

Title: CARDIOVASCULAR AND NEUROMUSCULAR EFFECTS OF BWA938U: COMPARISON WITH PANCURONIUM

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**Introduction.** BWA938U is a new long acting non-depolarizing relaxant.<sup>1,2</sup> The purpose of this study was to compare the cardiovascular and neuromuscular effects of large doses of BWA938U and pancuronium and to study the cumulative neuromuscular properties of repeat doses of BWA938U and pancuronium.

**Methods.** After the protocol was approved and written permission obtained, 39 ASA I or II patients, aged 18-60 years who required elective surgery, were divided into two groups; 27 patients received BWA938U, 12 patients received pancuronium.

The patients were premedicated with morphine (0.1 - 0.15 mg.kg<sup>-1</sup>) and atropine (0.004 - 0.01 mg.kg<sup>-1</sup>). Anesthesia was induced with thiopental and fentanyl (1-2 µg.kg<sup>-1</sup>), and maintained with additional doses of thiopental and 70% N<sub>2</sub>O. Neuromuscular responses of the adductor pollicis (square wave pulses from stimulation of the ulnar nerve at a frequency of .15 Hz, 20V above maximal response, and 0.2 msec duration) and cardiovascular data (heart rate by EKG and blood pressure by direct arterial measurements) were recorded on a Hewlett-Packard 4 channel recorder. Ventilation was assisted or controlled with end-tidal CO<sub>2</sub> maintained between 36-40 mm (mass spectrometer).

Fifteen minutes following induction, after baseline heart rate, arterial pressure and neuromuscular measurements were obtained, BWA938U 40 µg.kg<sup>-1</sup> (1.7 x ED95) or pancuronium 80 µg.kg<sup>-1</sup> (1.5 x ED95) was administered as a single intravenous bolus. The arterial pressure and heart rate were recorded each minute for ten minutes following the injection of either pancuronium or BWA938U. In the BWA938U group, serum histamine levels were measured prior to and at two and five minutes post-injection. All hemodynamic data was recorded prior to the start of elective surgery.

To determine cumulative properties, the neuromuscular recovery was followed until 25% twitch height recovery [(BWA938U) n = 9; (Pancuronium) n = 9] and then a supplemental dose of 5 µg.kg<sup>-1</sup> of BWA938U or 10 µg.kg<sup>-1</sup> of pancuronium was administered. The additional block produced and the time to 25% recovery was recorded for at least three supplemental doses of either BWA938U or pancuronium. Student's T-test was used to analyze data.

**Results.** The time to 90% block and max block for both drugs is presented in Table 1. The time to 25% recovery for BWA938U was 77.5 ± 7.5 min; for pancuronium 71.4 ± 6.3 min (Table 1).

The effects of the supplemental doses on the additional twitch suppression and the time for recovery to 25% twitch height appears on Table 2.

While BWA938U had no significant effect

on heart rate and blood pressure, pancuronium produced significant increases in heart rate and mean blood pressure (Fig. 1). Following pancuronium the maximum mean percent of control mean blood pressure (MBP) and heart rate (HR) at five minutes was 110 ± 5%, 116 ± 6% respectively. The maximum mean percent of control MBP and HR at five minutes following BWA938U was 92.5 ± 2%, 94.6 ± 1.0%, respectively.

**Discussion.** BWA938U is approximately twice as potent as pancuronium. With neuromuscular doses of BWA938U and pancuronium of comparable potency, the duration of neuromuscular block was similar. In this study, no cumulative relaxant effect occurred with either pancuronium or BWA938U. While increases in heart rate and blood pressure occurred with pancuronium, BWA938U had minimal cardiovascular side effects in healthy patients.

**References.**

1. Mehta MP, et al: Anesthesiology 65:A280, 1986
2. Basta SJ, et al: Anesthesiology 65:A281, 1986
3. Fahey MR, et al: Anesthesiology 66:6-11. 1981

TABLE 1

Comparative NMB Data For BWA938U and Pancuronium					
	Predicted Effective Dose	Time (min) to onset and recovery			
		90% Block	Max Block	Begin Recovery	25% Recovery
BWA938U 40 µg.kg <sup>-1</sup>	1.7 ED95	4.1 ± 0.2	7.6 ± 0.8	42.2 ± 4.9	77.5 ± 7.5
Pancuronium 80 µg.kg <sup>-1</sup>	1.5 ED95	2.3 ± 0.3	5.1 ± 1.0	48.6 ± 3.5	71.4 ± 6.3

<sup>a</sup> Derived from Log-Dose Probit Response Curves<sup>1,3</sup>

TABLE 2

Effect of Repeated Doses of BWA938U and Pancuronium

		Mean % Twitch Suppression at Time of Dose	Maximum % Twitch Suppression	Time to 25% recovery (min)
BWA938U (n = 9)	1st maintenance 5 µg.kg <sup>-1</sup>	70.1 ± 1.4	85.5 ± 1.3	28.9 ± 5.9
	2nd maintenance	73.5 ± 2.4	86.8 ± 1.8	28.6 ± 5.1
	3rd maintenance	72.6 ± 1.6	86.8 ± 1.4	23.7 ± 4.4
Pancuronium (n = 9)	1st maintenance 10 µg.kg <sup>-1</sup>	72.4 ± 2.0	92.5 ± 1.1	24.8 ± 1.5
	2nd maintenance	71.1 ± 2.5	90 ± 1.4	24.4 ± 4.4
	3rd maintenance	69.8 ± 2.5	89.4 ± 1.3	24.0 ± 2.8

Values are expressed as mean ± S.E.M.

