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ORIGINAL ARTICLE

Effect of magnesium sulphate on bleeding during lumbar discectomy

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Summary

We assessed the effect of magnesium on the amount of bleeding, coagulation profiles and surgical conditions during lumbar discectomy under general anaesthesia. Forty patients, of ASA physical status 1–2 and aged 18–65 years, undergoing single-level microscopic lumbar discectomy, were randomly assigned to magnesium sulphate (50 mg.kg^{-1} in 100 ml saline over 10 min followed by a continuous infusion of 20 mg.kg.h^{-1}) or saline. The mean (SD) estimated blood loss was 190 (95) and 362 (170) ml in the magnesium and saline groups, respectively (mean difference = 172 ml; 95% CI 84–260 ml). The median (IQR [range]) Fromme's scale score for surgical conditions for the magnesium and saline groups were 2 (2–3 [2–3]) and 3 (2–3 [3–4]), respectively ($p < 0.05$). The bleeding time, haemoglobin, platelet count, prothrombin time, international normalised ratio and fibrinogen levels were similar in the two groups. The activated partial thromboplastin time was prolonged in the magnesium group immediately postoperatively and at 6 h after surgery. After the bolus of magnesium, the heart rate was higher and the mean arterial pressure lower in the magnesium group. The use of magnesium sulphate during lumbar discectomy decreases blood loss, and provides better surgical conditions without marked haemodynamic effects.

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Reducing blood loss and improving operating conditions during microscopic lumbar discectomy are important, and controlled hypotension has been used to reduce bleeding. Spinal and epidural anaesthesia are associated with less bleeding than general anaesthesia, but the need to perform these operations in the prone position, combined with patients' preference, results in the use of general anaesthesia in most instances [1]. Magnesium is a well-known adjuvant with analgesic properties and anti-arrhythmic effects. However, the effects of magnesium on surgical bleeding are controversial. Some in vivo and in vitro studies have shown that magnesium causes a prolongation in bleeding time [2, 3]. On the other hand, it has been shown that magnesium has direct vasodilatory effect on peripheral vessels via calcium channel blockade resulting in hypotension and reduced blood loss [4]. In this randomised controlled study, the effect of magnesium sulphate infusion on intra-operative blood loss, surgical conditions, coagulation profiles and haemodynamic parameters in patients undergoing elective microscopic lumbar discectomy was assessed.

Methods

The study was approved by the Ethics Committee of the Ministry of Health DıskapıYıldırım Beyazıt Research and Training Hospital and written informed consent was obtained from each patient. The study was double-blind, randomised and prospective. Forty patients, of ASA physical status 1–2, aged 18–65 years, undergoing single-level microscopic lumbar discectomy, were included. The patients were assigned randomly to one of two groups using a computer-generated random number table, with 20 patients in each group. Patients with the following conditions were not studied:

hypermagnesaemia (on routine pre-anaesthetic biochemical screening); known hypersensitivity to magnesium sulphate; any degree of heart block; hypertension; diabetes mellitus; cardiovascular or renal disease; or a coagulation disorder.

All the patients were premedicated with intramuscular midazolam 0.05 $mg.kg^{-1}$ 30 min before the operation. Electrocardiogram, mean arterial blood pressure and peripheral oxygen saturation (S_pO_2) were monitored (Infinity Delta, Dragger, Germany) and baseline recordings of mean arterial pressure and heart rate were recorded. Following intravenous cannulation, 4 ml venous blood was withdrawn for the measurement of magnesium, haemoglobin, platelet count, prothrombin time (PT), activated partial thromboplastin time (aPTT), international normalised ratio (INR) and fibrinogen. The bleeding time was determined using the Ivy method [5] before induction of anaesthesia. The treatment group received magnesium sulphate infusion and the control group received an equivalent amount of saline in a double-blind fashion. The solutions were prepared by the study co-ordinator and the anaesthetist was blinded to the infused medication. The investigator who assessed blood loss, the surgeon and the investigator who reported the laboratory tests were also blinded to group allocation. The magnesium group received magnesium sulphate 50 $mg.kg^{-1}$ in 100 ml saline by slow infusion over 10 min, followed by a continuous infusion of 20 $mg.kg.h^{-1}$ of magnesium sulphate, and the control group received a saline bolus followed by a continuous infusion.

