8 per cent). All three confused patients had received general anaesthesia (12.5 per cent). None of the patients in the spinal anaesthesia groups showed signs of confusion. The three confused patients had predisposing personality traits; two had higher levels of anxiety, and one had a paranoid personality. Two of the three confused patients were receiving antidepressants, in contrast to the group without postoperative confusion of whom none was receiving antidepressants. The Mini Mental test showed that patients in the spinal anaesthesia groups scored better at all times compared with the general anaesthetic group. Mean change in the mental function score was statistically significant in the general anaesthetic group as compared to the spinal group at six hours postoperatively ($p < 0.001$) and at the third day ($p < 0.1$) (Figure). The anxiety score showed that patients undergoing transurethral resection of prostate and pelvic floor repair had a very low level of preoperative anxiety. The difference in degree of anxiety between preoperative and postoperative assessments was not statistically significant. There was no significant difference between preoperative and postoperative blood results. The requirement for postoperative analgesics and hypnotics was not significantly different between general anaesthetic and spinal groups. The requirement of antiemetics was significantly higher in the general anaesthetic group ($p < 0.005$).

Discussion

In this study, a higher percentage of patients who received general anaesthetic were confused as compared to those receiving spinal anaesthesia. Predisposing personality traits and preoperative use of antidepressants seemed to be the contributing factors in the confused patients. Mental recovery in the postoperative period was better with spinal anaesthesia as compared to general anaesthesia. Significant mental impairment still occurred at six hours after general anaesthesia.

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Measuring the volume of gastric contents under general anaesthesia: evaluation of two clinical methods

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Accurate measurement of the volume of gastric contents is of prime importance in anaesthesia to identify patient populations at increased risk of regurgitation and subsequent aspiration. Two methods are readily available in clinical practice to measure this volume: (1) gastric intubation and complete aspiration of fluid contained in the stomach and (2) indirect determination by a dye dilution method. Both methods have several drawbacks. Aspiration may be incomplete, especially with conventional Levin's tubes.[1] Dye dilution has been thoroughly investigated in the gastroenterology laboratory.[2–3] The method has been shown to be accurate when patients were kept sitting, when the position of stomach tube was checked radiologically, and when the previously determined optimal concentrations of the indicator dye were used. However, the method has never been validated in the operating room environment. Furthermore, division of the stomach into antral and fundal sacs in supine patients[4] may interfere with both aspiration and dilution. Thus, we believe that a re-evaluation of these experimental methods is necessary. This study attempts to prospectively validate both gastric fluid measurement techniques in the supine anaesthetized patient.

Methods

Ethics Committee approval and informed consent were obtained. Twenty-four ASA physical status I–III adult patients undergoing elective laparotomy, excluding surgery of the oesophagus and stomach, were studied.

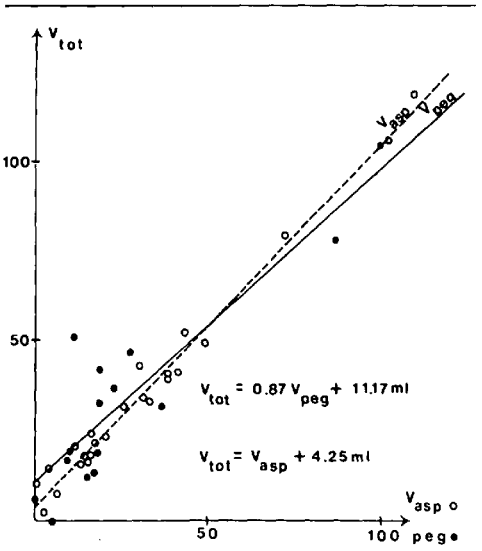

FIGURE Correlation of V_{asp} and V_{peg} with V_{tot}.

Anaesthetics were standardized. Mask ventilation was avoided to prevent gastric insufflation. After skin incision, an 18 Fr Salem Sump® tube (Argyle, St Louis, Mo.) was passed orally into the stomach. Gastric contents were aspirated as completely as possible (aspirated volume, V_{asp}) with a 50 ml syringe. The surgeon was then asked to inspect the stomach and ascertain complete gastric emptying. This direct inspection could lead to aspiration of additional gastric fluid (additional volume, V_{add}). The total volume ($V_{tot} = V_{asp} + V_{add}$) was then returned to the stomach and diluted with 100 ml of a 0.4 per cent polyethylene glycol (PEG) solution. PEG is a non-toxic, non-absorbable, water soluble polymer. Mixing was achieved by withdrawing and re-inserting five syringefuls of gastric contents, which were then aspirated as completely as possible ($V_{re\text{-}asp}$). PEG concentrations were determined by colorimetry in two 3 ml samples (laboratory blinded to V_{tot}). Knowledge of PEG concentration enabled calculation[2] of the volume diluting the indicator (V_{PEG}). Stastistical analysis was performed by the Department of Mathematics and Statistics.

Results

All results mean ± standard deviation

$V_{asp} = 31.10 \pm 28.77$ ml ($n = 24$)
$V_{add} = 4.05 \pm 3.93$ ml (significantly $\neq 0$, $p < 0.05$)
$V_{tot} = 35.48 \pm 29.15$ ml
$V_{PEG} = 26.2 \pm 28.78$ ml ($n = 15$).

