

TITLE: NEUROMUSCULAR EFFECTS OF BW A938U IN ANESTHETIZED CHILDREN

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**INTRODUCTION:** BW A938U (BW 938), a new long-acting nondepolarizing neuromuscular blocking agent, has minimal cardiovascular effects in adults at several multiples of the ED95. Efficacy and safety studies of BW 938 have not been described for children. We were interested in determining BW 938 dose-response relationship, onset times, and recovery times in children during halothane anesthesia.

**METHODS:** Eighteen children (ASA status I-II between 2 and 12 years old, having low risk elective surgical procedures were studied. No patient received aminoglycoside antibiotics or antihistamines within 48 hours of the study. The study was approved by the Human Rights Committee of the Children's Hospital of Pittsburgh. Informed consent was obtained from a parent. The children were not premedicated. Anesthesia was induced with nitrous oxide (70%), oxygen (30%) and halothane (up to 4% inspired). After induction, an intravenous catheter was placed, and atropine 10 ug/kg was given IV. After endotracheal intubation, the end-tidal halothane concentration was adjusted to  $0.8 \pm 0.05\%$  fentanyl (1-3 ug/kg) was given as needed.

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 thumb adduction was recorded using a Puritan-Bennett/Datex monitor. The degree of neuromuscular block was described as percent of control in that the height of the first train-of-four response was compared to the control EMG height. Cumulative dose-response curves for BW 938 were determined in nine children (Group I). Each patient received an intravenous bolus of BW 938 (0.01 mg/kg); additional incremental doses of BW 938 were given as neuromuscular blockade stabilized to produce at least 75% block. A dose-response curve for each patient was constructed by log-probit transformation of the data and calculation of least squares regression lines. Effective dose estimates were calculated for each patient. Another nine patients (Group II) were anesthetized in a similar manner and received the ED95 dose of BW 938. The onset time, maximum neuromuscular blockade, and time for neuromuscular transmission to return to 25% of control (T25) and 75% (T75) after the bolus was noted. Blood pressure and heart rate were recorded at one minute intervals for 10 minutes after the bolus. The recovery index (T25-T75) was calculated. Standard deviations are shown for all mean values. Student's t-tests and Mann-Whitney U tests were utilized where appropriate to compare means. Statistical differences were considered significant at  $p < 0.05$ .

**RESULTS:** The median ED 25 50, 75, and 95 during nitrous oxide halothane (0.8% ET) anesthesia were 0.011, 0.015, 0.019, and 0.0275 mg/kg respectively.

The onset time to maximum block, duration of block, and recovery data following a single bolus of 0.0275 mg/kg (Group II) are presented in Table 1 along with the recovery parameters following cumulative dosing (Group I). The maximum block and recovery indices (T75-T25) were comparable in the two groups. When the patient who developed 100% block was deleted from Group II, there was no longer a statistically significant difference in T25 between the two groups. There were no clinically significant changes in blood pressure, heart rate, or heart rhythm following a bolus of ED95 of BW 938. Full recovery of neuromuscular transmission occurred spontaneously in 4 of 18 patients. Neostigmine (up to 0.06 mg/kg) was given when block was between 03 and 47 percent of baseline and a T4/T1 ratio of greater than 75% followed within 0.2 to 2.3 minutes.

**DISCUSSION:** The dose-response relationship for BW 938 in children anesthetized with halothane and nitrous oxide (ED50 of 0.015 mg and ED95 of 0.0275 mg/kg) is similar to that seen in adults under balanced anesthesia.<sup>1,2</sup> It is to be expected that halothane potentiates the neuromuscular effects of BW 938, as has been demonstrated with isoflurane.<sup>3</sup> Therefore, it is likely that children anesthetized with balanced anesthesia would require more BW 938 to achieve the same degree of block than do children anesthetized with halothane or adults anesthetized with balanced anesthesia.

Both onset time to maximum block and recovery to 25% of baseline twitch height in these children were shorter than those reported in adults.<sup>2</sup> However, the recovery profile after BW 938 in children anesthetized with halothane (0.8% ET) appears quite similar to that in adults under balanced anesthesia.<sup>1</sup> Further study may better define age related differences in BW 938 pharmacokinetics and dynamics.

TABLE 1: Neuromuscular Data BW 938 (X  $\pm$  SD)

	Max Block %	Onset (min)	T25 (min)	T75-25 (min)
Group I				
0.026 $\pm$	88	--	16.3*	25.6
0.006 mg/kg	$\pm 7$		$\pm 8.8$	$\pm 6.3$
	(N = 9)		(N = 9)	(N = 8)
Group II				
0.0275 mg/kg	91	6.9	27.8	34.0
	$\pm 12$	$\pm 1.9$	$\pm 10.3$	$\pm 16.4$
	(N = 9)	(N = 9)	(N = 8)	(N = 7)

(\* significantly different  $p \leq 0.05$ )

#### REFERENCES

1. Mehta et al.: Anesthesiology 65: A280, 1986.
2. Basta et al.: Anesthesiology 65: A281, 1986.
3. Murray et al.: Anesth. Analg. 66: S126, 1987.