

Title: CARDIOVASCULAR EFFECTS OF BW B1090U DURING NITROUS OXIDE-OXYGEN-NARCOTIC ANESTHESIA

Authors: R.B. Forbes, M.D., W.W. Choi, M.D., M.P. Mehta, M.D., D.J. Murray, M.D., M.D. Sokoll, M.D., S.D. Gergis, M.D., C. Douglas, M.S., Martha Abou-Donia, Ph.D.

Affiliation: Department of Anesthesia, University of Iowa College of Medicine, Iowa City, Iowa 52242 and Wellcome Research Laboratories Co., Research Triangle Park, North Carolina 27709

**Introduction.** BW B1090U is a new non-depolarizing neuromuscular blocking agent currently under clinical evaluation. Previous clinical studies in human volunteers and healthy surgical patients indicate that the neuromuscular blockade produced by BW B1090U has a rapid<sup>1,2</sup> onset and a relatively short duration of action. The purpose of this study was to evaluate the cardiovascular responses that occur following the administration of BW B1090U to surgical patients during nitrous oxide-oxygen-narcotic anesthesia.

**Methods.** Fifty-four patients of either sex (excluding females with child-bearing potential), ASA Class I or II, aged 18-70 years, weighing less than 110 kg were studied after obtaining institutionally approved informed consent. Patients were premedicated with morphine (0.10-0.15 mg/kg) and atropine (0.004-0.008 mg/kg) IM 45-60 minutes prior to the induction of anesthesia. Anesthesia was induced with fentanyl (1-2 µg/kg), thiopental (4-8 mg/kg) IV and maintained with 70% nitrous oxide in oxygen. Additional thiopental and fentanyl were administered as clinically indicated. Ventilation was controlled to maintain end tidal CO<sub>2</sub> at 35-40 mmHg (Perkin-Elmer mass spectrometer). The twitch response of the adductor pollicis muscle to ulnar nerve stimulation was elicited by supramaximal square wave pulses of 0.2 msec duration at a frequency of 0.15 Hz quantitated using an FT10 transducer. Values obtained from analysis of the twitch recording included: onset time of maximal block, magnitude of maximal block, and duration of block from injection to 5%, 25% 50%, 75% and 95% recovery.

After stabilization of the twitch response each patient received one of six doses of BW B1090U (0.03, 0.04, 0.05, 0.08, 0.15 or 0.20 mg/kg) administered as an IV bolus over 5-10 seconds to establish a single dose-response relationship. The ECG and pulse (HR) were monitored continuously throughout the study. In the lower dose groups (0.03-0.05 mg/kg) blood pressure was monitored every minute using an automated oscillotonometer. In those patients that received drug doses estimated to equal or exceed ED<sub>95</sub> an indwelling radial artery catheter was placed for continuous monitoring and recording of systolic, diastolic and mean (MAP) arterial blood pressure. Data are expressed as mean ± S.E. and were analyzed using analysis of variance.

**Results.** The % change from control in mean arterial pressure and heart rate at 1, 2 and 5 minutes following bolus administration of BW B1090U are presented in Table 1. Preliminary analysis of the data indicate that at doses up to 0.15 mg/kg (approx. 2 x ED<sub>95</sub>) there was no significant change in MAP. At 0.20 mg/kg

administration of BW B1090U resulted in a significant fall in MAP at one and two minutes. This change was of short duration and within five minutes the MAP was within 20% of control in 8/9 patients in this group.

There was no significant change in heart rate at any time.

**Discussion.** Bolus administration of BW B1090U in doses up to 0.15 mg/kg had no significant effect on mean arterial pressure and heart rate at 1, 2 and 5 minutes following drug injection. Rapid administration of bolus doses, exceeding 2 x ED<sub>95</sub>, may be associated with a fall in blood pressure in some patients.

#### References.

1. Savarese JJ, Ali HH, Basta SJ, et al: Neuromuscular and cardiovascular effects of BW B1090U in anesthetized volunteers. *Anesth Analg* 64:A278, 1985
2. Basta SJ, Savarese JJ, Ali HH, et al: The neuromuscular pharmacology of BW B1090U in anesthetized patients. *Anesthesiology* 63:A318, 1985

Table 1. Percent Change in MAP and HR from Baseline following Bolus Doses of BW B1090U.

Dose mg/kg	% Control		
	1 min	2 min	5 min
MAP			
0.03	98.0±2.7	96.0±2.2	90.7±2.8
0.04	98.4±1.1	93.9±7.2	91.7±2.5
0.05	97.9±1.7	96.2±2.3	91.2±3.7
0.08	97.0±1.2	94.3±1.3	93.6±1.4
0.15	92.3±3.1*	96.3±1.6*	97.4±2.1
0.20	81.4±5.8	84.7±4.2	91.7±2.1
HR			
0.03	101.3±2.4	102.0±1.8	95.8±3.7
0.04	97.6±2.1	96.5±2.6	92.0±2.3
0.05	94.5±2.0	92.3±2.4	89.6±2.3
0.08	95.8±3.1	91.1±2.6	87.0±3.0
0.15	103.0±2.7	99.7±2.7	92.6±2.2
0.20	106.0±2.6	101.9±3.7	99.0±5.2

\*P < 0.05

Table 2. Number of patients exhibiting > 20% change in MAP following a bolus dose of BW B1090U.

Dose mg/kg	n	Number of patients		
		1 minute	2 minutes	5 minutes
0.03	9	0	0	0
0.04	9	0	0	0
0.05	9	0	0	0
0.08	9	0	0	0
0.15	9	1	0*	0*
0.20	9	3	3	1

\*Same patients as at one minute.