The first nine determinations of V_{PEG} were totally erratic, owing to a variety of technical difficulties, and were excluded.

V_{asp} correlated with V_{tot} ($r = 1.00$, $p < 0.001$)
V_{PEG} correlated with V_{tot} ($r = 0.89$, $p < 0.01$)
$V_{re\text{-}asp}$ correlated with V_{PEG} ($r = 0.89$, $p < 0.01$).

Conclusions

(1) Aspiration of gastric fluid with a large, vented, multi-orificed tube yields a very accurate estimate of the volume present in the stomach. The technique is simple, fast and inexpensive. We submit that previous concerns that the aspiration method will underestimate the volume of gastric fluid[1,5] may have been due to technical limitations. (2) The PEG dilution method yields slightly less precise, but still very adequate results. It is however more complicated and requires strict laboratory discipline to achieve accuracy.

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Monitoring for marrow embolism during cemented arthroplasty procedures

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Intraoperative hypoxaemia and hypotension has been reported during cemented arthroplasty procedures. The GUEPAR total knee replacement requires reaming of both tibial and femoral intramedullary canals and insertion of long-stemmed components. In theory, simultaneous insertion of two cemented prostheses would effectively double the potential for marrow embolism. We monitored a patient and demonstrated a reduced F_ETCO_2 after prosthesis insertion which coincided with hypoxaemia and hypotension. In this study we examine the sensitivity of F_ETCO_2 monitoring in detecting intraoperative marrow embolism during dual stemmed arthroplasty using a mongrel dog model.

Methods

Eight mongrel dogs were anaesthetized with pentobarbitone, paralyzed with pancuronium, and ventilated to a

normal $PaCO_2$. The pulmonary arterial (PAP), aortic (BP) and left atrial (LA) pressures were monitored continuously. Arterial and mixed venous blood samples were obtained and analyzed for PO_2 and PCO_2. Cardiac output ($\dot{Q}$) was determined using thermodilution technique.

After control data were obtained, both femurs were exposed and intramedullary cavities reamed to a depth of 10 cm with successively larger reamers. Low-viscosity bone cement was injected under manual pressure and bilateral contoured prostheses were inserted. The methylmethacrylate (MMC) components were mixed according to standard directions and injected to simulate the clinical situation. During mixing, the capnograph sampled vapour from the mixing bowl; and during insertion, $FETCO_2$ was continuously monitored (Beckman capnograph) as well as BP, PAP, and LAP. At 5, 15, 30 and 60 minutes after prostheses insertion measurements were repeated.

Post-mortem, lungs were fixed in inflation with ten per cent buffered formalin at a pressure of 25 cm H_2O and stained. Morphometric measurements were performed, and the number of fat and marrow emboli were counted.

Results

During mixing of MMC the capnograph did not detect any CO_2. The Table details some early cardiorespiratory changes noted immediately after cemented implant insertion. No change in LAP was noted and a slight increase in $FETCO_2$ was documented immediatedly. Massive marrow embolism was found on histological examination.

Discussion

Marrow embolism can result from pressurizing the reamed contents of the intramedullary cavity during cemented arthroplasty procedures. These data suggest that $FETCO_2$ monitoring may not detect haemodynamically significant marrow emboli. This contrasts with the clinical sensitivity of $FETCO_2$ in detecting air embolism. The insensitivity of $FETCO_2$ in this study was not an artifact produced by the vapour as the capnograph did not detect any of the products of mixing.

In four dogs $FETCO_2$ increased in spite of reduced $\dot{Q}$ and elevated PAP (Table). This suggests increased CO_2 production. MMC may be metabolized to CO_2 through the citric acid cycle or the heat generated polymerization could liberate CO_2 stored in bone and adjacent tissue.

If the syndrome results in catastrophic cardiovascular collapse, $FETCO_2$ will decrease but less profound reductions in $\dot{Q}$ may not be detected. If clinical studies verify the relevance of this model, anaesthetists should not rely on $FETCO_2$ to detect marrow emboli. Other continuous monitors (pulse oximeter, PA catheters) may be more sensitive during high risk procedures.

TABLE Results

	Control	*5 Minutes*	*15 Minutes*
BP (mmHg)	136.3 ± 5.5	124.4 ± 8.9*	126.1 ± 5.2
PAP (mmHg)	15.2 ± 1.2	25.1 ± 1.2*	22.5 ± 0.9*
$\dot{Q}$ ($L \cdot min^{-1}$)	4.43 ± 0.43	3.16 ± 0.36*	2.96 ± 0.34*
PaO_2 (mmHg)	94.1 ± 3.7	82.1 ± 3.6*	76.7 ± 3.4*
$FETCO_2$ (%)	4.5 ± 0.24	4.74 ± 0.2*	4.62 ± 0.27

Mean ± 1 SEM of values noted at 5 and 15 minutes after bilateral arthroplasties (n = 8).

*Denotes a significant change from control.