Title: HEMODYNAMIC EFFECTS OF BW A938U IN CORONARY ARTERY BYPASS GRAFT AND VALVE REPLACEMENT PATIENTS RECEIVING OXYGEN SUFENTANIL ANESTHESIA

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Introduction. BW A938U is an investigational nondepolarizing neuromuscular blocking drug. Its duration of action equals or exceeds that of pancuronium in equipotent doses, and it is not cumulative. (1,2) The drug has been shown to be devoid of cardiovascular side effects at modest doses in healthy patients not invasively monitored.(2) Animal studies have shown hemodynamic deviations from control of less than 5 per cent with doses 10 to 20 times the ED95.(3) However invasive hemodynamic studies in patients with cardiac disease are just beginning.

Methods. Fifteen patients 35 to 72 years of age ASA Class III or IV of either sex excluding females of childbearing potential were studied after obtaining an institutionally approved informed consent. Ten patients were scheduled for coronary artery bypass grafting, and 5 were undergoing aortic or mitral valve replacement. All patients met New York Heart Association criteria for functional Class I, II or III. Patients were excluded from the study for any of the following reasons: a history of chronic alcoholism and/or known drug abuse; evidence of renal or hepatic impairment; exposure to antibiotics except penicillin, cephalosporins, or tetracyclines; exposure to H1- or H2-receptor blockers within 48 hrs prior to anesthetic induction; exposure to antidepressants or phenytoin within 1 wk of entry into the study.

Preanesthetic medication administered 90 min prior to anticipated induction consisted of morphine 10 to 15 mg and scopolamine 0.4 mg intramuscularly along with lorazepam 2 to 4 mg orally. A peripheral intravenous infusion of Normosol-R was established in the operating room and a volume equal to the NPO deficit administered. The coronary patients were also hydrated with purified plasma protein fraction 1000 ml. Initial monitoring included leads II and V5 of the ECG, a radial intra-arterial catheter and an evoked electromyographic response of the adductor pollicis muscle following ulnar nerve stimulation at the wrist.

Anesthetic induction was accomplished intravenously with midazolam 0.2 to 0.3 mg/kg and sufentanil 0.1 to 1.5 ug/kg while the patient breathed 100 per cent oxygen via face mask. Tracheal intubation was facilitated by succinylcholine 1 mg/kg and topical lidocaine 4 per cent 4 ml. Anesthesia was maintained with an infusion of sufentanil 0.5 to 1.0 ug/min and controlled ventilation of the lungs to maintain end-tidal PCO2 near 30 mm Hg. A pulmonary artery catheter was passed via the right internal jugular vein, and a thermistor-equipped esophageal stethoscope was placed.

During a stable state of sufentanil anesthesia at least 15 min after tracheal intubation baseline measurements were made of the following hemodynamic variables: MAP, HR, MPAP, PAOP and RAP. Thermodilution cardiac output determinations were made in duplicate. Calculated variables including CI, SV, SVR and PVR were made after completion of the study.

There were 3 groups of 5 patients each. After baseline hemodynamic measurements the patients with coronary artery disease received BW A938U 25 ug/kg (Group A, n = 5) or 50 ug/kg (Group B, n = 5). The patients with valvular heart disease were given BW A938U 50 ug/kg (Group C, n = 5). These doses represent the ED95 and twice the ED95 of BW A938U.(1,2) All measurements and calculations were repeated at 2, 5 and 10 min after injection. Hemodynamic changes were analyzed by paired t-test with p less than 0.05 considered statistically significant.

Results. There were no statistically significant changes in any hemodynamic parameter over time.

Discussion. BW A938U has a wide hemodynamic and autonomic margin of safety in patients with coronary or valvular heart disease. Because of this lack of cardiovascular side effects BW A938U is an attractive alternative to the conventional long-acting nondepolarizers, especially in cardiac patients.

References.

1. Mehta MP, Murray D, Forbes R, et al. Anesthesiology 65:A280, 1986.
2. Basta SJ, Savarese JJ, Ali HH, et al. Anesthesiology 65:A281, 1986.
3. Savarese JJ, Wastila WB, Basta SJ, et al. Anesthesiology 59:A274, 1983.

Results (% Change from Control)

	Group A	25µg/Kg			(CABG)
	MAP	SV	SVR	PVR	CI
2 min	-6.50	-3.63	0.93	-1.24	-5.12
5 min	-7.29	1.01	0.89	35.47	-5.32
10 min	2.92	1.31	8.19	-10.65	-1.95
	Group B	50µg/Kg			(CABG)
	MAP	SV	SVR	PVR	CI
2 min	0.15	4.52	2.71	-22.43	-2.58
5 min	-1.19	3.73	2.68	-32.72	-3.82
10 min	-2.06	8.27	0.23	-32.83	-1.89
	Group C	50µg/Kg			(Valve)
	MAP	SV	SVR	PVR	CI
2 min	-1.87	6.58	-1.53	29.63	1.33
5 min	0.76	10.25	-1.65	12.26	4.62
10 min	1.64	8.97	0.35	16.64	3.14

St. Dev.'s Omitted to Save Space