Sedation and paralysis

193

USE OF PROPOFOL FOR SEDATION IN YOUNG CHILDREN.

Use of propofol for sedation for adults in the ICU is accepted as a good standard.
Propofol is registered for use in children of 3 years and older.
We used propofol in children who were intubated for epiglottitis or laryngotracheabronchitis and were spontaneous breathing and for children who were on mechanical ventilation. Our schedule is as follows:
Propofol bolus injection of 2-3 mg/kg BW., continued by an infusion of propofol 9 mg/kg BW, per hour.
We sedated: 3 newborn children,
8 children under 1 year of age,
15 children between 1 and 3 years of age
11 children over 3 years of age.
Results: We had no problems with the sedation, all the children showed a mild respiratory depression, end tidal CO_2 between 45 and 50 mm Hg.
After discontinuation the children were waking up within 15 minutes and full awake after 30 minutes to 2 hours. The smaller the child the longer was the time for full awakening.
Three children got problems with their temperature regulation, they needed extra artificial warming, because their body temperature fall under 36°C. The cause of this phenomena is not clear. There are to probable reasons for the drop in body temperature. The first is a direct deprivation of the temperature centre, the second is a general depression of the metabolic state.
Conclusion: Propofol is a good drug for sedation in young children, but need a good monitoring of respiration and body temperature.

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194

THE SPONTANEOUS RECOVERY OF NEUROMUSCULAR BLOKADE FOLLOWING AN INFUSION OF ATRACURIUM DURING THE EARLY POSTOPERATIVE PERIOD OF LIVER TRANSPLANTATION (LT) IN ICU

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The elimination rate of atracurium does not depends of liver function. It was shown in the studies performed intraoperatively during LT. The aim of this study is to confirm this findings during the early postoperative period of LX in the intensive care unit.
For this aim; in 7 patients, a constant infusion rate of atracurium with a 0.5 mg/kg/h was used as a routine practice during LT. Neuromuscular Transmission (NMT) monitoring was performed with Datex Relaxagraph through out of operation. The infusion of atracurium was discontinued at the end of the surgery and the patients were transferred to ICU. The assessment of the recovery index by NMT monitoring was continued in ICU. All NMT results were evaluated for each phases of transplantation and postoperative period.
During the operation T1/TC values were between 0-38%. The mean T1/TC level at the end of the operation was 4.8∓4% and the mean spontaneous recovery index was 26.7∓7 minutes.
In conclusion; Although during neohepatic period the level of neuromuscular blokade level profound, the spontaneous recovery index didn't prolonged than normal. This postoperative findings may be useful when an early extubation is planed during the postoperative period in the ICU.

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195

SAFETY AND EFFECTIVENESS OF VECURONIUM IN THE INTENSIVE CARE UNIT: A COMPARISON OF CONTINUOUS INFUSION AND INTERMITTENT BOLUSES

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Neuromuscular blocking (NMB) agents are often used in the ICU to prevent severe agitation in patients on mechanical ventilation. Several articles have questioned the safety of long term use of NMB agents in critically ill patients.

The neuromuscular blocking agent vecuronium bromide is ideally suited for the intensive care unit because of its short onset of action, relatively short half-life, and hemodynamic neutrality. The purpose of this study was to determine the optimum dose and most effective means of safely administering vecuronium in critically ill patients.

Methods: Eleven patients, requiring mechanical ventilation and ranging from 25 to 75 years, were randomized to receive vecuronium as a constant infusion or as intermittent intravenous boluses. The twitch response of the adductor pollicis muscle to train-of-four (TOF) stimulation was used to determine the appropriate dose. All patients received an initial bolus of 100 mcg/kg. After return of one twitch, patients randomized to the infusion arm received an infusion of 1 mcg/kg/min, and patients randomized to the bolus arm received a second bolus of 100 mcg/kg. Maintenance infusion and bolus doses were adjusted through hourly TOF monitoring, with the goal of maintaining one or two twitches.

Results: Five patients were randomized to the bolus group, and six patients were randomized to the infusion group. The average dose for bolus patients was 1.86 mcg/kg/min (range 1.24-2.99) and 0.950 mcg/kg/min (range 0.41-0.97) for infusion patients. Average recovery time (time to restoration of 4 twitches) for bolus patients was 103 minutes (range = 46-120) and 44 minutes (range = 15-85) for infusion patients. Neither of these differences was statistically significant. No correlation was found between total dose and recovery time or average dose and recovery time for either bolus patients ($r2$ = -0.876816 and 0.014637 respectively), or for infusion patients ($r2$ = 0.376886 and 0.184698 respectively). Vecuronium did not affect heart rate, blood pressure, or cardiac index.

