Anesthesiology
V 75, No 3A, Sep 1991

A802

TITLE: DO ANTIARRHYTHMIC DOSES OF MAGNESIUM (MG) POTENTIATE VECURONIUM (V) NEUROMUSCULAR BLOCK?

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Introduction: Mg salts are often administered to treat ventricular arrhythmias after myocardial infarction or cardiovascular surgery. Although the doses used (typically 1-2 g $MgSO_4$) are much smaller than those used for toxemia of pregnancy, whether such low-dose Mg therapy might potentiate neuromuscular blockade and lead to unacceptable postoperative muscle weakness remains unknown.[1] We tested whether small doses of $MgSO_4$ would reduce the ED_{95} or increase the duration of V paralysis in elective surgical patients.

Methods: After IRB approval, we randomly assigned 20 consenting patients to receive either $MgSO_4$ (30 mg/kg) or placebo in a blinded fashion. ED_{95} of V was determined during thiopental-fentanyl anesthesia in both groups by administering 10 μg/kg boluses until 95% twitch depression was measured. Trains of 4 supramaximal stimuli were delivered to the ulnar nerve while adductor pollicis isometric tension was measured using a strain gauge. Venous blood obtained at baseline, 5 min after the bolus of either $MgSO_4$ or placebo, and 30 min after the bolus was centrifuged and filtered for measurement of ultrafilterable Mg concentration (Mg_u). Mg_u approximates ionized Mg concentration, the active Mg species.[2] Data are reported as means ± SEM. Groups were compared using Mann-Whitney U and student's t tests. $P<.05$ was considered significant.

Results: ED_{95} of V was 57±3 μg/kg after $MgSO_4$ and 66±5 μg/kg after placebo ($p=.2$). The delay to 25% twitch height recovery was 25±4 min ($MgSO_4$+V) and 24±5 min (placebo+V) ($p=.9$). Mg_u at baseline was similar in the two groups. Mg_u increased significantly in the patients given $MgSO_4$ (from .98±.06 to 1.90±.27 and 1.75±.13 mg/dl); Mg_u did not change significantly in the placebo patients (from .95±.07 to .80±.08 and .80±.04 mg/dl). Mg_u in the 2 groups differed significantly at both 5 and 30 min, indicating a sustained elevation in Mg_u in the $MgSO_4$-treated group.

Discussion: Our data show no adverse neuromuscular effects following administration of antiarrhythmic doses of $MgSO_4$ to elective, carefully monitored patients during V administration. This is consistent with the conclusions of a recent report of pancuronium-Mg interaction in which ED_{95} was not determined.[3] We conclude that there appears to be no significant adverse interaction between low doses of $MgSO_4$ and V. We would caution against extrapolating these findings to other neuromuscular blockers or to higher doses of V. We recommend careful neuromuscular monitoring whenever $MgSO_4$ and a nondepolarizing neuromuscular blocker will be co-administered.

References:

1. Sinatra et al: Anesth Analg 64:1220-2, 1985
2. Zaloga et al: Crit Care Med 15:813-6, 1987
3. James et al: Br J Anaesth 66:247-9, 1991

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Title: INFLUENCE OF BLOOD SAMPLING SCHEDULE ON VECURONIUM KINETIC (PK) AND DYNAMIC (PD) PARAMETERS

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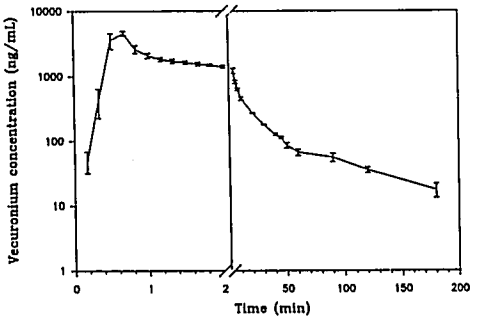
The importance of the duration of blood sampling to characterize the elimination phase of a drug is well established. However, little attention has been directed towards the timing of the first blood samples. This study investigates the influence of early blood sampling on vecuronium PK-PD modeling.

Methods. Five consenting ASA I-II patients scheduled for elective surgery were anesthetized with thiopental, fentanyl, nitrous oxide and isoflurane. Single twitch stimulation (0.1 Hz) was applied to the ulnar nerve and the force of contraction of the adductor pollicis was recorded. Following a 0.1 mg/kg vecuronium IV bolus, arterial blood samples were obtained every 10 sec for the first 2 min, then frequently until 180 min. Vecuronium plasma levels were measured by HPLC.



Results. Peak plasma concentrations of vecuronium were generally reached 40 sec post-dose. If during the first 2 min only the 1 and 2 min samples are considered, the area under the curve (AUC) for the first 10 min is underestimated by 22%. The mean residence time (MRT) and the AUC to infinity were less influenced by the sampling schedule. The K_{e0} estimated by a non parametric method[1] were greatly affected. Sigmoidal Emax modeling of neuromuscular blockade (NMB) vs vecuronium effect compartment concentrations indicated comparable EC_{50} for the onset and recovery phases (160 ± 11 vs 165 ± 11 ng/mL) but different slopes (6.4 ± 0.6 vs 4.7 ± 0.2). Significant differences were observed for all parameters (mean ± SEM; paired t-test, $p<0.05$).

		Blood sampling interval for the first 2 min	
		10 sec	1 min
MRT	*min*	44.5 ± 5.1	47.8 ± 5.7
AUC 0-10 min	*ng.min/mL*	10119 ± 431	7843 ± 317
0-inf		25633 ± 621	23862 ± 437
K_{e0}	min^{-1}	0.059 ± 0.007	0.092 ± 0.014

Discussion. Early 10 sec sample collection provides valuable information otherwise not obtained with 1 min sampling. A well-defined initial portion of the plasma concentration vs time curve is a prerequisite for PK-PD modeling and especially for error-free estimation of K_{e0}. In addition, the steeper sigmoid during the onset of NMB emphasizes the need for a more thorough investigation of plasma concentrations during this phase.

[1] Clin Pharmacol Ther 1986; 40: 86-93.

Funded by MRC (grant MA-10274)