

Is it Feasible to Use Magnesium Sulphate as a Hypotensive Agent in Oral and Maxillofacial Surgery?

G M Sanders,**FRCA*, K M Sim,***M Med (Anaes)*

Abstract

We report the results of a feasibility study using intravenous magnesium sulphate for deliberate hypotension in 16 ASA 1 patients undergoing major oral and maxillofacial surgery. All the patients received a standard nitrous oxide, oxygen, isoflurane, opioid and muscle relaxant anaesthetic. Magnesium sulphate was infused at 40 g/h until the mean arterial pressure reached 55 ± 5 mmHg, followed by a maintenance dose of 5 g/h until 30 minutes prior to the end of surgery.

The mean arterial pressure was significantly ($P < 0.01$) reduced by the magnesium sulphate when compared to baseline values. Control of the mean arterial pressure was satisfactory. No patient had reflex tachycardia, cardiac arrhythmia or rebound hypertension. In 14 patients the surgeons thought that the blood loss was less than when using other hypotensive anaesthetic techniques. In 2 patients the surgeons thought the blood loss was excessive. In another 2 patients, the surgeons thought that there was excessive facial swelling on completion of surgery. Postoperative muscle weakness and sedation were not problems clinically. Fourteen patients were extubated immediately after surgery and another 2 patients an hour later in the recovery room. Intraoperative urine output was well maintained. On completion of surgery, the prothrombin time was significantly increased ($P < 0.05$), and the partial thromboplastin time significantly decreased ($P < 0.05$) in all the patients (when compared to preoperative values); the clinical significance of this is unclear.

The use of intravenous magnesium sulphate for deliberate hypotension is feasible in ASA 1 patients using a standard nitrous oxide, oxygen, isoflurane, opioid and muscle relaxant technique. This study forms the basis for a larger controlled study where the issues of postoperative sedation and weakness and coagulopathy can be dealt with in greater detail.

Ann Acad Med Singapore 1998; 27:780-5

Key words: Blood loss, Deliberate hypotension, Hypotensive anaesthesia, Vasodilator

Introduction

Although deliberate hypotension during surgery may potentially cause organ ischaemia, in particular of the myocardium and cerebrum, it is widely used as an adjuvant technique in oral and maxillofacial surgery aimed at reducing blood loss and improving the surgical field. Deliberate hypotension was reported as the fourth commonest cause of anaesthetic death in the United Kingdom,¹ and hypotensive techniques using drugs which depress the myocardium are associated with more complications than those that decrease the systemic vascular resistance.² Intravenous magnesium sulphate may be a good agent for deliberate hypotension because magnesium acts as a vasodilator by increasing the synthesis of prostacyclin³ as well as inhibiting angiotensin converting enzyme activity.⁴ In addition, it has minimal myocardial depressant effects.⁵ More importantly, studies have suggested that magnesium may

have beneficial effects on ischaemic neurons⁶ and myocardium.⁷

There is no previous study employing intravenous magnesium sulphate for deliberate hypotension in ASA 1 patients using a nitrous oxide, oxygen, isoflurane, opioid and muscle relaxant technique. The only study employing intravenous magnesium sulphate for deliberate hypotension has demonstrated the problem of prolonged postoperative sedation in patients undergoing cerebral aneurysm clipping,⁵ however, anaesthesia was maintained utilizing an uncommon total intravenous anaesthetic technique with fentanyl and midazolam. Furthermore, it has long been known that magnesium prolongs blood clotting time as well as inhibiting platelet aggregation,⁸⁻¹¹ though the clinical relevance of these phenomena is unclear.¹² Based on their experience, the experience of others in the treatment of pre-eclampsia,^{13,14} and the intraoperative management of

* Senior Medical Officer
Department of Anaesthesia
Queen Elizabeth Hospital, Hong Kong

** Consultant Anaesthetist
Private Practice, Singapore

Address for Reprints: Dr G M Sanders, Anaesthetic Department, Queen Elizabeth Hospital, 30 Gascoigne Road, Kowloon, Hong Kong SAR.

phaeochromocytomas¹⁵ utilizing intravenous magnesium sulphate, we conducted a series of cases to assess the feasibility of using intravenous magnesium sulphate for intraoperative deliberate hypotension with an anaesthetic technique we are familiar with (i.e. nitrous oxide, oxygen, isoflurane, opioid and muscle relaxant technique). We selected to study oral and maxillofacial surgery because of the relative abundance of American Society of Anesthesiologists (ASA) 1 patients requiring major surgical procedures where hypotensive anaesthesia is routinely used.