Anaesthesia was induced with propofol 2–4 $mg.kg^{-1}$ and fentanyl 1 $\mu g.kg^{-1}$ and vecuronium 0.1 $mg.kg^{-1}$ was used to provide neuromuscular blockade. The lungs were ventilated to maintain the end-expiratory partial pressure of carbon dioxide at 4.0–4.6 kPa and anaesthesia was maintained with oxygen 50%, nitrous oxide 50%, sevoflurane and intermittent boluses of fentanyl 0.5 $\mu g.kg^{-1}$. Dose adjustments of sevoflurane and fentanyl were based on clinical signs and haemodynamic measurements. Signs of inadequate analgesia were defined as an increase in heart rate and mean arterial pressure > 20% from baseline. Fentanyl was given first and then the sevoflurane concentration was increased if the response to fentanyl was inadequate. If there was a decrease in mean arterial pressure > 20% from baseline, the patient received a saline infusion and then, if necessary, ephedrine 5 mg. If the heart rate decreased to 45 $beats.min^{-1}$, atropine 0.5 mg was given.

Mean arterial pressure and heart rate were recorded after the initial bolus of magnesium sulphate (or saline), after induction of anaesthesia, after tracheal intubation and every 10 min during surgery. The end-tidal concentration of sevoflurane was recorded every 10 min. Intra-operative blood loss was measured using graduated suction bottles and weighing the swabs, and corrected by subtracting the amount of saline wash used during surgery. Surgical conditions were assessed by one of two neurosurgeons using Fromme's scale (0 = no bleeding, virtually bloodless area; 1 = mild bleeding, not a surgical nuisance; 2 = moderate bleeding, a nuisance but without interfering with accurate dissection; 3 = moderate bleeding that moderately compromised surgical dissection; 4 = heavy bleeding but controllable, significantly interfered with dissection; 5 = massive uncontrollable bleeding) at the end of surgery [6]. The magnesium or saline infusions were stopped at the end of surgery. The coagulation studies, Ivy bleeding time and magnesium levels were repeated after extubation and 6 h after surgery. The duration of surgery and anaesthesia was noted and adverse events or side effects were recorded during the peri-operative period.

The primary outcome was difference in the blood loss. A previous study that compared magnesium and placebo reported a mean (SD) blood loss of 165 (19) ml vs 257 (21) ml [7]. On the basis of this and our own pilot study, a power analysis indicated that a minimum of 14 subjects per group would be sufficient to detect a 50% difference in blood loss with a study power of 90% and $\alpha = 0.05$. We included six additional patients in each group in case of drop-outs. Data analysis was performed using the Statistical Package for Social Sciences V11.5 software (SPSS Inc. Chicago, IL, USA). The Shapiro–Wilk test was used to test the normality of distribution of continuous variables. The mean differences were compared using Student's t-test. Nominal data were analysed using Pearson chi-squared or Fisher's exact tests, as appropriate. Group differences in mean arterial pressure, heart rate and sevoflurane concentration were analysed using a repeated measures ANOVA with Benferroni adjustment for multiple comparisons or Friedman test with Benferroni adjusted Wilcoxon signed-rank test. A p value < 0.05 was considered significant.

Results

Patients' characteristics and duration of surgery and anaesthesia are summarised in Table 1. Heart rate and

Table 1 Patients' characteristics and duration of surgery and anaesthesia in patients undergoing lumbar discectomy and receiving magnesium or saline. Values are mean (SD) or number.

	Magnesium (n = 20)	Placebo (n = 20)	p value
Age; years	48 (9)	49 (11)	N/A
Sex; M/F	10/10	9/11	N/A
ASA physical status; 1/2	14/6	10/10	N/A
Duration of surgery; min	67 (13)	77 (19)	NS
Duration of anaesthesia; min	78 (13)	86 (20)	NS

N/A, not applicable.

mean arterial pressure are shown in Figs 1 and 2. After the bolus of magnesium, the heart rate was higher and the mean arterial pressure was lower in the magnesium group compared with the placebo group. Mean (SD) fentanyl consumption was 100 (31) and 147 (52) μg in the magnesium and saline groups, respectively (difference in means = 47 μg; 95% Cl 25.4–68 μg). Intra-operative end-tidal sevoflurane concentrations are shown in Fig. 3.

There were no differences in the mean (SD) magnesium concentrations pre-operatively (0.89 (0.12) and 0.83 (0.12) $mmol.l^{-1}$) and 6 h after surgery (1.02 (0.20) and 0.86 (0.13) $mmol.l^{-1}$) in the magnesium and saline groups, respectively. The immediate postoperative magnesium levels were 1.57 (0.23) and 0.81 (0.13) $mmol.l^{-1}$ in the magnesium and saline groups, respectively (mean difference 0.76 $mmol.l^{-1}$; 95% CI 0.63–0.88 $mmol.l^{-1}$).

The mean (SD) estimated blood loss was 190 (95) and 362 (170) ml in the magnesium and saline groups, respectively (mean difference = 172 ml; 95% CI 84–260 ml). The median (IQR [range]) Fromme's scale score for surgical conditions for the magnesium and placebo groups were 2 (2–3 [2–3]) and 3 (2–3 [3–4]), respectively ($p < 0.05$). The activated partial thromboplastin time immediately postoperatively and 6 h after surgery was prolonged in the magnesium group, but the values were within the reference range (21–36 s). The bleeding time, platelet count, haemoglobin, PT, INR and fibrinogen levels were similar in the two groups at all times (Table 2).

