TITLE: PHARMACOLOGY OF BW 954U

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BW 954U is a bis-benzylisoquinolium diester whose structure differs from that of mivacurium (BW B1090U) by the absence of a double bond in the bridging alkyl chain.

In experiments performed in anesthetized and ventilated cats, arterial BP, and ECG were monitored and isometric twitch (at 0.1 Hz) was recorded from soleus and tibialis anterior muscles. Intermittent stimulation of the soleus at 400 Hz • 10 sec. was done to evoke post-tetanic twitch potentiation (PTP) in order to assess prejunctional effects[1]. A dose response curve was constructed for soleus (n=5) and tibialis anterior (n=5) muscles.

In ventilated rhesus monkeys under halothane anesthesia, tibialis anterior twitch (at 0.15 Hz), BP and HR were recorded.

Data are summarized in the tables.

In the cat, the tibialis anterior was more resistant to the effects of BW 954U than the soleus. PTP was ablated by sub-blocking doses, suggesting a significant prejunctional effect[1]. At up to 0.32 mg/kg average changes in heart rate and arterial pressure were less than 8%. These changes were brief, lasting 2 - 5 minutes. At 0.64 mg/kg iv, (approx 8 x ED95) MAP fell 8.6% ±.09%.

The duration of block in monkeys is 25% longer than than that of succinylcholine and about 50% shorter than that of mivacurium.

Conclusion: BW 954U is a potent nondepolarizing neuromuscular blocking drug with short duration, minimal cummulative effect and reasonable cardiovascular safety.

Reference:

1. J. Gen. Physiol. 47: 53 - 70, 1963.

Experiments in cats

DOSE mg/kg	%Block Soleus	% Block Tibialis Ant	Duration* Soleus	Duration* Tibialis Ant	MAP** % control
0.02	25	-	9.9		100
0.04	59	42	12.9	7.86	104
0.06	98	73	19	10.1	107
0.08	99.6	90	20.8	15.0	103
0.16	100	100	28.3	21.1	104
0.32	100	100	40.7	25.1	101

* all times are in minutes(injection to 95% twitch recovery
**Soleus and tibialis anterior preparations combined.

Experiments in monkeys (n=4)

Dose, mg/kg	TibialisTwitch***	HR***	BP***
0.05	80	100	100
0.1	33	96	99
0.2	100	96	99
0.4	100	99	99
0.8	100	95	97
1.6	100	100	82

*** Results are given as a % of control.

TITLE: VISUAL ASSESSMENT OF FADE WITH LOW INTENSITY STIMULATING CURRENT

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Introduction. Following general anesthesia and intraoperative use of muscle relaxants, it is not uncommon for patients to evidence partial residual blockade. Train-of-four (TOF) testing with a mechanogram has documented that, following general anesthesia with nondepolarizing muscle relaxants, the incidence of residual curarization (i.e., TOF<0.70) is between 16-42%.[1,2] Train-of-four monitoring is the most common technique of assessing such patients, as it does not require a pretesting baseline. Unfortunately, it has two significant limitations: a) tactile or visual assessment often misses significant reduction in the T_4/T_1 ratio; and b) stimulation at supramaximal current can be quite uncomfortable. In a recent study,[3] unmedicated subjects, using a visual analog scale of 0 (minimum discomfort) to 10 (maximum), rated 50 mA TOF stimulation at a score of 5.0. Of note, comparable stimulation at 20 mA resulted in a mean score of 2.0. The purpose of the present study was to document visual assessment of accelographic TOF-elicited fade at lower (thus more comfortable) stimulating currents.

Methods. Following institutional IRB approval, data were collected on 15 patients undergoing general anesthesia. Patients were induced with thiopental 5 mg/kg, and intubation was facilitated with succinylcholine 1 mg/kg. Anesthesia was maintained with isoflurane 0.75-1.00% end-tidal and 70% N_2O in O_2. A vecuronium infusion was begun to achieve a TOF ratio of 0.1-0.7, determined by an Accelograph (Biometer, Denmark). An anesthesiologist who was unaware of the presence or degree of neuromuscular blockade was asked to assess the existence of fade in the train-of-four evoked responses delivered at random current intensities of 20, 30, 50 and 60 mA. The data were grouped by current (20 and 30 mA vs. 50 and 60 mA) and by accelographically determined T_4/T_1 ratio (0.0-0.4 and 0.4-0.7).

Results. There were 25 patients in the 50 and 60 mA group who were judged to have no fade by the blinded observers, whereas there were 9 in the 20 and 30 mA group (Table).

Discussion. The present data suggest that in the degree of blockade tested (0.1-0.7), visual assessment of fade to TOF stimulation tended to be more sensitive at lower currents. Although the incidence of falsely identifying "no fade" in the T_4/T_1 0.1-0.4 group was similar in the low current (20+30 mA) and the supramaximal current (50+60 mA) groups, three times as many anesthesiologists incorrectly assessed the patients as exhibiting "no fade" when using 50 or 60 mA currents in the T_4/T_1 0.4-0.7 group (20 vs. 7). Thus, if TOF stimulation were employed to evaluate an awake patient suspected of having residual neuromuscular blockade, the use of low current may be preferable. It provides for sensitive visual detection of fade while being associated with less discomfort.

Current	Visual Assessment	T_4/T_1 0.1-0.4	T_4/T_1 0.4-0.7
20+30 mA	Fade	27	28
	No fade	2	7
50+60 mA	Fade	26	18
	No fade	5	20

References
1. Anesthesiology 50:539-541, 1979
2. Anesthesiology 69:272-276, 1988
3. Anesth Analg 70:S68, 1990