Materials and Methods

The study was approved by the Ethics Committee of Singapore General Hospital. Consecutive ASA class 1 adult patients of either sex, who were scheduled for Le Fort I maxillary osteotomy operations with bilateral sagittal osteotomies for correction of malocclusion, were selected for the study. The same surgeon in each case carried out the operation. All of the patients gave written consent. Arrangement was made for the patients to predonate 1 or 2 units of blood for perioperative autologous blood transfusion. They were fasted overnight and premedicated with intramuscular morphine 0.1 mg/kg and hyoscine 5 µg/kg one hour prior to their arrival in the operating theatre. Under local anaesthesia, a peripheral vein was cannulated with a 14 gauge cannula for infusion of fluids and blood products, another vein was cannulated with an 18 gauge cannula for the magnesium sulphate infusion, and the left radial artery was cannulated with a 20 gauge cannula for invasive blood pressure monitoring and blood sampling.

After 3 minutes of pre-oxygenation, anaesthesia was induced with intravenous thiopentone 4 mg/kg, fentanyl 1 µg/kg and suxamethonium 1 mg/kg. The patients were intubated nasally and a throat pack placed. They were ventilated to maintain an end-tidal carbon dioxide level of 4.0 to 4.5 kPa. Anaesthesia was maintained with 33% oxygen in nitrous oxide, isoflurane (end tidal concentration of 0.8%), and intermittent bolus doses of fentanyl 0.5 µg/kg. The isoflurane was discontinued 30 minutes prior to the end of surgery. A single dose of atracurium 0.5 mg/kg was given to each patient after intubation; no more was required due to the muscle relaxing properties of the magnesium.¹⁶

Each patient was catheterized with an indwelling urinary catheter. Measures to conserve the patient's body temperature were instigated, namely the use of a warming blanket, intravenous fluid warmer, and heat and moisture exchanger. Intraoperative monitoring comprised electrocardiography, pulse oximetry, invasive arterial blood pressure measurement, capnography, inspired oxygen concentration measurement, and rectal body temperature measurement (all Hewlett Packard

model 66S). A peripheral nerve stimulator (Fisher Paykel model NS242) was placed over the common peroneal nerve to monitor neuromuscular function. Hourly urine output was measured until 6 hours postoperatively. Total intraoperative blood loss was estimated by weighing swabs and measuring suction drainage. Intraoperative fluid loss was replaced with crystalloids, colloids, autologous whole blood and packed red blood cells according to the overall fluid balance.

At the end of surgery, each patient was given 10 ml of 10% calcium gluconate, neostigmine 2.5 mg and atropine 0.9 mg to reverse the effects of magnesium on the neuromuscular junction.^{16,17} The patients were extubated when adequate tidal volume and good gag and cough reflexes were observed.

Magnesium Sulphate Infusion

Magnesium sulphate (50% solution) was infused immediately after induction with a syringe pump (Terumo STC-523) through the dedicated 18 gauge peripheral intravenous cannula. The initial loading infusion rate was 40 g/h until the goal mean arterial pressure of 55 mmHg was reached, followed by a maintenance infusion rate of 5 g/h. The infusion was stopped 30 minutes prior to the end of surgery. Close titration of the mean arterial pressure could be achieved with either intermittent bolus doses of intravenous fentanyl 0.5 µg/kg (if inadequate analgesia was suspected), or intravenous bolus doses of 0.5 to 1 g magnesium sulphate if there was breakthrough hypertension. Hypotension (a mean arterial pressure of less than 50 mmHg) was treated with 250 ml intravenous boluses of 5% human albumin solution or intravenous boluses of 5 ml of 10% calcium gluconate. It must be noted here that calcium gluconate would have an immediate effect in reversing hypotension due to magnesium sulphate.¹⁶