Conclusions: Vecuronium can be used safely as an intermittent bolus or constant infusion when TOF monitoring is employed. An initial bolus of 100 mcg/kg followed by an infusion of 1 mcg/kg/min or hourly boluses of 100 mcg/kg is an effective and safe starting regimen. Although recovery times may vary widely, they do not appear to be dose related.

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196

INTRACRANIAL PRESSURE IN HEAD INJURIED PATIENTS UNDER CONTINUOUS SEDATION WITH PROPOFOL

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Introduction:
Sedation is a major problem in neurotrauma patient because of the conflict between the necessities to ensure adequate artificial ventilation and neurological assessment simultaneously. This study was aimed to detect the influence of propofol on intracranial pressure (ICP) and cerebral perfusion pressure (CPP).
Patients and Methods:
22 patients admitted to ICU after a severe head injury, subarachnoidal hemorrhage or intracerebral hemorrhage had a continuous and simultaneous monitoring of ICP and cerebral perfusion pressure (CPP). Cholesterine, triglyceride, lactate, ASAT, ALAT, lipase and amylase were measured routinely. They were divided into two groups; (A) initially the patients were sedated with propofol (300-600-(1000)mg/h) + fentanyl (0.05-0.3mg/h) and (B) with midazolam (5-30mg/h) + fentanyl (0.05-0.3mg/h). Every 24 hours the sedation design changed from propofol+fentanyl to midazolam+fentanyl and vice versa. The results were analysed statistically by U-test (Wilcoxon-Whitney-Mann).
Results:
There was no increase or decrease of the ICP and CPP during the application of propofol and also not after the change from benzodiazepine+fentanyl to propofol+fentanyl ($p<0.01$). Within about 2 hours after ending sedation with propofol the patient could be examined neurologically. However propofol seems to prolong the intervall of the vulnerability of the brain in severe head injured patients. There was a reversible increase in triglyceride.
Conclusion:
Propofol seems to be a useful agent for continuous sedation in neurotraumatized patients. But it can not barostabilize ICP peaks, so that the application of barbiturates might be prefered. Patients sedated with Propofol can be examined in a shorter time than these patients sedated with benzodiazepine, so that a faster and careful neurological examination is possible.

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197

PHARMACOKINETICS OF MIDAZOLAM IN INFUSION FOR LONG-TERM SEDATION OF VENTILATED PATIENTS IN ICU.

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Sedation is necessary to improve patient comfort, atenuate the strees — response and facilitate mechanical ventilation. Midazolam a water soluble benzodiacepine with a faster onset of action and a shorter elimination - half-life than other drugs, has become popular and is now increasing its usage in the ICU setting. The aim of our paper is the quantitation of — plasmatic concentration of Midazolam needed to obtain adequate sedation. Six patients who were due for ventilation for at least 24h., age 66 ± 9, weight 73 ± 13, Apache II index 23 ± 5, received one initial dose of Midazolam 0.3mg/kg followed 15 min after by continous infusion. During the — first 24h to facilitate mechanical ventilation, a initial bolus dose of - the neuromuscular blocking drug Vecuronium 0.1mg/kg were administered followed by continous infusion (abolition of the 3º or 4º response to ulnar nerve train of four supramaximal stimulation) during at least 24h. Determinations of Midazolam were carried out by extraction of 5ml of bood, centrifuged, plasma separated and stored deep-frozen until analysis. Blood samples were taken at the following intervals: pre dose -2-5-15-30 min - 1-2-4-8-12-24-36-48-60h. A sensitive and selective HPLC assay using UV detection at 254 nm for quantitation was used. (Hewlett-Packard 1050 Autosampler, U-Bondapack columns C18, 10 um.). Pharmacokinetics parameters were calculated from each patient according to standard formulae. The data were fitted to a bicompartmental model using an own program based on iterative methods.

Midazolam Infusion range was 30-164h (mean 63h). During the initial bolus phase: V_d cent.compart.=233ml/Kg. $T_{1/2\alpha}$ = 6.5 min and Mean Residence Time (T_{res} med) = 90min. During the infusion phase: Clearance = 94ml/kg/h V_d steady state = 109ml.kg. The mean plasma concentration for therapeutic window was 430 ± 126 ng/ml. At the end of infusion, recovery was obtained without antagonize in 53 ± 26 min.

