Recurarization in the recovery room following the use of magnesium sulphate

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A 67-yr-old man weighing 104 kg, with a history of hypertension, underwent laparoscopic cholecystectomy. His preoperative serum potassium was 3.4 mmol litre$^{-1}$. The patient received cisatracurium 14 mg, which was antagonized with neostigmine 2.5 mg and glycoprolate 0.5 mg at the end of the procedure. A repeat dose of neostigmine 2.5 mg and glycoprolate 0.5 mg was required 5 min later, as the neuromuscular block was incompletely antagonized. He was transferred to the recovery room about 10 min after the end of surgery, having had recovery of neuromuscular function demonstrated with no fade on peripheral nerve stimulation at 50 Hz for 5 s. Five minutes later he developed rapid atrial fibrillation, which was treated over 5 min with magnesium sulphate 2 G i.v.. Within the next 3 min, the patient developed marked neuro-
muscular weakness of a non-depolarizing pattern leading to respiratory arrest. This necessitated re-intubation of the trachea and artificial ventilation for 20 min, until there was spontaneous recovery of neuromuscular function demonstrated by peripheral nerve stimulation. Administration of magnesium appears to have caused recurarization in this patient. The dose of magnesium alone would not be expected to cause muscle weakness. Potentiation of neuromuscular blocking drugs by magnesium is well recognized, and we recommend its use is avoided for at least 30 min after reversal of neuromuscular block.

**Keywords**: anaesthesia; complications, morbidity; neuromuscular block, cisatracurium; pharmacology, magnesium

Accepted for publication: May 9, 2003

The use of parenteral magnesium has increased over the last few years, particularly in obstetrics, in surgery for phaeochromocytoma, and in the management of patients with tetanus.1 Magnesium also has a role in cardiology,1 especially in the treatment of arrhythmias including atrial fibrillation.2

The depressant effects of magnesium at the neuromuscular junction were first described in the 1950s,3 when it was shown to cause a reduction in pre-junctional acetylcholine release, with consequent potentiation of non-depolarizing neuromuscular blocking drugs.4 5 These effects necessitate neuromuscular monitoring when magnesium and neuromuscular blocking drugs are given together. The following case report illustrates that even when magnesium is administered after neuromuscular function has recovered postoperatively, if the patient has recently received neuromuscular blocking drugs, then synergism between the two agents may lead to recurarization.

**Case report**

A 67-yr-old man was to undergo for laparoscopic cholecystectomy. He had a history of hypertension, which was well controlled (arterial pressure 140/85 mm Hg). He had no prior cardiovascular symptoms and a good exercise tolerance. He was obese, weighing 104 kg, with a height of 1.81 m (body mass index of 31.5 kg m⁻²), and had a hiatus hernia. His medication at the time of surgery was enalapril and lansoprazole. He had undergone several uneventful anaesthetics in the past. There was no recorded difficulty with tracheal intubation. Physical examination was unremarkable. The resting ECG showed sinus rhythm with a rate of 80 beats min⁻¹, with a normal QRS axis. There were voltage criteria for left ventricular hypertrophy, and some lateral lead ST depression. His serum potassium was 3.4 mmol litre⁻¹, with the rest of his biochemistry within normal limits.

Following pre-oxygenation, anaesthesia was induced with propofol 200 mg, alfentanil 1 mg, granisetron 1 mg, and cisatracurium 14 mg. Cricoid pressure was applied until the trachea was intubated, and the patient’s lungs were ventilated with nitrous oxide 67%, oxygen 33%, and isoflurane to an end-tidal concentration of 1%. A total of morphine 10 mg of was administered during the operation. Anaesthesia and surgery were uneventful apart from a fall in the patient’s oxygen saturation to 91% after pneumoperitoneum, requiring an increase in PₐO₂ to 50%. Isoflurane was increased to an end-tidal concentration of 1.3%. Oxygen saturation remained at 94–96% thereafter. He remained in sinus rhythm throughout, and his arterial pressure remained within normal limits.

At the end of surgery, 40 min later, neuromuscular block was antagonized with glycopyrrolate 0.5 mg and neostigmine 2.5 mg. A few minutes after this, some tracheal tug was noted. Peripheral nerve stimulation showed a train-of-four (TOF) count of four twitches at 2 Hz, but with obvious fade at 50 Hz for 5 s. A repeat dose of glycopyrrolate 0.5 mg and neostigmine 2.5 mg was administered. Five minutes later there was no demonstrable fade at 50 Hz and the patient’s respiratory pattern was normal. The trachea was extubated and the patient transferred to the recovery room.

On arrival in the recovery room he had an oxygen saturation of 94%, a heart rate of 100 min⁻¹ and an arterial pressure of 160/90 mm Hg. He remained stable for about 5 min, when his heart rate suddenly became irregular and increased to 170 beats min⁻¹, with an arterial pressure of 194/110 mm Hg. He received oxygen 60%. ECG confirmed rapid atrial fibrillation. The patient was treated with an i.v. bolus of magnesium sulphate 2G i.v. over 5 min, and the ventricular response rate slowed over the next minute to 120 beats min⁻¹ and an arterial pressure of 154/88 mm Hg. However, 3 min later the patient’s respirations became shallow, and he became agitated before respirations ceased and his oxygen saturation fell to 80%. Cricoid pressure was re-applied and his trachea re-intubated, following which he was given midazolam 5 mg. The urgency of the situation did not permit administration of anaesthetic agents before re-intubation. Peripheral nerve stimulation detected only the
first twitch of the TOF, and marked fade on stimulation at 50 Hz. The patient’s lungs were ventilated with oxygen and the patient was sedated with boluses of propofol 30–50 mg every 5 min. No further neostigmine or glycopyrrolate was administered and after 20 min, neuromuscular monitoring demonstrated four twitches and no fade on tetanic stimulation. At this point, his heart rate was 100 beats min\(^{-1}\) in atrial fibrillation and arterial pressure 130/77 mm Hg. Spontaneous ventilation resumed shortly after and his trachea was extubated. He remained in recovery for a further 2 h. He was discharged back to the ward in atrial fibrillation at a rate of 100 beats min\(^{-1}\), having received digoxin 500 μg i.v., with potassium chloride 40 mmol i.v. in progress. His oxygen saturation was 94% on air and a 12 lead ECG showed no changes other than atrial fibrillation.