Arterial blood samples were taken at specific times for laboratory investigations. Arterial blood gases, serum magnesium, potassium and ionized calcium levels were determined pre-induction, at T1 (defined as 30 minutes after the goal mean arterial pressure was reached), on completion of the surgery, and 6 hours postoperatively. The prothrombin time and partial thromboplastin time were measured preoperatively and on completion of surgery. The patients' sedation scores were recorded pre-induction, upon completion of the surgery, and one and six hours postoperatively. The surgeon's opinion of the blood loss and overall satisfaction with the hypotensive technique were recorded. The presence of postoperative nausea and vomiting were also recorded.

The paired *t*-test was used for comparing the data (using the SPSS PC+ statistical package on an IBM compatible personal computer). A *P* value of less than 0.05 was considered statistically significant.

Results

Sixteen ASA 1 patients (age range 14 to 40 years; body weight range 39 to 77 kg; 5 males and 11 females) were co-opted into this case series. The mean duration of the surgery was 282 ± 45 minutes. The mean arterial pressure was lowered smoothly and reliably in all patients by the magnesium sulphate infusion. The mean arterial pressure at T1 was significantly lower than baseline values ($P < 0.01$). The mean time taken to reach the goal mean arterial pressure of 55 ± 5 mmHg was 28 minutes ($SD \pm 12$ min). The mean arterial pressure returned to baseline values 26 minutes ($SD \pm 11$ min) after discontinuing the magnesium sulphate infusion. Two patients developed a single episode each of hypotension (mean arterial pressure < 50 mmHg) which required treatment with an intravenous bolus of 250 ml of 5% human albumin solution; neither patient required calcium gluconate. No patient had arrhythmia or reflex tachycardia during the magnesium sulphate infusion, and no patient had rebound hypertension upon discontinuation of the magnesium sulphate infusion. Cardiovascular parameters are shown in Table I. The mean urine output was good during surgery (1426 ± 690 ml) and this diuresis lasted for up to 6 hours into the postoperative period. The mean urine output in the first 6 postoperative hours was 1182 ml ($SD \pm 460$ ml). The total magnesium sulphate dose given was 20 to 51.5 g (mean 33.5 g). Serum magnesium levels were as shown in Table II. Serum calcium levels remained unchanged throughout the surgery. Serum potassium levels measured during surgery showed a gradual decline due to the diuresis; all 16 patients needed 20 mmol of potassium supplementation intraoperatively to maintain normal serum potassium levels. Compared to the pre-induction values, there were no clinically significant changes in the arterial blood gases during and after the surgery. There

was no clinically significant metabolic acidosis and no patient required intravenous sodium bicarbonate solution.

The first 2 patients were left intubated and breathing on a T-piece at the end of surgery due to excessive sedation (i.e. they responded to pain only); they were both extubated within 1 hour postoperatively. The other 14 patients were extubated at the end of surgery. Clinical assessment showed that all patients had normal respiratory rates, adequate tidal volumes and normal sized pupils on completion of surgery. All patients were awake and alert 6 hours postoperatively. Sedation scores are given in Table III. No patient had recall of intraoperative events despite the isoflurane being discontinued 30 minutes prior to completion of surgery. Monitoring with a peripheral nerve stimulator showed no response to train of four or tetanic stimulation during the magnesium sulphate infusion in all 16 patients. On terminating the infusion, first tetanic contraction with no fade appeared, followed by train of 4 stimulation patterns similar to that seen with depolarizing neuromuscular blockers (i.e. 4 weak twitches with no fade). Once neostigmine and calcium gluconate were given, 4 strong twitches were seen in all the patients.