During the initial infusion of magnesium, three patients complained of localised pain and a sensation of

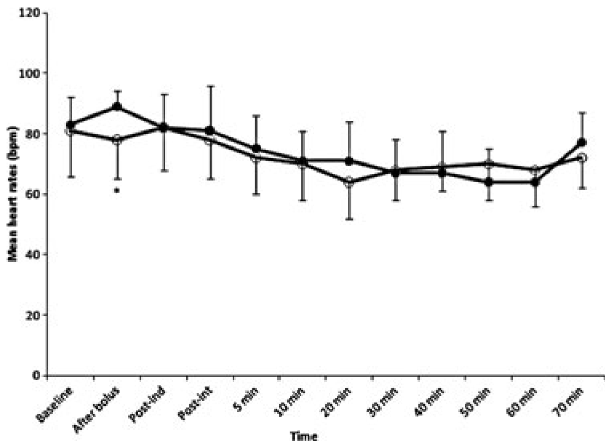

Figure 1 Heart rate after infusion of magnesium (closed circle) or saline (open circle) during lumbar discectomy surgery. Data are mean (SD). ⋆$p < 0.05$.

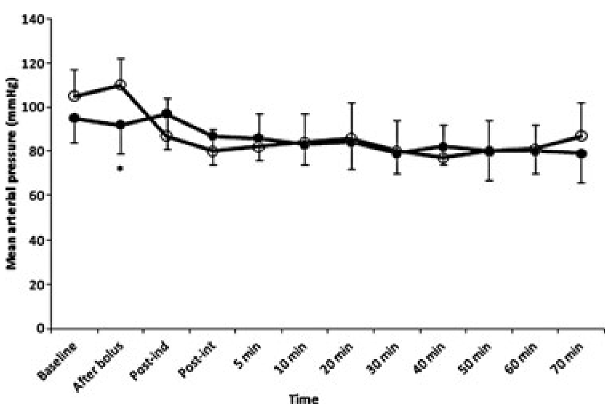

Figure 2 Mean arterial pressure after infusion of magnesium (closed circle) or saline (open circle) during lumbar discectomy surgery. Data are mean (SD). ⋆$p < 0.05$.

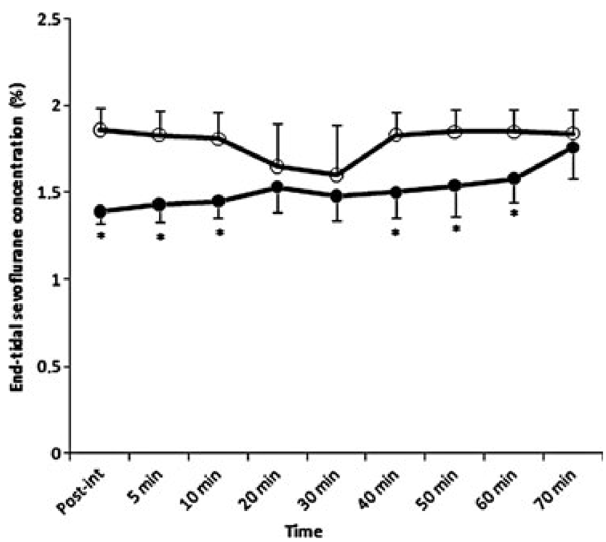

Figure 3 Intra-operative end-tidal sevoflurane concentrations of magnesium (closed circle) and control (open circle) groups Data are mean (SD). ⋆$p < 0.05$.

Table 2 Changes in bleeding time and coagulation parameters during surgery and immediately afterwards in patients receiving magnesium or saline for lumbar discectomy surgery. Values are mean (SD).

