Title: NEUROMUSCULAR EFFECTS OF BW1090U IN PATIENTS UNDER NARCOTIC-N_2O ANESTHESIA

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Introduction. BW1090U is a new nondepolarizing neuromuscular blocking relaxant.[1] Preliminary data in human studies indicate that it is potent and short-acting with an estimated ED_{95} of 0.09-0.10 mg/kg and a 25-75% recovery index of 5-7 min.[2] This is a progress report of an independent study of its basic clinical neuromuscular pharmacology in surgical patients.

Methods. Fifty-two elective surgical patients, ASA I-II, aged 19-65 years, weighing 50-110 kg gave informed consent and were studied. The protocol was approved by institutional committees. Premedication consisted of meperidine 50-75 mg i.m. and/or diazepam 10 mg p.o. Anesthesia was induced and maintained with 2.5-5 mg/kg meperidine with supplemental fentanyl 2-12 μg/kg followed by thiopental 4-10 mg/kg, and N_2O 50-67% in O_2. Ventilation was controlled manually before intubation of the trachea, and with a ventilator afterwards at 10-15 ml/kg, 8-12 breaths/min. Core temperature was 35-36.5°C. The systolic, mean and diastolic blood pressures were determined at one minute intervals. ECG was continuously monitored. All patients received 0.5-0.7 L. of 5% dextrose in lactated Ringers or saline solutions during the preparation. Vital signs and neuromuscular response was stabilized for 5 minutes before study began. The trachea was intubated after the initial dose of BW1090U or the reblocking dose of BW1090U, whichever produced greater than 85% neuromuscular block first. BW1090U was the sole relaxant used in all patients. It was injected i.v. and flushed rapidly (5-10 seconds). The ulnar nerve was stimulated with 0.2 ms supramaximal electric pulses at 0.1 Hz. The muscle response was quantified electromyographically (EMG). Forty-three patients (Group I-V) were observed through spontaneous recovery from the initial dose of BW1090U to greater than 95% of control. They then received a reblocking dose of BW1090U. The remainder of patients were not allowed complete spontaneous recovery. All patients then received BW1090U to maintain 90-99% block by additional bolus injections or by infusion. At the end of surgery, residual neuromuscular block was reversed as needed. All data were (mean ± SEM) or otherwise specified.

Results. (1) Potency, onset and duration of action of BW1090U are presented in Table 1. The ED_{25}, ED_{50}, ED_{75} and ED_{95} determined by log-probit regression analysis were 0.037, 0.049, 0.071, and 0.12 mg/kg in that order. (2) Characteristics and reversibility of block: absence of fasciculation, train-of-four fade, and reversibility with clinical doses of edrophonium indicate that the block is nondepolarizing. Edrophonium 0.3-0.5 mg/kg was given to 17 patients during 95-25% residual block. EMG response reached 90% of control within 9 ± 2 minutes. (3) BW1090U by infusion: seventeen patients received additional BW1090U by infusion. The infusion rate for 90-99% block was 4.8 ± 0.5 μg/kg/min. (4) Reblocking dose: reblocking dose (0.075, 0.1, or 0.15 mg/kg) invariably produced a block greater than 93% within 70-90 seconds of injection. (5) Cardiovascular responses: no patients had irregular ECGs or any cardiovascular or hyperthermic responses following BW1090U. With the highest dose (0.15 mg/kg), the mean BP were 89 ± 4, 81 ± 4, 85 ± 4, and 87 ± 4 torr at -1, 1, 3, and 5 min. The one-minute pre- and post-BW1090U values were significantly different ($p < 0.004$) but needed no clinical intervention. (6) Other observations: five of the 52 patients reacted with flushing of the upper part of the body. No patients had wheezing.

Discussion. Our data indicate that BW1090U is a potent, short-acting, reversible, nondepolarizing neuromuscular blocking relaxant with cardiovascular margin of safety no less than that of atracurium. The onset is slow when the dosage is low. But it is comparable to that of other nondepolarizing relaxants currently available. The reblocking dose has accelerated onset and greater block than the initial dose. Neuromuscular effects of BW1090U in larger doses, by infusion, during other anesthetic courses, in various patient populations, as well as cumulativeness, "priming", and so forth await further study. In agreement with other reports, we conclude that BW1090U is likely a clinically useful compound with a unique duration of action between the ultrashort-acting (succinylcholine) and the intermediate-acting (vecuronium, atracurium) neuromuscular relaxants.

References.

1. Savarese JJ, Wastilla WB, El-Sayad HA, et al: Anesthesiology 61:A306, 1984
2. Basta SJ, Savarese JJ, Ali HH, et al: Anesthesiology 63:A318, 1985

Table 1. Potency, Onset and Duration of BW1090U

Group		I	II	III	IV	V	VI
Dose (mg/kg)		0.03	0.05	0.06	0.08	0.15	0.15
n		(9)	(9)	(7)	(9)	(9)	(9)
EMG block, full effect (%)	Mean	18	54	68	83	97	97
	SEM	8	11	11	7	2	3
Inj. to full effect (min)	Mean	6	8	5	6	5	5
	SEM	1	1	1	0.3	1	1
Inj. to recovery to 75% (min)	Mean		15	13	17	22	
	SEM	-	2	2	2	3	-
*Recovery Index 25-75% (min)	Mean		6	4	6	6	
	SEM	-	1	1	1	1	-

* overall, Recovery Index for n=20 is 6 ± 0.4 min mean ± SEM