TABLE III: SEDATION SCORES

Preinduction	10A 6D
Completion of surgery	14D 2P
One hour postoperatively	9A 7D
Six hours postoperatively	16A

A: awake and alert;
D: drowsy but cooperative;
P: responds to pain only;
U: unconscious

TABLE I: CARDIOVASCULAR PARAMETERS AND BLOOD LOSS (MEAN \pm SD)

Baseline mean arterial pressure (mmHg)	85 ± 14
T1 mean arterial pressure (mmHg)	$55 \pm 4^*$
Recovery room mean arterial pressure (mmHg)	78 ± 11
Baseline heart rate (beats/min)	81 ± 12
T1 heart rate (beats/min)	71 ± 8
Recovery room heart rate (beats/min)	83 ± 9
Intraoperative blood loss (ml)	1597 ± 1232

* $P < 0.01$ when compared to the baseline mean arterial pressure.

TABLE II: MAGNESIUM LEVELS IN MMOL/L (MEAN \pm SD)

Preoperative	$0.81 (\pm 0.12)$
T1	$5.94 (\pm 1.50)$
Recovery room admission	$4.12 (\pm 0.96)$
Six hours postoperatively	$1.72 (\pm 0.37)$

When compared to the preoperative values (prothrombin time 12.2 seconds ± 0.5 , partial thromboplastin time 25.6 seconds ± 1.6), the postoperative prothrombin times were increased (postoperative prothrombin time 13.9 seconds ± 1.4) ($P < 0.05$) and the partial thromboplastin times decreased (postoperative partial thromboplastin time 21.4 seconds ± 2.8) ($P < 0.05$) in all 16 patients. In 12 of the 16 patients who received magnesium sulphate, the dental surgeons were satisfied with the operating conditions and thought that the blood loss was less than with other hypotensive anaesthetic techniques. In 2 patients the surgeons thought the blood loss was excessive. In another 2 patients, the surgeons thought that there was excessive facial swelling on completion of surgery. The patients were given autologous and donor blood transfusions as required; no patient received any fresh frozen plasma. Postoperative nausea and vomiting do not appear to be a major problem with this technique; 4 out of 16 patients complained of nausea.

Discussion

The arterial blood pressure can be lowered by either decreasing the systemic vascular resistance and/or reducing the cardiac output. A wide variety of drugs are currently used to achieve this goal, namely:

- 1) volatile anaesthetic agents such as halothane and isoflurane,
- 2) directly acting vasodilators such as sodium nitroprusside, glyceryl trinitrate and hydralazine,
- 3) alpha and/or beta adrenergic blockers such as labetalol, esmolol and propranolol,
- 4) the neuromuscular blocking agent d-tubocurarine, and
- 5) combinations of the above.

This long list of drugs used in hypotensive anaesthesia suggests that there is as of now no ideal method of inducing deliberate hypotension. All the drugs currently in use have their drawbacks, such as impaired vital organ perfusion (with oliguria), myocardial depression, cardiac arrhythmia, cyanide toxicity, rebound hypertension, bronchospasm and tachyphylaxis. The main reasons that magnesium sulphate was chosen for this study were: 1) magnesium sulphate has been shown to protect ischaemic neurons and myocardium,^{6,7} and 2) magnesium sulphate is a vasodilator with minimal myocardial depression.³⁻⁵ Our main concerns were the ability of magnesium sulphate to control the blood pressure, its effects on neuromuscular junctions, postoperative sedation, and its effects on blood coagulation and platelet aggregation.

When compared with deliberate hypotension induced by sodium nitroprusside, the control of the blood pressure by magnesium sulphate infusion is not as tight. Indeed, as it takes approximately half an hour to reach the desired mean arterial pressure with magnesium sulphate, we recommend that the infusion be started immediately after the induction of anaesthesia; this gives time for the magnesium to work while preparations are being made for the surgery. Nitroprusside infusion, however, is associated with rebound hypertension and reflex tachycardia because sustained renin release, which causes vasoconstriction via angiotensin I and II, is stimulated by nitroprusside infusion. Angiotensin I and II act both as direct vasoconstrictors and also by causing release of catecholamines from the adrenal glands.¹⁸ There is no rebound hypertension or reflex tachycardia associated with magnesium sulphate infusion probably because hypermagnesaemia is associated with inhibition of angiotensin converting enzyme activity, sympathetic blockade, slowing of sino-atrial node transmission, depression of carotid baroreceptors, and diminished release of adrenal catecholamines.^{4,16}

