

Title: DOSE-DURATION RELATIONSHIP OF BW1090U BY BOLUS INJECTIONS
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Introduction. BW1090U is a new nondepolarizing neuromuscular blocking relaxant which is hydrolyzed by human plasma cholinesterase at about 90% the rate of succinylcholine.^{1,2} Its duration of action is short, about 1/2 that of atracurium or 2X that of succinylcholine. The ED₉₅ appears to be around 0.09-0.10 mg/kg.³ This pharmacological profile suggests that the duration of action of BW1090U may not increase proportionately with the dose. We examined the dose-duration relationship of BW1090U up to 0.20 mg/kg bolus doses in elective surgical patients under narcotic-N₂O anesthesia.

Methods. The study was approved by the institution and all patients signed informed consent. Fifty-eight ASA I-II patients, age 19-65 yrs., weight 50-110 kg, received mainly meperidine 50-75 mg I.M. for premedication. Anesthesia consisted of meperidine or fentanyl or both, totaling the equivalent of 150-250 mg meperidine, followed by thiopental 4-8 mg/kg and N₂O 40-67% in O₂. Ventilation was controlled manually until the trachea was intubated, and with a ventilator afterwards, both aiming at normocarbida. BW1090U was the sole relaxant used. The trachea was intubated 5-6 minutes after either the initial dose or the reblocking dose of BW1090U, depending on which dose produced the desired degree of block. The initial dose, the reblocking dose, and the maintenance dose were varied to define the dose requirement of the sample population. All doses were injected i.v. rapidly (5-10 seconds) and flushed. The reblocking dose was given on complete or near complete (>95%) recovery of neuromuscular transmission from the initial dose. The first maintenance dose was given on recovery of neuromuscular transmission from the reblocking dose to 10% of control. In all patients arterial blood pressure was measured once every one minute; ECG and core temperature were monitored continuously. The ulnar nerve was stimulated at the wrist with needle electrodes, by 0.2 ms supramaximal electric pulses at 0.1 Hz from a Grass 88 stimulator. The compound electromyographic twitch response (EMG) of the first interphalangeal muscle of the hand was quantified. Originally each group consisted of 9 patients and was assigned to receive a progressively increasing dose. For this study, data were collected from all incidents wherein the initial dose produced a block greater than 50% (Table 1), wherein the reblocking dose produced a block greater than 90% (Table 2), and wherein the first maintenance dose returned the block to greater than 95% depression (Table 3).

Results. Table 1 presents the durations of action of the initial bolus dose of BW1090U. Table 2 presents the duration of action of the reblocking dose of BW1090U. Table 3 presents the duration of action of the first maintenance dose of BW1090U.

Discussion. Our results confirm that BW1090U has a short duration of action and that the initial and the reblocking doses of BW1090U

do not last proportionately longer with increasing dose. This dose-duration relationship is probably related to the first-order kinetics of BW1090U. It is an advantage for tracheal intubation because it allows use of large doses to speed up the onset of block without risking protracted paralysis. It would be a disadvantage for maintenance of neuromuscular block during prolonged surgery because large doses are uneconomical and the inconvenience of frequent injections is always there. Continuous infusion then becomes the obvious method of choice. In perspective, we recommend that BW1090U be used in bolus doses of 0.075-0.15 mg/kg intraoperatively for rapid reestablishment of a profound block after neuromuscular transmission has once been blocked but has since recovered, or in bolus doses of 0.05-0.10 mg/kg for briefly extending a profound block of 10-15 minutes duration during short surgical procedures. Continuous infusion is recommended for prolonged relaxation. Details of BW1090U infusion and its use in large doses for tracheal intubation with or without "priming" are currently under multicenter investigations.

References.

1. Savarese JJ, Wastilla WB, El-Sayad HA, et al: *Anesthesiology* 61:A306, 1985
2. Ali HH, Savarese JJ, Embree PB, et al: *Anesthesiology* 65:A282, 1986
3. Basta SJ, Savarese JJ, Ali HH, et al: *Anesthesiology* 63:A318, 1985

Table 1: Duration of action of initial dose of BW1090U (inj. to recovery to 50% of control):

Dose (mg/kg)	0.03	0.05	0.06	0.075	0.08	0.15	0.20
Duration (min) mean	11	13	10	14	15	20	25
SEM	—	1	2	—	2	2	3
n =	1	5	6	2	8	8	4

Table 2: Duration of action of reblocking dose of BW1090U, (inj. to recovery to 5% of control):

Dose (mg/kg)	0.075	0.1	0.15	0.20
Duration (min, mean ± SEM)	12 ± 1	14 ± 1	15 ± 1	24 ± 5
n =	8	19	16	4

Table 3: Duration of action of first maintenance dose of BW1090U, (inj. to recovery to 10% of control):

Dose (mg/kg)	0.05	0.075	0.1
Duration (min, mean ± SEM)	8 ± 1	13 ± 1	15 ± 2
n =	7	8	11