	Magnesium (n = 20)	Control (n = 20)	p value
Bleeding time; s			
Pre-operative	238 (59)	246 (67)	NS
Immediately postoperative	297 (64)	265 (62)	NS
6 h after surgery	263 (80)	255 (55)	NS
Platelet count; $\times 10^9.l^{-1}$			
Pre-operative	220 (56)	233 (67)	NS
Immediately postoperative	210 (54)	229 (58)	NS
6 h after surgery	202 (44)	227 (57)	NS
Haemoglobin; $g.dl^{-1}$			
Pre-operative	14.2 (1.5)	13.7 (1.6)	NS
Immediately postoperative	12.5 (1.6)	11.7 (1.7)	NS
6 h after surgery	12.9 (1.9)	12.6 (1.8)	NS
Prothrombin time; s			
Pre-operative	11.9 (0.7)	12.1 (0.7)	NS
Immediately postoperative	12.5 (1.0)	12.6 (0.8)	NS
6 h after surgery	11.7 (0.9)	12.2 (0.6)	NS
Activated partial thromboplastin time; s			
Pre-operative	25.1 (3.5)	23.6 (2.0)	NS
Immediately postoperative	26.0 (2.9)	24.3 (2.1)	0.038
6 h after surgery	24.5 (2.7)	22.6 (1.6)	0.010
INR			
Pre-operative	1.01 (0.1)	1.05 (0.1)	NS
Immediately postoperative	1.06 (0.1)	1.09 (0.1)	NS
6 h after surgery	1.02 (0.1)	1.05 (0.1)	NS
Fibrinogen; $g.l^{-1}$			
Pre-operative	3.0 (0.8)	3.2 (0.7)	NS
Immediately postoperative	2.6 (0.6)	2.8 (0.7)	NS
6 h after surgery	2.7 (0.7)	3.0 (0.6)	NS

heat that resolved spontaneously. One patient in the magnesium group developed profound bradycardia during prone positioning requiring atropine 0.5 mg.

Discussion

We have shown that magnesium sulphate infusion reduces bleeding and provides better surgical conditions without a marked effect on haemodynamic parameters during one-level microscopic lumbar discectomy. The magnesium infusion did not affect coagulation parameters or the bleeding time.

Magnesium produces vasodilation by a direct action, as well as indirectly by sympathetic blockade and inhibition of catecholamine release [8], which may be responsible for hypotension and tachycardia produced by magnesium administration. There are studies that have reported no haemodynamic changes besides very small changes in heart rate and mean arterial pressure [9, 10]. We found no haemodynamic changes except mild hypotension and tachycardia that lasted a short period and resolved spontaneously. Elsharnouby et al. used magnesium sulphate as a vasodilator to produce hypotension and reduce blood loss during endoscopic sinus surgery without any adverse effects [7]. Ryu and colleagues reported a comparison of remifentanil with magnesium for middle ear surgery and found magnesium as effective as remifentanil in sustaining deliberate hypotension during surgery and proper surgical condition [2]. Reducing blood loss provides a better surgical field, which is important in microscopic lumbar discectomy operations. This might be from a decrease in venous pressure in the surgical field. Thus, the mechanism by which magnesium reduces bleeding may due to local vasodilation or a systemic hyptensive effect. We are unable to determine which of these is more important from our study.

As magnesium is a 'natural physiological calcium antagonist' and regulates calcium influx into cells, it may affect the coagulation cascade [3, 11–13]. We measured the haemoglobin, bleeding time, platelet count, PT, aPTT, INR and fibrinogen, which were not different between the groups. Reviewing the literature, we found studies in pregnant women that showed an increased bleeding time. Harnett et al. demonstrated that the time to first clot formation was slower in pregnant patients treated with magnesium sulphate [14], and Fuentes et al. found that the bleeding time was prolonged by ~1 min in pregnant patients who received magnesium sulphate [15]. Kynczl et al. showed that the bleeding time was more than twice as long in women with pregnancy-induced hypertension after magnesium sulphate infusion[16]. Falck et al. studied healthy male volunteers and found no effect on their bleeding time [17]. James and Neil found that magnesium had only minimal effect on coagulation, which was unlikely to be important clinically. With serum magnesium level < 3 $mmol.l^{-1}$, there were no significant effects on coagulation [18]. We did not detect any change in bleeding time, and magnesium levels were < 3 $mmol.l^{-1}$ at all time points. The only parameter of coagulation that was different between the groups was aPTT; however, we believe that difference was not clinically important as all values remained within the reference range at our institution.

Çizmeci et al. established that use of magnesium sulphate reduced the total amount of propofol used for induction and maintenance and that patients reported less postoperative pain [10]. The use of magnesium as an adjuvant in the peri-operative period is related to its actons as an N-methyl-D-aspartate (NMDA) receptor antagonist and calcium channel inhibitor [19]. We found that fentanyl consumption was less in the magnesium group. As expected, blood magnesium concentrations were increased postoperatively in the magnesium group, but there were no reports of symptoms of hypermagnesaemia (such as nausea, vomiting, somnolence or respiratory paralysis). In accordance with other workers [20], we found that magnesium levels had returned to pre-operative levels 6 h after surgery.

In conclusion, administration of a magnesium sulphate (50 $mg.kg^{-1}$ bolus followed by a contiunous infusion of 20 $mg.kg.h^{-1}$) decreases blood loss and provides better surgical conditions without marked haemodynamic effects in patients undergoing microscopic lumbar discectomy.

Competing interests

No external funding or competing interests declared.

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