Crozier et al⁵ employed magnesium sulphate infusions for deliberate hypotension in patients undergoing

cerebral aneurysm clipping. They used an initial magnesium sulphate dose of 40 g/h until a mean arterial pressure of 70 mmHg was reached, followed by 20 g/h until the goal mean arterial pressure was reached, and then 10 g/h for the duration. We modified the dosing regimen to 40 g/h until the goal mean arterial pressure was reached, followed by a maintenance infusion of 5 g/h. With this regimen we found that our T1 serum magnesium levels were lower than with Crozier et al's patients without loss of the hypotensive effect.

Magnesium is a central nervous system depressant and causes a reduced anaesthetic requirement.¹⁹ All of our patients were drowsy postoperatively, but this did not prove to be a problem clinically. Fourteen were judged to be suitable for extubation on the operating table at the end of surgery and 2 were extubated within an hour in the recovery room. All were awake and alert within 6 hours. The absence of signs of narcotic overdose and normal train of 4 patterns excluded fentanyl overdose and residual neuromuscular blockade as causes of drowsiness. We would, however, advocate that all patients undergoing a hypotensive anaesthetic technique based on the use of magnesium be admitted to a high dependency area for the first 12 hours postoperatively. This would allow respiratory monitoring, regular arterial blood gas estimations and tight control of fluid and electrolyte balance. In addition, we recommend that magnesium sulphate not be used as a hypotensive agent during neurosurgical procedures where immediate postoperative neurological assessment is required.

Magnesium suppresses the release of acetylcholine and blocks transmission at the neuromuscular junction.²⁰ It also causes increased acetyl cholinesterase activity.²¹ This causes prolonged neuromuscular blockade and paralysis of skeletal muscles with respiratory failure. For this reason the dose of neuromuscular blocking agent must be reduced. Indeed, we found that we only needed a single bolus dose of atracurium at the start of surgery to cover the period of the loading magnesium dose. It must be noted here that all the effects of magnesium can be reversed by the administration of calcium. Mordes and Wacker¹⁶ have detailed the effect of calcium gluconate on neuromuscular function in hypermagnesaemic patients. Brosnan and Boyd¹⁷ demonstrated that physostigmine could also reverse the neuromuscular effects of magnesium to a certain extent.

Hypermagnesaemia has been reported as causing reduced cardiac output, but cardiac output actually increased in the patients in some studies.^{5,13} Hypermagnesaemia has also been reported to cause cardiac arrhythmias. All the arrhythmias reported were in the context of renal failure with its accompanying acidosis and hyperkalaemia, and probably not caused by high magnesium levels alone.⁵ Magnesium is in fact used to treat certain arrhythmias, namely those associ-

ated with digoxin toxicity and torsade de pointes.²² It may also decrease the incidence of malignant arrhythmias in patients with acute myocardial infarction.²³ None of our patients had perioperative cardiac arrhythmias. Our observation confirms similar observations in previous studies.^{5,15}

The major excretory pathway for magnesium is renal.¹⁶ We therefore cannot recommend the use of magnesium sulphate in patients with compromised renal function. Magnesium sulphate infusion causes a profound diuresis, which persists for up to 6 hours after surgery in patients with normal renal function. This is probably caused by renal artery dilatation.²⁴ Oliguria is a common problem during prolonged hypotensive anaesthesia using other drugs (e.g. with labetalol and sodium nitroprusside). In contrast, we found that it was necessary to keep a close watch on intraoperative fluid and electrolyte balance during the magnesium sulphate infusion. Serial serum potassium estimations are therefore recommended during the magnesium sulphate infusion and potassium replacement administered as required. The replacement of potassium is important to avoid the muscle weakness and cardiac arrhythmias associated with hypokalaemia; all of our patients had normal serum potassium levels in the perioperative period.

