

Title: CLINICAL PHARMACOLOGY OF VECURONIUM (ORG NC45) IN ANESTHETIZED INFANTS AND CHILDREN

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Introduction. Vecuronium (Org NC45) is a non-depolarizing muscle relaxant undergoing extensive clinical evaluation. We have determined the clinical pharmacology of vecuronium in anesthetized children and compared these results with known values for adults.

Methods. After obtaining approval of the committee on human research and informed consent, 40 patients 8 weeks to 8 years of age were studied. The patients consisted of two equal groups: infants, less than one year; and children, older than one year. Anesthesia was maintained with 70% N₂O and halothane, 0.9 MAC (age-adjusted), measured by mass spectrometry. End-tidal PCO₂ was maintained at 30-40 mmHg and nasopharyngeal temperature maintained at 35-37° C. Heart rate and arterial blood pressure were monitored throughout the studies. Supramaximal 0.15 ms stimuli were administered to the ulnar nerve at 0.15 Hz and the response of the adductor pollicis was measured with a Grass FT10 transducer. To determine potency we administered a single dose of vecuronium, 15, 20, or 25 µg/kg, to 29 patients. Maximal twitch depression was plotted against log dose and least squares regression lines were determined. These dose response curves were compared by analysis of covariance to adult values obtained under comparable anesthetic conditions(1). To determine the time course of large doses, 11 patients received a single dose of vecuronium, 70 µg/kg. Onset (time to peak effect), duration (time from injection to 90% recovery of twitch height), recovery time (time from 25% to 75% twitch height) and peak effect were recorded. These values and onset of 20 µg/kg doses were compared by ANOVA and the Student-Newman-Keuls test. A P < 0.05 was considered statistically significant.

Results. ED50 was 18.3, 18.2 and 15.0 µg/kg for infants, children and adults respectively. The dose response curve differed by analysis of covariance. Onset of vecuronium, 20 µg/kg, was shorter in infants (4.6 min) and children (4.8 min) than in adults (6.0 min)(Table 1). Onset of vecuronium, 70 µg/kg, was shorter in infants (1.4 min), than in adults (3.8 min). Duration was markedly longer in infants (73 min) than in children (36 min) and adults (34 min). Recovery time was longer in infants(Table 2). Twitch tension was depressed 100% in all patients receiving vecuronium, 70 µg/kg. No changes in heart rate or blood pressure were observed.

Discussion. The response of infants and children to vecuronium differs from that of adults. Larger doses are required in pediatric patients to achieve 50% neuromuscular blockade. The rapid onset of paralysis in infants and children may result from elevated cardiac output compared to adults. The

duration of action of vecuronium, 70 µg/kg, was markedly longer in infants. Vecuronium has no cardiovascular effects following the administration of doses used clinically. We conclude that vecuronium can be used in pediatric patients in doses similar to or slightly larger than those used for adult patients. One advantage of vecuronium in adult patients is its shorter duration compared to other muscle relaxants. In patients older than one year, duration of action is similar to that in adults. However, in patients less than one year of age, the duration of action is markedly longer and doses will be required less frequently. Further investigation is necessary to determine if the prolonged duration of action of vecuronium in infants can be explained on a pharmacokinetic or pharmacodynamic basis.

Reference.

1. Fahey MR, Morris RB, Miller RD, et al: Clinical pharmacology of Org NC45 (Norcuron): A new nondepolarizing muscle relaxant. *Anesthesiology* 55:6-11, 1981

Table 1. Onset Time and Magnitude of Peak Effect of Vecuronium (Mean ± SD)

	n	Dose (µg/kg)	Onset (min)	Peak (%)
Infants	4	15	5.4 ± 1.9	23 ± 19
	5	20	4.6 ± 0.8*	68 ± 14
	5	25	3.5 ± 1.5	93 ± 8
Children	5	15	5.6 ± 1.1	39 ± 31
	5	20	4.8 ± 0.7*	50 ± 26
	5	25	5.2 ± 1.6	77 ± 10
Adults [@]	6	10	6.7 ± 2.2	25 ± 11
	7	14	6.3 ± 1.9	36 ± 18
	7	20	6.0 ± 0.8	76 ± 15

* Different from adults
@ From previous study(1)

Table 2. Onset, Duration and Recovery Times of Vecuronium, 70 µg/kg (Mean ± SD)

	n	Onset (min)	Duration (min)	Recovery (min)
Infants	6	1.4 ± 0.5*	73 ± 28 [#]	20 ± 9 [#]
Children	5	2.6 ± 1.4	36 ± 6	10 ± 3
Adults [@]	10	3.8 ± 1.4	34 ± 9	8 ± 3

* Different from adults
Different from children and adults
@ From previous study(1)