POSTER SESSION III

A963

TITLE: EFFECTS OF DISEASE ON PROTEIN BINDING
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INTRODUCTION: Alfentanil is a short-acting opioid whose pharmacokinetic properties make it a useful anesthetic agent for pediatric patients. Studies in pediatric patients with normal and abnormal hepatic and renal function have not demonstrated any differences in the pharmacokinetic profile of alfentanil. There have been no studies evaluating the effect of disease on alfentanil protein binding. This study was performed in order to evaluate the effects of hepatic and renal disease on protein binding.

METHODS: After approval from the hospital's IRB, patients scheduled for renal transplantation (group R, N=6), liver transplantation (group L, N=10), or repair of an asymptomatic atrial septal defect (group A, N=8) were entered into the study. All patients underwent an inhalational induction of anesthesia with nitrous oxide, oxygen, and halothane. After an intravenous and an arterial catheter were inserted, atropine and atracurium were administered to prevent bradycardia and to facilitate tracheal intubation. A 1 ml blood sample was obtained from either the intravenous or the arterial catheter. In all patients anesthesia was maintained with inhalational anesthetics. No narcotics were administered until after the plasma sample was obtained.

The blood samples were obtained in a heparinized syringe and immediately centrifuged, and the plasma was separated and stored at -60°C. Alfentanil (100 ng/ml) was added to the plasma samples, and equilibrium dialysis was performed using a Dianorm system. These cells were rotated at 20 RPM in a thermostat bath at 37°C for 4 h. At equilibrium (4 h) the drug in the buffer cell half equals the free drug concentration (Cf) and the drug in the plasma cell half equals the sum of the concentration of both free and bound drug (Cf + Cb = C). Therefore, the % of free drug = Cf/C x 100 and the % of bound drug = C-Cf/C x 100. Alfentanil concentrations in each half of the cell were determined with a specific radioimmunoassay. This assay accurately detects 0.1 ng/ml of alfentanil, and its coefficient of variation is 5% at 0.1 ng/ml. The loss of alfentanil to nonspecific cell binding was small (<4%). Alpha 1 acid glycoprotein AAG was also measured with a radial immunoassay.

RESULTS: Table 1 lists the age, weight, percent binding, and AAG levels of the 3 groups. There were no differences in weight between the 3 groups; however, patients in group R were older than patients in groups A and L. AAG levels were significantly greater in group R compared with groups A and L.

DISCUSSION: Although patients in group R tended to have higher protein binding, these values were not statistically different from patients with liver disease and healthy children undergoing ASD repair (P=.06). A larger patient sample size, however, may demonstrate an increase in binding for patients with renal disease. At present, our findings of normal or possibly increased alfentanil binding in pediatric patients with kidney disease contrast with the findings in adults. Adult studies of patients with renal disease demonstrated an increased AAG but an unexplainable decrease in alfentanil protein binding (1).

REFERENCE

1. Anesth Analg 66:53, 1987.

Table 1.

Group	Age (yrs)	Weight (kg)	Binding (%)	AAG (mg/dl)
A	4.3 ± 1.9	17.5 ± 4.1	88.9 ± 4.6	52.9 ± 13.4
L	5.2 ± 4.3	20 ± 12	84.4 ± 6.9	65.4 ± 16.1
R	9.5 ± 4.1*	27.9 ± 22	91 ± 2.1	89.9 ± 13.4*

* P < 0.05 compared with group A and L (ANOVA).

A964

TITLE: REVERSAL OF DEEP NEUROMUSCULAR BLOCKADE WITH 40 µg/kg VS. 70 µg/kg NEOSTIGMINE IN INFANTS AND CHILDREN

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Introduction: Standard texts of pediatric anesthesia vary greatly in the recommended dose of neostigmine required to antagonize neuromuscular blockade. These recommendations range from 40-70 µg/kg. We have previously studied reversal of deep neuromuscular blockade with 40 µg/kg neostigmine in infants and children[1]. In this study, we compare the higher and lower recommended neostigmine doses in terms of adequacy and time to reversal.

Methods: With IRB approval, 40 pediatric patients, ages 2 months to 8 years, physical status I or II were studied. Anesthetic induction and maintenance were accomplished with 30% O_2, 70% N_2O, and halothane. Neuromuscular function was monitored with a Puritan-Bennett relaxograph. T_1% of control and the T_4/T_1 ratio were followed. Intubation was performed after relaxation with atracurium. A continuous infusion of relaxant was titrated to keep one twitch present with T_1 < 10% of control. At the completion of surgery, the relaxant infusion was discontinued and neuromuscular blockade reversed with 20 µg/kg atropine and either 40 µg/kg or 70 µg/kg neostigmine IV. Reversal was deemed to be adequate when the T_4/T_1 ratio exceeded 70%, and extubation was accomplished at this time, provided the clinical criteria for extubation were also present.

Results: Results are summarized as follows:

Reversal Dose of Neostigmine	# Patients	Age	Reversal Time (minutes) mean ± SEM
40 µg/kg	10	2-11 mo	5.3 ± 0.5†
	10	13 mo - 8 yr	9.0 ± 0.5†‡
70 µg/kg	10	3-11 mo	3.9 ± 0.7*
	10	13 mo - 7 yr	6.1 ± 0.6*‡

* P<0.05 by unpaired two-tailed t-test; † P<0.01 by unpaired two-tailed t-test; ‡ P<0.01 by unpaired two-tailed t-test

Discussion: All patients had adequate reversal of neuromuscular blockade as measured by EMG as well as clinical criteria, even when the lower dose of neostigmine was used, supporting the findings of our previous study.[1] That 40 µg/kg of neostigmine provided adequate reversal of neuromuscular blockade in infants is in agreement with others who suggest that neostigmine dose requirements are smaller in infants when compared with children and adults.[2] In the infant group, there was no significant time advantage to using the larger dose of 70 µg/kg neostigmine for reversal of neuromuscular blockade. In the older group of patients studied, 70 µg/kg of neostigmine provided adequate reversal of neuromuscular blockade in a shorter period of time than did the 40 µg/kg dose. This is not unexpected since the ED_{50} of neostigmine is greater in children when compared with infants, and here an increased dose might be expected to offer some time advantage. We recommend 40 µg/kg neostigmine as an adequate dose for reversal of deep neuromuscular blockade in infants and children. If reversal is required in a shorter period of time, the 70 µg/kg dose of neostigmine is suggested for children, but provides no advantage in the infant group.

References: 1. Anesth Analg 72:S21, 1991
2. Anesthesiology 59:220-225, 1983

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