We cannot explain the postoperative prothrombin time and partial thromboplastin time changes and we did not measure platelet aggregation. The excessive facial swelling and blood loss reported in 4 of our patients might be due to the effects of magnesium on blood coagulation or platelet aggregation. Although reports have shown that hypermagnesaemia affects platelet aggregation and blood coagulation *in vitro* and *in vivo*,⁸⁻¹¹ previous studies employing magnesium sulphate infusions did not report the problem of excessive intraoperative bleeding.^{5,15} Recently, James and Neil¹² have demonstrated increased *r* and *k* times with thromboelastography, and decreased maximum amplitude at serum magnesium levels from 5 to 7 mmol/l. The speed of clot formation as measured by the α angle remained unchanged at serum magnesium levels less than 7 mmol/l and thrombolysis was unaffected by magnesium. Others have also found that platelet function as measured by the bleeding time and blood coagulation function as measured by thromboelastography remained unchanged during magnesium infusions.^{25,26} Nevertheless based on our experience, we cannot recommend the use of magnesium sulphate during surgical procedures where meticulous haemostasis is important.

Other possible benefits of the magnesium sulphate hypotensive technique are:

- (a) Magnesium is a potent bronchodilator and is used in the management of severe acute asthmatic attacks.^{27,28} It may therefore be the agent of choice in asthmatic

patients in whom beta adrenergic blockade is obviously not suitable.

- (b) Magnesium depresses epileptic foci.²⁹ It may thus be the hypotensive agent of choice for epileptic patients.
- (c) Magnesium is a cerebral artery dilator.³⁰ This may reduce the chances of a patient having a cerebrovascular accident whilst undergoing hypotensive anaesthesia.
- (d) Magnesium sulphate is inexpensive. In addition, savings can be made on muscle relaxants.

In conclusion, the results of this preliminary study have demonstrated that the use of intravenous magnesium sulphate infusion for intraoperative deliberate hypotension is feasible in ASA 1 patients undergoing standard nitrous oxide, oxygen, isoflurane, opioid and muscle relaxant anaesthesia. Blood loss appears to be less than with other hypotensive anaesthetic techniques. Intraoperative control of blood pressure was satisfactory without undesirable cardiovascular side effects. Postoperative muscle weakness was not a problem clinically. All patients had a degree of sedation immediately postoperatively. This study forms the basis for a larger controlled study where the issues of postoperative sedation and weakness and coagulopathy can be dealt with in greater detail.

Acknowledgements

The assistance and patience of the surgeons in the Department of Oral and Maxillofacial Surgery of the Government Dental Clinic are appreciated; Dr R Peck and Dr L Y Teh receive special thanks. This study was supported by a grant from the Division of Surgery, Singapore General Hospital.

REFERENCES

1. Utting J E. Pitfalls in anaesthetic practice. *Br J Anaesth* 1987; 59:877-90.
2. Aitkenhead A R. The pattern of litigation against anaesthetists. *Br J Anaesth* 1994; 73:10-21.
3. Nadler J L, Goodson S, Rude R K. Evidence that prostacyclin mediates the vascular action of magnesium in humans. *Hypertension* 1987; 9:379-83.
4. Fuentes A, Goldkrand J W. Angiotensin-converting enzyme activity in hypertensive subjects after magnesium sulfate therapy. *Am J Obstet Gynecol* 1987; 156:1375-9.
5. Crozier T A, Radke J, Weyland A, Sydow M, Seyde W, Markakis E, et al. Haemodynamic and endocrine effects of deliberate hypotension with magnesium sulphate for cerebral-aneurysm surgery. *Eur J Anaesthesiol* 1991; 8:115-21.
6. Kass I S, Cottrell J E, Chambers G. Magnesium and cobalt, not nimodipine, protect neurons against anoxic damage in the rat hippocampal slice. *Anesthesiology* 1988; 69:710-5.
7. Shechter M, Kaplinsky E, Rabinowitz B. The rationale of magnesium supplementation in acute myocardial infarction. *Arch Intern Med* 1992; 152:2189-96.
8. Huntsman R G, Hurn B A L, Lehmann H. Observations on the effect of

