

Administration of magnesium sulphate before rocuronium: effects on speed of onset and duration of neuromuscular block

B. KUSSMAN, G. SHORTEN, J. UPPINGTON AND M. E. COMUNALE

Summary

The speeds of onset of pancuronium, atracurium and vecuronium are increased by prior administration of magnesium sulphate. A prospective, randomized, double-blind, controlled, clinical study was performed to examine the effects of prior i.v. administration of magnesium sulphate 60 mg kg⁻¹ on the neuromuscular blocking effects of rocuronium 0.6 mg kg⁻¹ during isoflurane anaesthesia. Neuromuscular function was measured electromyographically (Relaxograph) in 30 patients who received either magnesium sulphate 60 mg kg⁻¹ or normal saline, 1 min before rocuronium 0.6 mg kg⁻¹. Mean onset times were similar in the two groups (magnesium sulphate 71 (SD 20) s; normal saline 75 (23) s), but times to initial, 10% and 25% recovery from neuromuscular block were significantly longer in the magnesium sulphate group (42.1 (16.3), 49.0 (12.4) and 56.5 (13.2) min, respectively) than in the saline group (25.1 (9.1), 33.0 (11.1) and 35.6 (13.2) min, respectively) ($P < 0.05$ in all three cases). Administration of magnesium sulphate was not associated with adverse haemodynamic effects. Prior administration of magnesium sulphate, under the study conditions described, prolonged rocuronium-induced neuromuscular block but did not increase speed of onset. (*Br. J. Anaesth.* 1997; 79: 122–124).

Key words

Ions, magnesium. Pharmacology, magnesium sulphate. Neuromuscular block, rocuronium. Neuromuscular block, measurement of response.

The action of non-depolarizing neuromuscular blockers is potentiated by magnesium sulphate (MgSO₄)¹ and the speeds of onset of pancuronium, atracurium and vecuronium are increased by prior administration of MgSO₄.^{2–4} The aims of this study were to determine the effects of prior administration of MgSO₄ 60 mg kg⁻¹ i.v. on the onset and duration of rocuronium-induced neuromuscular block, and to quantify the haemodynamic effects of bolus i.v. administration of MgSO₄ 60 mg kg⁻¹ on heart rate and arterial pressure.

Methods and results

After obtaining Institutional Review Board approval and written informed consent, we studied 30 ASA I or II patients, aged 18–65 yr, undergoing surgery requiring tracheal intubation. A prospective, randomized, double-blind study was performed.

Patients received midazolam < 0.05 mg kg⁻¹ i.v. as premedication if indicated clinically. After 3 min of preoxygenation, anaesthesia was induced with thiopentone 4 mg kg⁻¹ and fentanyl 1.5 µg kg⁻¹, and maintained with 1–1.5% isoflurane (inspired concentration) and 66% nitrous oxide in oxygen.

The response of the first dorsal interosseous muscle of the hand to supramaximal train-of-four (TOF) stimulation of the ulnar nerve at the wrist at 10-s intervals was measured electromyographically (Relaxograph, Datex Instrumentarium, Helsinki, Finland). The forearm was wrapped with a cotton blanket to minimize cooling. After induction of anaesthesia and having established a stable twitch response (at least three successive equal responses to TOF stimulation), either MgSO₄ 60 mg kg⁻¹ or normal saline (NaCl) was given i.v. over 1 min according to random allocation. One minute after completion of this infusion, rocuronium 0.6 mg kg⁻¹ was administered via a fast flowing i.v. infusion over 5 s. The times to 90% (T₁ = 10%) and complete (T₁ = 0%) single twitch depression, and to initial, 10% and 25% spontaneous recovery were measured. Heart rate and arterial pressure were measured immediately before and after induction of anaesthesia, 30 s after administration of MgSO₄ 60 mg kg⁻¹ or NaCl, and at 1-min intervals for 3 min after administration of rocuronium (Hewlett Packard Component System, Andover, MA, USA). The minimum nasopharyngeal temperature measured with a thermistor temperature probe during the study was recorded (Hewlett Packard, part no. 21075A, Andover, MA, USA).

Sample size was calculated based on the following: taking the level of statistical significance as $\alpha = 0.05$ and $\beta = 0.2$, where $1 - \beta$ = the

BARRY KUSSMAN, MB, BCH, FFA(SA), GEORGE SHORTEN, MD, JEFFREY UPPINGTON, MD, MARK E. COMUNALE, MD, Department of Anaesthesia and Critical Care, Beth Israel Hospital, and Harvard Medical School, Boston, MA 02215, USA. Accepted for publication: March 6, 1997.

Correspondence to G. S.

power of the study, a difference of 20% between two groups in onset time was sought.

Effect size (onset time) = $108 \times s \times 20\% = 21.6$.

Standardized effect size = effect
size/SD = $21.6/24^* = 0.9$

*Based on previous data.⁵

Data were analysed using unpaired (pharmacodynamic variables) and paired (within-patient comparison of heart rate and arterial pressure) two-tailed Student's *t* tests. Significance was defined as $P < 0.05$.

