PRIMING OF PANCURONIUM WITH MAGNESIUM

M. F. M. JAMES, P. A. SCHENK AND B. W. VAN DER VEEN

SUMMARY
Magnesium inhibits the release of acetylcholine from the motor nerve terminal and thus potentiates the action of the non-depolarizing neuromuscular blocking drugs. We have examined the possibility that this effect might enhance the speed of onset of non-depolarizing block with pancuronium. Following the administration of pancuronium 100 μg kg⁻¹, 95% depression of thumb twitch occurred in 68.3 (SD 25.9) s in magnesium-pretreated subjects and in 73.7 (19.5) s in a group given a priming dose (10 μg kg⁻¹) of pancuronium. Trachea/intubation was performed after 97.8 (22.5) s in the magnesium group and in 121.0 (37.5) s in the control group (ns). It is concluded that pretreatment with magnesium does not usefully increase the speed of onset of action of pancuronium.

KEY WORDS

Suxamethonium has remained the agent of choice for rapid sequence tracheal intubation techniques for emergency anaesthesia, primarily because of its extremely rapid onset of action and the profound nature of the neuromuscular block produced. Unfortunately, the well-known adverse reactions to this drug and the less common idiosyncratic responses are major disadvantages [1]. Non-depolarizing neuromuscular blockers (NDNMB) are devoid of many of the side effects of suxamethonium. However, despite intensive research, the development of an NDNMB capable of producing profound neuromuscular block with a speed of onset of action comparable to that achieved with suxamethonium has remained elusive. Investigation into this problem concentrated on the modification of administration schedules of established NDNMB, for example: supra-normal bolus doses, the priming principle and the use of combinations of two different NDNMB (purportedly with varying activity at different, specific receptor sites). None of these manoeuvres seriously challenges the role of suxamethonium for rapid sequence tracheal intubation [2]. The effect of NDNMB at the motor end-plate is potentiated by magnesium ions, which interfere with release of acetylcholine from the presynaptic terminal [3]. Conceivably, the reduced release of acetylcholine which magnesium produces, as opposed to the reduced mobilization produced by the NDNMB [4], could result in accelerated onset of paralysis. It is well known that the action of NDNMB is potentiated by magnesium in both animals and man [1], but the influence of the ion on the onset of action of NDNMB has not been studied.

This study compared the effect of magnesium sulphate (MgSO₄) pretreatment on the rate of onset of neuromuscular block produced by an intubating dose of NDNMB with a technique using the priming principle.

METHODS AND RESULTS
The study was approved by the Human Experimentation Ethics Committee of the Medical School, University of the Witwatersrand.

We studied patients (ASA I or II) of both sexes, aged 18–50 yr, undergoing elective surgery requiring tracheal intubation. Subjects meeting the inclusion criteria for the study were asked to give informed consent and were allocated randomly to one of two study groups (A and B) with 10 subjects in each group. Exclusion criteria included absence of informed consent, significant inter-
current disease, pregnancy or possible pregnancy, medication which could affect neuromuscular function, history of previous adverse reactions whilst under general anaesthesia and known allergy to any of the drugs to be used in the study.

Premedication consisted of hydroxyzine 1 mg kg\(^{-1}\) i.m., 1 h before induction of anaesthesia. All patients underwent preoxygenation for not less than 3 min. Three minutes before induction, group B subjects were given pancuronium 10 µg kg\(^{-1}\) i.v., whilst group A subjects received an equivalent volume saline. Anaesthesia was induced with propofol 2-3 mg kg\(^{-1}\) given over 30 s to loss of the eyelash reflex. Anaesthesia was maintained with 50% nitrous oxide in oxygen administered via a Mapleson A breathing system with supported ventilation as required, supplemented by an infusion of propofol 100 µg kg\(^{-1}\) min\(^{-1}\). Subjects in group A then received a “pretreatment” of MgSO\(_4\) 60 mg kg\(^{-1}\) (0.25 mmol kg\(^{-1}\)) i.v. over 1 min, and patients in group B received an equivalent volume of saline. One minute after completion of the pretreatment, both groups received an “intubating dose” of pancuronium bromide 100 µg kg\(^{-1}\) as a bolus.

Twitch height was monitored continuously after induction using a single, repetitive, supra-maximal twitch stimulus applied to the ulnar nerve at 2-s intervals, and the force of contraction in the adductor pollicis muscle was recorded using a Myograph strain gauge transducer attached to the thumb in the normal manner with a continuous written record made on the Myotest chart recorder. The time from administration of the 100-µg kg\(^{-1}\) bolus of pancuronium to 5% control twitch height was determined. At this time, direct laryngoscopy was performed by an investigator blind to the patient group, and intubating conditions were assessed on a five-point scale: 1 = no jaw relaxation, unable to insert laryngoscope; 2 = gross movement in response to laryngoscopy; 3 = marked movement of vocal cord on visualization; 4 = minimal cord movement; 5 = ideal intubating conditions, with no movement.