- magnesium on blood coagulation. *J Clin Pathol* 1960; 13:99-101.
9. Greville G D, Lehmann H. Cation antagonism in blood coagulation. *J Physiol (Lond)* 1944; 103:175-84.
10. Hughes A, Tonks R S. Platelets, magnesium, and myocardial infarction. *Lancet* 1965; 1:1044-6.
11. Davies D T P, Hughes A, Lomax G D, Tonks R S. Hypermagnesaemia and platelet function in uraemic bleeding. *Lancet* 1968; i:301-2.
12. James M F M, Neil G. Effect of magnesium on coagulation as measured by thromboelastography. *Br J Anaesth* 1995; 74:92-4.
13. Cotton D B, Gonik B, Dorman K F. Cardiovascular alterations in severe pregnancy-induced hypertension: acute effects of intravenous magnesium sulfate. *Am J Obstet Gynecol* 1984; 148:162-5.
14. Sibai B M. Magnesium sulfate is the ideal anticonvulsant in preeclampsia-eclampsia. *Am J Obstet Gynecol* 1990; 162:1141-5.
15. James M F M. Use of magnesium sulphate in the anaesthetic management of phaeochromocytoma: A review of 17 anaesthetics. *Br J Anaesth* 1989; 62:616-23.
16. Mordes J P, Wacker W E. Excess magnesium. *Pharmacol Rev* 1977; 29: 273-300.
17. Brosnan J J, Boyd T E. Agents which antagonize the curare-like action of magnesium. *Am J Physiol* 1937; 119:281-2.
18. Khambatta H J, Stone J G, Khan E. Propranolol alters renin release during nitroprusside-induced hypotension and prevents hypertension on discontinuation of nitroprusside. *Anesth Analg* 1981; 60:569-73.
19. Thompson S W, Moscicki J C, DiFazio C A. The anesthetic contribution of magnesium sulfate and ritodrine hydrochloride in rats. *Anesth Analg* 1988; 67:31-4.
20. Del Castillo J, Engbaek L. The nature of the neuromuscular block produced by magnesium. *J Physiol (Lond)* 1954; 124:370-84.
21. Nachmansohn D. Action of ions on cholinesterase. *Nature* 1940; 145:513-4.
22. McLean R M. Magnesium and its therapeutic uses: a review. *Am J Med* 1994; 96:63-76.
23. Ott P, Fenster P. Should magnesium be part of the routine therapy for acute myocardial infarction? *Am Heart J* 1992; 124:1113-8.
24. Kelly H G, Cross H C, Turton M R, Hatcher J D. Renal and cardiovascular effects induced by intravenous infusion of magnesium sulphate. *Can Med Assoc J* 1960; 82:866-71.
25. Kelleher J F, Millar W L, Reisner L S. Effects of intravenous magnesium sulfate on the bleeding time in healthy volunteers. *Anesthesiology* 1989; 71:A887.
26. Wall M H, Chadwick H S, Chandler W, Ross B K. Thromboelastography in healthy laboring women and in women receiving magnesium for premature labor. *Anesthesiology* 1993; 79:A993.
27. Noppen M, Vanmaele L, Impens N, Schandevyl W. Bronchodilating effect of intravenous magnesium sulphate in acute severe bronchial asthma. *Chest* 1990; 97:373-6.
28. Skobeloff E M, Spivey W H, McNamara R M, Greenspon L. Intravenous magnesium sulfate for the treatment of acute asthma in the emergency department. *J Am Med Assoc* 1989; 262:1210-3.
29. Borges L F, Gucer G. Effect of magnesium on epileptic foci. *Epilepsia* 1978; 19:81-91.
30. Altura B T, Altura B M. Interactions of magnesium and K on cerebral vessels—aspects in view of stroke. Review of present status and new findings. *Magnesium* 1984; 3:195-211.