The two groups were similar in age, weight, sex distribution and minimum nasopharyngeal temperature. Mean onset times to T1 = 10% (MgSO₄ 71 (SD 20) s, NaCl 75 (23) s) and T1 = 0% (MgSO₄ 105 (36) s, NaCl 107 (30) s) were similar in the two groups. The time to initial recovery was longer in the MgSO₄ group (42.1 (16.3) min) compared with the NaCl group (25.1 (9.1) min) (fig. 1). Similarly, times to 10% and 25% single twitch recovery in the MgSO₄ group (49.0 (12.4) and 56.5 (13.2) min, respectively) were greater than those in the NaCl group (33.0 (11.1) and 35.6 (13.2) min, respectively) (fig. 1).

Recovery data to 25% twitch suppression were not obtained in two patients. One patient with normal renal function, who received MgSO₄ and who was not receiving magnesium-containing medications, had a markedly prolonged block. The first evidence of spontaneous recovery occurred 65 min after administration of rocuronium. Plasma magnesium concentration was 4.0 mmol litre⁻¹, 75 min after administration of MgSO₄ 60 mg kg⁻¹; baseline plasma magnesium concentration had not been obtained. The Relaxograph was accidentally disconnected in the second (NaCl group) patient during complete ablation of twitch response. Although arterial pressures were similar in the two groups throughout the study, heart rates in the MgSO₄ group were significantly greater than those in the NaCl group immediately after induction of anaesthesia (mean 83 (SD 9) and 74 (10) beat min⁻¹,

respectively; $P = 0.014$), after administration of MgSO₄ or NaCl (92 (12) and 78 (16) beat min⁻¹, respectively; $P = 0.013$), and 1 min after administration of rocuronium (91 (11) and 77 (16) beat min⁻¹, respectively; $P = 0.01$).

Comment

We have demonstrated that prior administration of MgSO₄ did not increase speed of onset, but prolonged duration of action of rocuronium-induced (0.6 mg kg⁻¹) neuromuscular block.

In the presence of high concentrations of magnesium, fewer calcium ions bind to acetylcholine containing vesicles, thus decreasing acetylcholine release from the nerve ending.⁶ Postsynaptically, magnesium ions may compete with calcium ions for activation sites on the myosin ATPase necessary for excitation-contraction coupling.⁷

Previous studies of the effect of MgSO₄ on onset times for non-depolarizing neuromuscular blocking agents have produced conflicting results.²⁻⁴ It appears that the shorter the "baseline" onset time, the less effect MgSO₄ pretreatment has on its reduction. This may be because the time of delivery of the neuromuscular blocking agent is unaffected. The remaining portion of onset time, which can be influenced by the pharmacodynamic effect of MgSO₄, is short, approximately 30–40 s. Similar proportionate decreases in onset time result in smaller absolute effects for fast compared with slow onset agents. For example, administration of MgSO₄ 60 mg kg⁻¹ before pancuronium 0.1 mg kg⁻¹ resulted in a fast onset time (68.3 (25.9) s). The results of this study are consistent with those of others who have shown that prior administration of MgSO₄ consistently prolongs neuromuscular block induced by intermediate-acting, non-depolarizing neuromuscular blocking agents.³ In contrast, MgSO₄ 60 mg kg⁻¹ did not prolong the neuromuscular blocking effects of pancuronium 0.1 mg kg⁻¹.² One possible explanation is that the effects of a bolus dose of MgSO₄ are diminished by the time that spontaneous recovery from the longer acting pancuronium begins to take place. The differences in heart rate between the MgSO₄ and NaCl groups immediately after induction of anaesthesia were not clinically significant. The small samples used in this study increased the likelihood of encountering such a difference randomly.

In summary, MgSO₄ did not increase the speed of onset, but prolonged the duration of rocuronium-induced neuromuscular block. Administration of MgSO₄ at this dose before rocuronium offered no clinical advantage and because an unanticipated, prolonged neuromuscular block could result, is potentially harmful.

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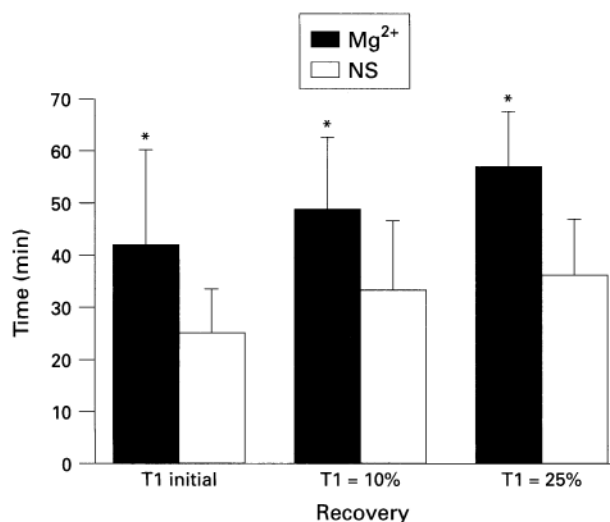


Figure 1 Times to initial recovery (T1 initial) and to T1 = 10% and T1 = 25% in the magnesium sulphate (Mg²⁺) and normal saline (NS) groups. * $P < 0.05$.

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