Title: A STUDY OF THE HEMODYNAMIC EFFECTS OF BW A938U - A NEW LONG ACTING NONDEPOLARIZING MUSCLE RELAXANT

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Introduction The currently used long acting nondepolarizing muscle relaxants all have associated hemodynamic effects. In patients with cardiovascular disease, these effects may be poorly tolerated.[1] BW A938U is a new long acting nondepolarizing muscle relaxant that in healthy volunteers is devoid of cardiovascular effects and does not cumulate during repeated dosing. The purpose of this study was to evaluate the hemodynamic effects of BW A938U in ASA physical status class III and IV patients undergoing coronary artery bypass graft (CABG) surgery and valvular replacement (VR) during O_2/fentanyl/diazepam anesthesia.

Methods Eight patients scheduled for elective CABG or VR were studied. Written informed consent was obtained from each patient and the protocol was approved by the institution's Human Investigations Committee. The patients were premedicated with combinations of morphine (0.08 to 0.10 mg/kg IM), scopolamine (0.003 to 0.005 mg/kg IM), diazepam (0.07 to 0.15 mg/kg PO) or lorazepam (0.5 to 4.0 mg IM) as determined individually for each patient. Cardiac medications were continued up to the time of surgery. Each patient was monitored by electrocardiographic lead V_5, and radial and pulmonary arterial catheters (PAC) connected to aneroid-calibrated transducers zeroed at the level of the right atrium. In patients with sinus rhythm, a rapid response thermistor PAC capable of measuring right ventricular ejection fraction (RVEF), stroke volume (RVSV), end-diastolic volume (RVEDV) and end-systolic volume (RVESV) was used (n=6).

Anesthesia was induced with a combination of 100% oxygen, fentanyl (30-75 mcg/kg), and diazepam (2.5-20 mg). Succinylcholine (1 mg/kg) was used to facilitate endotracheal intubation. The patients were then mechanically ventilated to maintain normocarbia. In a steady state after recovery from the succinylcholine, baseline measurements (A) were performed: heart rate (HR, bpm), mean arterial pressure (MAP, mmHg), pulmonary capillary wedge pressure (PCWP, mmHg), central venous pressure (CVP, mmHg), cardiac output (CO, L/M - performed by thermodilution in triplicate with iced D5W and averaged), and RVEF, RVSV(ml), RVEDV(ml) and RVESV(ml). An intravenous bolus of 0.05 mg/kg of BW A938U (approximately 2 X ED_{95}) was then administered. Hemodynamic measurements were repeated at 2 minutes (B), 5 minutes (C), and 10 minutes (D) after the study drug administration. Data were analyzed by repeated-measures ANOVA and significance was defined as $p < 0.05$.

Results After administration of BW A938U there were statistically significant decreases in HR (10 min), MAP (2,5,10 min), PAP (5,10 min), CVP (2,5,10 min), and PCWP (2,5,10 min). There were no significant changes in CO, stroke volume, systemic vascular resistance, pulmonary vascular resistance, RVEF, RVSV, RVEDV, and RVESV. Pertinent data are presented in the table. There were no allergic reactions or complications attributable to the drug.

Discussion The administration of BW A938U resulted in several statistically significant hemodynamic observations. However, the magnitude of these changes were small and not clinically significant. Additionally, no single patient demonstrated hemodynamic instability. There are two likely explanations for our observations. BW A938U may possess an intrinsic mild vasodilatory property or the decreases in the hemodynamics may be due to a progressive decrease in sympathetic tone after the induction of anesthesia and intubation. In a study of similar design, Girard et al demonstrated reductions in HR, MAP, and CO during placebo infusion after the induction of anesthesia.[2] In conclusion, with a dose approximately two times ED_{95}, BW A938U appears to have minimal hemodynamic effects on ASA physical status Class III and IV patients.

References

1. Thomson IR, Putnins CI: Adverse effects of pancuronium during high-dose fentanyl anesthesia for coronary artery bypass grafting. Anesthesiology 62:708-713, 1985.
2. Girard D, Shulman BJ, Thys DM et al: The safety and efficacy of esmolol during myocardial revascularization. Anesthesiology 65:157-164, 1986.

Table Means ± S.D. *=$p < 0.05$

	A	B	C	D
HR	52±7	51±8	50±6	49±7*
MAP	78±13	74±16*	74±13*	72±13*
PAP	24±13	22±12	21±11*	21±11*
PCWP	17±8	15±7*	15±7*	14±7*
CVP	12±5	10±4*	10±5*	10±5*
CO	3.28±0.77	2.98±0.63	2.86±0.54	2.89±0.56
RVEF	37±5	35±7	34±7	34±7