He was discharged the next day on a maintenance dose of digoxin. There were no new changes on his ECG. On direct questioning, he admitted to having had palpitations several times in the preceding 3 months, lasting for up to 1 h at a time. He was later seen by a cardiologist, who commenced the patient on warfarin and arranged an echocardiograph.

**Discussion**

A patient is described in whom late recurarization occurred following the use of magnesium sulphate for treatment of atrial fibrillation. It is highly likely that magnesium caused the recurarization.

Reversal of neuromuscular block was initially inadequate, demonstrated by tracheal tug and fade with peripheral nerve stimulation. Various factors may have contributed to this: the first dose of glycopyrrolate and neostigmine was probably administered in the presence of considerable neuromuscular block, as a large initial dose of cisatracurium was antagonized within 40 min. In addition, the patient had hypokalaemia, which potentiates neuromuscular block. However, adequate return of neuromuscular function was demonstrated before leaving the operating theatre.

Magnesium has a well-documented effect at the neuromuscular junction, where it inhibits pre-junctional acetylcholine release with consequent potentiation of non-depolarizing neuromuscular blocking drugs.\(^3\)\(^-\)\(^5\) Following antagonism of residual neuromuscular block by neostigmine, adequate neuromuscular function was confirmed by the ability of the patient to sustain tetanus at 50 Hz for 5 s. This correlates well with other clinical tests, such as sustained headlift, which indicate return of normal neuromuscular function, in particular respiratory function and airway protection.\(^6\) Although magnesium alone may cause muscle weakness if administered in large doses,\(^1\) this would be unlikely with the modest dose used in this patient (2G).

Following the administration of magnesium sulphate, the patient redeveloped a non-depolarizing block that took 20 min to resolve spontaneously. We attribute this to a reduction in acetylcholine release at the neuromuscular junction, which under usual circumstances would have had no demonstrable effect. However, in a patient in whom there is still non-depolarizing neuromuscular blocking drug present at the neuromuscular junction, and hence acetylcholine receptor occupancy, even a relatively small dose of magnesium was enough to cause weakness.

Recurarization is a well-documented phenomenon, and was particularly common with the older neuromuscular blocking drugs such as pancuronium, d-tubocurarine, and gallamine. In 1979, Viby-Mogensen demonstrated an incidence of residual curarization of 42% in the recovery room.\(^7\) Later studies confirmed his findings, with an incidence of between 20 and 50% with these drugs.\(^8\)-\(^11\) This problem is less common as the advent of atracurium and vecuronium, possibly as a result of other factors such as improved neuromuscular monitoring and awareness of the problem, with an incidence of residual recurarization of 0–12%.\(^8\)-\(^12\) Indeed, an editorial questioned whether or not we need to antagonize residual neuromuscular block.\(^13\) We think it is unlikely that recurarization was spontaneous as the dose of cisatracurium was given 50 min earlier, and the drug undergoes organ independent biotransformation. Moreover, the onset of recurarization was rapid, dramatic, and closely related to administration of magnesium sulphate.

Use of magnesium sulphate to treat atrial fibrillation merits discussion. There were several therapeutic options including cardioversion. The authors’ familiarity with the drug was a key reason for its use, as it is useful for the termination of many arrhythmias including atrial fibrillation,\(^2\) particularly if hypokalaemia exists.\(^1\) Moreover the drug’s vasodilator and sympatholytic properties are useful in a patient with hypertension and presumed ischaemic heart disease. Other treatment options were amiodarone, \(\beta\) blockade, or digoxin. Cardioversion was not used because the urgency of the situation did not warrant it, and there is a small risk of an embolic event if there is mural thrombus present.

The use of glycopyrrolate and neostigmine is standard to reverse neuromuscular block, and yet it is not without risk. Nausea and vomiting, bronchospasm, and anastomotic dehiscence are all potential problems of neostigmine,\(^13\) as is tachycardia with glycopyrrolate. In this patient, it is possible that glycopyrrolate caused a tachycardia, which then predisposed to the onset of atrial fibrillation, in an individual who may have had episodes of atrial fibrillation in the past. However, glycopyrrolate is associated with greater heart rate stability than atropine.

There is now increased understanding and use of magnesium as a therapeutic agent. The potentiation of neuromuscular blocking drugs by magnesium is well recognized, but it must be remembered that a significant amount of neuromuscular blocking drug may still be present at the neuromuscular junction after apparently normal
muscle tone has returned, and even at this stage muscle weakness may recur. In future, we would avoid the use of magnesium sulphate for at least 30 min after reversal of residual neuromuscular block, to minimize the risk of this recurring.

References
3 Jenkinson DH. The nature of the antagonism between calcium and magnesium ions at the neuromuscular junction. J Physiol 1957; 138: 434–44
7 Viby-Mogensen J, Jørgensen BC. Residual curarization in the recovery room. Anesthesiology 1979; 50: 539–41
11 Jensen E, Engbaek J, Andersen BN. The frequency of residual neuromuscular blockade following atracurium (A), vecuronium (V) and pancuronium (P). A multicenter randomized study. Anesthesiology 1990; 73: A914