TITLE: THE CUMULATIVE DOSE-RESPONSE RELATIONSHIP OF PIPECURONIUM BROMIDE (ARDUAN®) IN INFANTS AND CHILDREN

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INTRODUCTION. Pipecuronium bromide (Arduan®) is a new long-acting steroidal nondepolarizing muscle relaxant devoid of cardiovascular side effects. We studied the cumulative dose-response relation of pipecuronium in infants and children during halothane anesthesia.

METHODS. Twenty-nine patients were studied during elective surgery with informed consent obtained from a parent and after approval by the Human Rights Committee of Children's Hospital of Pittsburgh. They were grouped according to age: 3-6 mos (N=10), 1-3 yrs (N=10), and 3-6 yrs (N=9). Each patient was anesthetized with nitrous-oxide (70%) and halothane (up to 4% inspired). An intravenous catheter was placed, atropine and fentanyl (1-3 μg/kg) given IV, and intubation accomplished without the use of relaxant. Following intubation, end-tidal halothane concentration was adjusted to 0.8%. The ulnar nerve was stimulated supramaximally with repetitive trains-of-four stimuli (2 Hz for 2 sec at 10-sec intervals) at the wrist with surface electrodes. The evoked compound electromyogram of the thenar area was recorded using a Datex NMT monitor.

Cumulative dosing was accomplished with 5 or 10 μg/kg doses of pipecuronium until complete neuromuscular blockade was established. A dose-response (DR) curve for each patient was constructed by log-probit transformation of the data and calculation of least squares regression lines. Effective dose (ED) estimates were calculated for each patient. Mean ED values for each group were compared using t-test with Bonferroni correction (Table 1). Statistical differences were considered significant at $p < 0.01$.

RESULTS.

Table I	3-6 mos++	1-3 yr	3-6 yr
ED_{50} (μg/kg)	18	21	24+
ED_{95} (μg/kg)	33+	47	49
ED_{50} (μg/m^2)	358+	502	589
ED_{95} (μg/m^2)	663+	1102	1224

\+ statistically significant difference from other groups
++ DR curve not parallel to other two groups

DISCUSSION. The pipecuronium dose requirement for our children age 1-6 years during halothane anesthesia is 10-20% greater than that reported in geriatric and younger adults during balanced anesthesia.[1,2] This is likely due to age-related differences in volume of distribution of the drug.

Comparison of our data for 3-6 mos infants to other groups is difficult because the slopes of the DR curves were not parallel. However, the increased sensitivity to pipecuronium we observed in infants 3-6 months of age compared to older children 1-6 years of age is similar to that noted previously in this age group with vecuronium.[3] Decreased dosage requirement in this group is also noted on a μg/m^2 basis, and can therefore not be explained by age-related differences in volume of distribution.

REFERENCES. 1. Anesthesiology 65:A116, 1986
2. Anesthesiology 67:A370, 1987
3. Anesth Analg 67:21-6, 1988

A779

TITLE: NEUROMUSCULAR EFFECT OF PIPECURONIUM IN INFANTS AND CHILDREN DURING NITROUS OXIDE-ALFENTANIL ANESTHESIA

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Pipecuronium (PIP) is a new steroidal neuromuscular (NM) blocking agent which has widely been studied in adults (1,2,3). There are only few data available in children (4) and no data in neonates and infants. We therefore evaluated and compared the potency and duration of the PIP-induced NM blockade in neonates, infants and children during balanced anesthesia.

We obtained approval from the local ethic committee on pediatric research and informed consent from parents to study 32 ASA 1 or 2 children undergoing elective minor surgery. Group A included 12 infants, 0 to 3 months old, weighing 5.2±0.3 kg (mean ± SE), group B, 10 infants, 3 to 12 months old, 6.9±0.4 kg, and group C, 10 children 2 to 9 yrs old, 19.6±2.2 kg. Anesthesia was induced with thiopental 5 mg/kg and alfentanil 15 μg/kg i.v., and maintained with nitrous oxide and O_2 (60:40) supplemented with repeated i.v. doses of alfentanil (10 μg/kg). End-tidal CO_2 was maintained between 4.3-4.8 vol% and rectal temperature between 36-37.5 °C. NM transmission was measured by electromyography (Relaxograph, Datex) at the ulnar nerve adductor pollicis muscle using transcutaneous electrodes. Train-of-four stimulation was applied at supramaximal level at 2 Hz every 20 sec. The first of the four responses was considered as the twitch height (TH). All TH were referred to those measured before administration of PIP. Incremental i.v. doses of PIP were given to reach a 95±2% TH depression. The time from this point to 25% recovery (CD), to 75% recovery (D_{75}), and from 25 to 75% recovery (RI) was determined. Individual dose-response curves were constructed after logit transformation of TH responses. Comparisons between groups were made using a one way ANOVA (significance: $P < 0.05$).

Results are summarized in Table 1. Dose requirements of PIP in both groups of infants were significantly lower than in children. CD and D_{75} were also significantly shorter in infants than in children.

This study demonstrates that the NM potency of PIP is increased in both groups of infants compared to children. Furthermore, contrary to children, PIP is not a long- but rather an intermediate-acting NM blocking agent in infants.

References: 1.Agoston S, Clin Anesth 3:361-369,1985
2.Caldwell JE, Br J Anaesth 61:693-697,1984
3.Tassonyi E, Anesthesiology 69:793-796,1988
4:Tassonyi E, Anesthesiology 69:A491,1988

Table 1: Potency of pipecuronium and duration of the neuromuscular blockade in infants and children during N_2O-alfentanil anesthesia

	Infants		Children
	0-3 months	3-12 months	
ED_{50} (μg/kg)	23.7 ± 1.7*	25.8 ± 1.5*	43.9 ± 4.7
ED_{95} (μg/kg)	46.5 ± 2.9*	48.7 ± 3.5*	79.3 ± 9.8
CD (min)	13.2 ± 1.8*	13.4 ± 2.2*	38.7 ± 5.9
RI (min)	27.0 ± 4.6*	31.8 ± 4.1*	23.1 ± 1.4
D_{75} (min)	38.7 ± 5.7*	43.8 ± 5.3*	62.3 ± 7.8

mean ± SE of 12 patients in infants less than 3 months and 10 patients in others;
* significantly different from children ($P < 0.05$)