Title: VERAPAMIL-MAGNESIUM NEUROMUSCULAR BLOCK IN VIVO

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Introduction. Verapamil, a calcium channel blocker, produces a dose related depression of indirect muscle twitch in vivo[1] and in vitro.[2] It also potentiates neuromuscular relaxants.[3] Its interaction with magnesium sulfate (Mg) has not been studied. This is of particular interest to us since pregnant women receiving verapamil to treat supraventricular tachycardia in the mother or fetus in utero could be administered $MgSO_4$ for pregnancy-induced hypertension. We investigated the neuromuscular effects of verapamil and its effects on: the ED_{50}, concentration at 50% block, and the time for 25-75% recovery of magnesium-neuromuscular block in rabbits.

Methods. Twenty healthy male New Zealand white rabbits were anesthetized with chloralose 60 mg/kg and pentobarbital 15 mg/kg injected intraperitoneally. Ventilation was controlled via tracheostomy. Esophageal temperature was maintained between 36-38°C. The carotid artery was cannulated for arterial blood pressure (BP) and heart rate (HR) monitoring and the jugular vein for drug administration. The sciatic nerve was stimulated with 0.2 ms supramaximal electric pulse once every 10 seconds, and the tibialis anterior muscle twitch was quantified both electromyographically (EMG) and mechanomyographically (MMG). The animals were divided into 3 groups. Group I (n=7) animals received only Mg; its ED_{50} and spontaneous recovery of 25-75% block were determined. This group served as control. Group II (n=7) received verapamil 0.2 mg/kg I.V. in 0.1 mg/kg increments every 5 min. Thirty minutes later, Mg was administered and parameters as in Group I determined. Group III (n=6) received verapamil 0.5 mg/kg I.V. in a similar manner. Thirty minutes later Mg was administered and parameters as in Group I were measured. In all rabbits after dose response studies, Mg was infused to maintain a 50% neuromuscular block for 30 min at which point blood was sampled for determination of serum concentration of Mg. Data was analyzed by unpaired t test, $p < 0.05$ was considered significant.

Results. Verapamil in doses administered caused a prompt and brief (2-5 min) decrease in BP. There was no significant change in HR (Table I). Hemodynamic parameters were at control levels when Mg infusion was started 30 min later. There was no significant decrease in EMG or MMG following verapamil alone. There was no significant change in the ED_{50} of Mg in the presence of verapamil 0.2 or 0.5 mg/kg. The serum concentration of Mg at 50% block likewise showed no verapamil effect. Verapamil also did not significantly affect the 25-75% recovery time of Mg. Although at the higher dose there was a tendency for the recovery time to increase, this was not statistically significant (Table II).

Discussion. Verapamil in doses of 0.2 and 0.5 mg/kg administered I.V. to rabbits failed to significantly inhibit neuromuscular transmission. These results agree with those of others.[3] The same doses however were shown to potentiate the effects of curariform relaxants and succinylcholine. Since calcium antagonizes Mg, one would expect a Ca channel blocker to enhance the neuromuscular effects of magnesium. Our results did not show any potentiation. This could be due to verapamil blocking Mg ion entry as well as Ca, so that the balance of ions is maintained. In patients treated with verapamil, the neuromuscular effects of Mg may essentially remain unaffected. Its therapeutic index in terms of neuromuscular transmission probably will remain the same.

References.

1. Lawson NW, Kraynack BJ, Gintautas J: Neuromuscular and electrographic responses to verapamil in dogs. Anesth Analg 62:50-54, 1983
2. Kraynack BJ, Lawson NW, Gintautas J, et al: Effects of verapamil on indirect muscle twitch responses. Anesth Analg 62:627-630, 1983
3. Durant NN, Nguyen N, Briscoe JR, et al: Potentiation of pancuronium and succinylcholine by verapamil. Anesthesiology 57:A267, 1982

TABLE I.

Gp	Drug	BP Before Drug	BP After Drug	HR Before Drug	HR After Drug
I	Mg --	95 ± 4.36 *	66 ± 5.98 *	214 ± 16 *	258 ± 4.0 *
II	$V_{0.2}$ mg/kg	91 ± 4.8 *	49 ± 4.8 *	217 ± 10	219 ± 13
	$V_{0.2}$ + Mg	88 ± 4.8 *	61 ± 5.4 *	230 ± 8	257 ± 16
III	$V_{0.5}$ mg/kg	83 ± 3.8 *	38 ± 2.95 *	220 ± 18	224 ± 16
	$V_{0.5}$ + Mg	74 ± 2.3 *	47 ± 3.3 *	237 ± 15	230 ± 15

Data = Mean ± SEM
* P <0.05 - * vs *

Table II

Gp	V mg/kg		Twitch depression % change	Mg ED_{50} mg/kg	Mg conc at 50% blk. meq/l	T25-75%/Rec. (min.)
I n=7	—	EMG:	—	79.1 ± 7.8	6.55 ± 0.34	7.8 ± 1.0 *
		MMG:		72.0 ± 8.2		7.6 ± 1.0
II n=7	0.2	EMG:	7.7 ± 2.9	68.3 ± 3.04	6.84 ± 0.4	7.7 ± 0.7
		MMG:	3.29 ± 1.36	63.6 ± 4.0		7.67 ± 1.0
III n=6	0.5	EMG:	3.83 ± 1.42	82.8 ± 9.03	6.88 ± 0.5	8.83 ± 1.47
		MMG:	5.67 ± 2.48	81.0 ± 6.0		8.25 ± 1.0

Data are in Mean ± S.E.M.
All P values comparing effects of V. on Mg are > 0.2