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198

PROPOFOL versus MIDAZOLAM IN SEDATION OF CRITICALLY ILL PATIENTS. COST-BENEFIT ANALYSIS

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Propofol (2,6-di-isopropylphenol) is an intravenous anaesthetic agent which has been favourably compared with midazolam in continuous sedation of patients undergoing mechanical ventilation. Its use reduces the time needed for recovery of spontaneous respiration. One of the disadvantages which can limit its general use in critical medicine is its high cost. So far, no clinical study has been able to demonstrate whether a possible reduction in length ICU stay in patients sedated with propofol would be of benefit in reducing the economical cost of such stays.

The purpose of this study is to evaluate and compare the safety, clinical effects and economical cost of propofol and midazolam in the sedation of ICU patients undergoing mechanical ventilation.

One hundred-fifty critically ill patients were studied and randomly allocated to receive short-term (less than 24 hours), medium-term (24 hours-7 days) and prolonged (more than 7 days) continuous sedation with propofol (n= 78) or midazolam (n= 72). Both groups were comparable with respect to age, sex, weight, diagnosis at admission, severity of illness (valued following the Simplified Acute Physiologic Score) and basal conscience levels (determined by the Glasgow Coma Score modified by Cook). Mean duration of sedation with propofol (11.8 hours, 117.1 hours and 313.5 hours for the subgroups of short, medium and prolonged-term sedation, respectively) was similar to that of subgroups treated with midazolam (11.7 hours, 113.1 hours and 342.3 hours, respectively). Mean doses required were 2.36 mg/kg/hr of propofol and 0.17 mg/kg/hr of midazolam. Patients in the propofol group showed a percentage of sedation hours at the desired level of 93%, compared with 82% ($p<0.05$) in the midazolam group. No differences between groups were observed with respect to hemodynamics, O2 transport and analytical parameters. Both agents were considered safe with respect to the induction of adverse reactions during their use in prolonged sedation.

Recovery after interrupting sedation was significantly faster in patients treated with propofol (1.0±0.2, 2.8±1.0, 5.2±2.1 hours for extubation, and 2.1±0.5, 5.5±1.9, 9.9±3.6 hours for total recuperation, for short-term, medium-term and prolonged-term sedation subgroups, respectively) than in those sedated with midazolam (3.6±0.8, 20.6±5.6, 46.6±12.2 hours for extubation, and 6.3±1.5, 26.2±6.2, 68.4±13.8 hours for total recovery, for short-term, medium-term and prolonged-term sedation subgroups, respectively). In patients sedated with propofol, total consciousness recovery was predictable according to sedation time (r= 0.97, 0.99, 0.92 for short, medium and prolonged-term sedation subgroups, respectively), while this correlation was not observed in the midazolam group. Compared with midazolam, in subgroup of sedation of less than 24 hours, propofol provided a cost-savings of approximately 1,900 pts per patient, due to shorter ICU stays. In the subgroup of more than 24 hours sedation, and compared with midazolam, propofol had the same quantifiable cost, but constituted a greater indirect benefit due to money saved on the cost of antagonisation with flumazenil.

In our hospital environment, propofol is a sedative agent with the same safety, higher clinical effectiveness and better cost-benefit ratio than midazolam in continuous sedation of critically ill patients.

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Cardiovascular assessment II

199

THORACIC ELECTRICAL BIOIMPEDANCE (TEB) vs THERMODILUTION (TD) FOR CARDIAC OUTPUT (CO) MEASUREMENT DURING MECHANICAL VENTILATION

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TEB is a non-invasive technique for haemodynamic monitoring. Some reports concern situations influencing the measurements performed with TEB, particularly in critically ill patients (pts) (sepsis, haematocrit variations and mechanical ventilation). In this study we compared CO measurements obtained with TEB and with TD in pts under mechanical ventilation. CO was measured before induction of general anaesthesia and about 10 minutes after orotracheal intubation and connnection to ventilator. 17 pts (age 46-72, BSA 1.6-1.97 m2, haematocrit 30%-40%) were included in our study. All the pts underwent the same kind of ventilation: 12 breaths/min with tidal volume 8-10 ml/kg. CO measurements with TD were performed injecting 10 ml of saline solution at room temperature. The recorded value is the average of three measurements. TEB data were recorded using a BoMed NCCOM3 device, considering the average of one minute recording. In non-ventilated pts the mean TD-CO was 5.96±1.29 (SD) l/min and the mean TEB-CO 5.77±1.52. The equation is Y=1.059 X - 0.537 with r=0.896 ($p<0.0001$). In the same pts under mechanical ventilation the mean TD-CO value was 5.67±1.44 l/min, while the mean TEB-CO was 5.89±1.88. The equation is Y=0.896 X + 0.813, with r=0.688 ($p<0.002$). For a more accurate evaluation of the data we plotted the difference between the two measurements (TD-CO - TEB-CO) by mean CO (TD-CO + TEB-CO /2) as suggested by Bland and Altman (Lancet, 1986). We obtained the following information: the mean difference between the techniques in non-ventilated pts was 0.18±0.16, while in ventilated pts was -0.22±0.33. The CO values measured using these two methods are similar; the differences are quite slight and there are no major variation for different flow levels. In ventilated pts the difference, though increasing, remains acceptable for clinical purposes. Only in one case the results of the two techniques disagreed. Therefore it can be stated that, due to its easy use, non-invasivity, continuous data reading, and relatively low cost, TEB can be considered a useful technique for haemodynamic monitoring of critical pts.