If the intubating conditions were scored at 3 or greater, tracheal intubation was performed. If the score was 2 or less, laryngoscopy was terminated and intubation reattempted after a further 30 s. The time from administration of the intubating dose of pancuronium to intubation was noted. Blood samples, taken before induction of anaesthesia, after induction, after intubation and at the end of the procedure were analysed for serum concentrations of magnesium by atomic absorption spectrophotometry.

The ECG was monitored continuously and arterial pressure measured at 1-min intervals using a Dynamap automated arterial pressure recording device.

Statistical analysis of the numerical data was performed using Student’s t test, and Fisher’s exact test was used for testing distributions. Significance was defined as \(P < 0.05\). Results for numerical data are presented as mean (sd).

Following administration of MgSO\(_4\), there was a small, non-significant reduction in twitch height, and the mean serum concentration of magnesium at the time of intubation in group A was 2.34 (0.63) mmol litre\(^{-1}\). Serum concentration of magnesium before operation was in the normal range (0.8-1.1 mmol litre\(^{-1}\)) in both groups. The interval from induction to 95% depression of twitch height was 68.3 (25.9) s in the magnesium group and 73.7 (19.5) s in the control group. Intubation was performed after 97.8 (22.5) s in the magnesium group and after 121.0 (37.5) s in the control group.

### Table 1. Cardiovascular responses in the two groups (mean (sd)). SAP, DAP = Systolic and diastolic arterial pressures; HR = heart rate

<table>
<thead>
<tr>
<th></th>
<th>Group A (Magnesium)</th>
<th>Group B (Control)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SAP (mm Hg)</td>
<td>DAP (mm Hg)</td>
</tr>
<tr>
<td><strong>Baseline</strong></td>
<td>141.9 (20.0)</td>
<td>90.0 (16.2)</td>
</tr>
<tr>
<td><strong>Induction</strong></td>
<td>118.5 (22.5)</td>
<td>77.0 (25.2)</td>
</tr>
<tr>
<td><strong>Agent</strong></td>
<td>118.5 (28.7)</td>
<td>77.8 (23.7)</td>
</tr>
<tr>
<td><strong>Intubation</strong></td>
<td>135.8 (18.4)</td>
<td>85.6 (16.6)</td>
</tr>
</tbody>
</table>

BRITISH JOURNAL OF ANAESTHESIA
Six patients in the magnesium group coughed with intubation, compared with four in the control group. No patient in either group was judged to be ready for tracheal intubation, with our scoring system, in less than 75 s. Loss of thumb twitch did not appear to be a reliable guide to laryngeal or diaphragmatic paralysis, particularly in the magnesium group. At the end of the procedure, approximately 50 min after induction, neuromuscular block was antagonized easily in both groups and there was no evidence of prolongation of the effect of pancuronium in the magnesium group. At this time the serum concentration of magnesium in the magnesium group was 1.23 (0.07) mmol litre⁻¹. There were no significant differences in cardiovascular variables between the groups (table I).

**COMMENT**

This study has demonstrated that, whilst magnesium may have some effect on the speed of onset of NDNMB, it is unlikely to produce significant, clinically useful effects on onset time with pancuronium. The serum concentrations of magnesium obtained were considerably less than the 5 mmol litre⁻¹ at which neuromuscular weakness occurs and the 10–12 mmol litre⁻¹ at which serious cardiac problems are seen [5]. It is conceivable that greater concentrations of magnesium could have produced a different result, but at the risk of significant paralysis occurring before administration of the blocking drug. It might be argued that there was a trend towards shorter onset times in the magnesium group, and that a larger sample size might have produced a statistically significant result. However, even if a statistically significant result was obtained, the reduction in onset time would still not be sufficient to allow this technique to be advocated for rapid sequence tracheal intubation, although it could be argued that the technique was marginally superior to the priming principle. Even in hypertensive obstetric patients in which MgSO₄ has been used for control of convulsions, suxamethonium remains the neuromuscular blocking drug of choice for rapid sequence tracheal intubation. It is of interest that, although subjects were judged to be ready for intubation earlier in the magnesium group, slightly more of them coughed, suggesting that the diaphragm may be more resistant than the adductor pollicis to magnesium. This is similar to the effect described for the non-depolarizing neuromuscular blockers [6], and might suggest varying sensitivity according to muscle type.

**REFERENCES**