Title: INTERACTION BETWEEN MAGNESIUM AND VECURONIUM IN RABBITS

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INTRODUCTION: Magnesium sulfate is widely used in the treatment of pre-eclamptic and eclamptic toxemias. It is also well known that Magnesium (Mg) enhances succinylcholine and d-tubocurarine neuromuscular block.[1,2] The purpose of this study is to examine the interaction of magnesium with vecuronium (ORG-NC45), a new nondepolarizing muscle relaxant of intermediate duration of action.

METHOD: The sciatic nerve and the tibialis anterior muscle of twenty male New Zealand rabbits ranging from 3-4.2 kg in weight were used to determine neuromuscular block. These rabbits were anesthetized with alpha-chloralose 50 mg/kg and pentobarbital 25 mg/kg injected into the peritoneal cavity. The animals were then tracheostomized and mechanically ventilated with room air. The esophageal temperature was maintained between 38-40°C. Drugs were administered through the cannulated jugular vein. Arterial blood pressure and heart rate were continuously monitored from a cutdown of carotid artery. Sciatic nerve was stimulated by a Grass S88 stimulator with supramaximal electric pulses of 0.2 ms duration generated at 0.1 Hz. The response of the ipsilateral tibialis anterior muscle was quantified electromyographically. Groups of rabbits received intravenous doses of magnesium sulfate either 25(n=4), 50(n=4), 100(n=4), 200(n=4) or 400(n=4) mg/kg, injected as incremental doses of 25 mg/kg. Thirty minutes after complete recovery of the blood pressure, heart rate and the magnesium induced neuromuscular block, blood sample was obtained for determination of serum magnesium concentration. The dose requirements of vecuronium corresponding to those serum concentrations of magnesium were determined by construction of a cummulative dose response curve for each rabbit. The ED_{50} of vecuronium was determined by log-profit dose response analysis. An additional twelve rabbits received vecuronium under the same conditions without magnesium pretreatment as control. Linear regression analysis was used to construct the relationship of ED_{50} of vecuronium to the magnesium concentration.

RESULTS: Data are summarized in Table I. All results are presented as the mean ± S.E.M. Figure below shows the relationship between the serum concentration of magnesium and the ED_{50} of vecuronium based on data in Table I. Two rabbits died after receiving a total dose of 400 mg/kg of magnesium sulfate.

DISCUSSION/CONCLUSION: One specific effect of magnesium is to block neuromuscular junction by (1) Decreasing the amount of acetylcholine liberated from the motor nerve endings. (2) Decreasing the endplate response to the available acetylcholine. (3) Decreasing the muscle fiber excitability. The results of this study indicate that the serum concentration of magnesium and the dose requirements of vecuronium is linearly and inversely related. The higher the magnesium concentration, the lower the dose of vecuronium is required. Our data confirms the previous observations that magnesium sulfate treated patients require less muscle relaxants during surgery. The use of a peripheral nerve stimulator is recommended to avoid an excessive dose of vecuronium and profound paralysis.

REFERENCES:

1. Ghoneim MM, Long JP: The interaction between magnesium and other neuromuscular blocking agents. Anesthesiology 32:23-27, 1970.

2. Giesecke, Jr AH, Morris RE et al.: Of magnesium, muscle relaxants, toxemic parturients, and cats. Anesth Analg 47:689-695, 1968.

TABLE I

		MAGNESIUM SULFATE PRETREATMENT				
	Control (n=12)	25 mg/kg (n=4)	50 mg/kg (n=4)	100 mg/kg (n=4)	200 mg/kg (n=4)	400 mg/kg (n=2)*
Serum MG (mEq/l)	2.21±.10	3.25±.33	3.55±.53	3.70±.10	4.50±.13	5.85±.75
ED_{50} of Vecuronium (µg/kg)	8.47±.32	7.65±.29	6.15±.80	5.65±.50	5.03±.67	4.40±.60

Values are mean ± S.E.M.

* 2 rabbits died