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200

DETERMINATION OF CARDIAC OUTPUT, OXYGEN CONSUMPTION AND OXYGEN DELIVERY: A SIMULTANEOUS COMPARISON OF THREE DIFFERENT NON-INVASIVE METHODS WITH STANDARD METHODS:

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Evaluation of oxygen transport variables cardiac output (C.O.), oxygen consumption ($\dot{V}O2$), and oxygen delivery ($DO2$) is a tool to guide therapy and predict outcome for critically ill patients. Standard methods with considerable invasiveness for measurement of these variables are:

- C.O. by thermodilution (CO_TD, HP CMS Monitor Hewlett Packard)
- $\dot{V}O2$ by indirect Calorimetry ($\dot{V}O2$_CAL, Datex Deltatrac Metabolic Monitor)
- arterial ($SaO2$_H) and mixed venous ($SvO2$_H) oxygen saturation and hemoglobin concentration (Hb_H) by hemoximetry (OSM 3 Hemoximeter, Radiometer Copenhagen)

Methods:

In this study the reliability of three different non-invasive methods for determination of C.O., $\dot{V}O2$ and $DO2$ were examined by simultaneous measurement of $\dot{V}O2$ by indirect calorimetry, measurement of mixed expiratory carbon dioxide concentration ($FECO2$) by a capnometer (Datex Normocap) and measurement of minute ventilation (VE) by a flow calibrated ventilator (Evita, Dräger). Oxygen saturations were measured by pulse oximetry ($SaO2$_POX, HP CMS Monitor) and by hemoximetry from a central venous blood sample ($ScvO2$_H). C.O. was also measured by thoracic bioimedance (AVL 2001 Monitor, BoMed, CO_BI).

In 15 postoperative mechanical ventilated patients with hemodynamic monitoring including radial artery and pulmonary artery catheters all these mentioned variables were simultaneously determined in 88 cases and calculated according to the formula:

Standard:	C.O.	=	CO_TD
	$\dot{V}O2$	=	$\dot{V}O2$_CAL
	$DO2$	=	CO_TD•$SaO2$_H•13.9•Hb_H/100
Fick-method:	CO_FICK	=	$\dot{V}O2$_CAL/($SaO2$_POX-$ScvO2$_H)/13.9/Hb_H•100
	$\dot{V}O2$	=	$\dot{V}O2$_CAL
	$DO2$	=	CO_FICK•$SaO2$_POX•13.9•Hb_H/100
Modified Fick-method:	CO_FickM	=	($FECO2$•VE)/($SaO2$_POX-$ScvO2$_H)/13.9/Hb_H•100
	$\dot{V}O2$	=	$\dot{V}O2$_FickM = $FECO2$•VE/0.9 [$FECO2$ conv.to STPD]
	$DO2$	=	CO_Fick2•$SaO2$_POX•13.9•Hb_H/100
Bioimpedance:	C.O.	=	CO_BI
	$\dot{V}O2$	=	$\dot{V}O2$_FickM
	$DO2$	=	CO_BI•$SaO2$_POX•13.9•Hb_H/100

Results:

Standard vs.	C.O.	$\dot{V}O2$	$DO2$
Fick-Method	r=0.83	-	r=0.81
Modified Fick-Method	r=0.86	r=0.81	r=0.85
Thoracic bioimpedance	r=0.66	r=0.81	r=0.58

Conclusion:

In our experience we found the non-invasive determination of C.O., $\dot{V}O2$ and $DO2$ by the Fick-method using indirect calorimetry, pulse oximetry and a centr.ven.blood sample and by a modified Fick-method using capnometry and spirometry as well as pulse oximetry and a centr.ven.blood sample to be reliable alternatives to thermodilution-derived parameters. Thoracic bioimpedance did not correlate with T.D. as close as the Fick-methods.