Title: THE CUMULATIVE DOSE-RESPONSE OF PIPECURONIUM BROMIDE IN CHILDREN

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Introduction: Pipecuronium bromide, a nondepolarizing neuromuscular (NM) blocking agent with similar chemical and pharmacological properties to pancuronium, has been investigated clinically in adults (1,2). It has been reported that the NM potencies of vecuronium in infants and children are not different from those in adults (3). Goudsouzian and his associates (4) found, however, that in children the dose-response regression line of vecuronium was shifted to the right from that of adolescents, indicating that the dose requirement of vecuronium in children was more than in adolescents. The present study was designed to determine whether there are any age related differences in the NM effects of pipecuronium.

Methods: This study, approved by the Institutional Review Board was carried out on 21 ASA classification 1, 2 and 3 children of 1 to 14 years of age whose guardians signed informed consents. Patients were premedicated with 1.0-1.5 mg/kg diphenhydramine, 1.0-1.5 mg/kg meperidine and 0.01 mg/kg atropine intramuscularly an hour prior to surgery. All drugs administered during anesthesia were given intravenously. Anesthesia was induced with 0.05 mg/kg droperidol, fractional doses of fentanyl and N_2O-O_2. To facilitate early application of electrical stimulation of ulnar nerve, 2.0 mg/kg of thiopental was added to the induction agents. Anesthesia was maintained with 4 l/min N_2O-2 l/min O_2 and fentanyl. After induction of anesthesia, electrodes were placed over the ulnar nerve at the wrist and stimulated with train-of-four (TOF) supramaximal square wave pulses of 0.1 msec duration administered at 2 Hz every 10 sec. The elicited electromyogram (EMG) of the adductor pollicis muscle was continuously recorded. After obtaining a control tracing 10 µg/kg pipecuronium followed by 5 to 10 µg/kg increments were injected i.v. until greater than 85% block developed. Each dose was injected when the maximal effect of the previous dose had developed. The "cumulative" log dose-response (T1 of TOF) regression lines of pipecuronium were determined for each subject and ED50 and ED90 values were calculated. To maintain surgical relaxation 15 µg/kg increments of pipecuronium were administered whenever T1 returned to 25% of control. When T4/T1 ratio was < 0.75 at end of anesthesia the residual NM block was antagonized with a mixture of 40 µg/kg neostigmine and 15 µg/kg atropine. The results obtained were compared (Student's t test) with those obtained in adults (2).

Results: As indicated in the table, pipecuronium is less potent in children than in adults. In contrast to adults the clinical duration of successive maintenance doses of pipecuronium was unchanged in children. Residual NM block could be antagonized equally well in adults and children.

Discussion: The findings presented indicate that in children pipecuronium is less potent than in adults. Our findings are in contrast to those reported by Fisher (3) indicating that the ED50 of vecuronium does not change with age. They stated that this was due to the fact that age-related changes in the steady state volume of distribution and plasma concentration of the relaxant, that caused 50% depression of the twitch, counterbalance each other and result in no change in ED50 values. In contrast to the considerable cumulative effect of pipecuronium observed in adults (2), there was no cumulative effect in children.

References

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Neuromuscular Parameters in Children and Adults

Parameters	Children	Adults	p <
ED50 (µg/kg)	28.3±2.0(21)*	20.3±1.1(28)	0.001
ED90 (µg/kg)	55.8±4.6	35.1±1.7	0.001
Clinic Durat(min)			
Maintenance Doses			
1st Dose	29.8±3.0(12)	31.3±2.9(21)	n.s.
All Doses	26.8±1.5	47.1±2.0(38)	0.001
Recovery Rate(min)	24.5±10.7(3)	44.5±8.2(3)	n.s.

*Mean±SEM of number of observations in parenthesis.