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Research Article

Evaluation of Different Doses of Intravenous Magnesium Sulfate on Intraoperative Anesthetic Drugs Usage and Postoperative Pain in Posterior Spinal Fusion Surgery

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ABSTRACT

Background: In this study, the effect of different doses of magnesium sulfate on the consumption of anesthetic drugs during surgery and pain after spine surgery has been investigated. In complex spine surgeries, a large amount of sedative and analgesic drugs is prescribed, which will have various systemic effects during and after the operation.

Methods: This study was a double-blind clinical trial, and 80 patients who were candidates for posterior spinal fusion surgery at Luqman Hakim Hospital were included in the study. Patients were randomly divided into four groups (20 people in each group): Group M received magnesium sulfate in three doses (M1=10mg/kg/hr), (M2=15mg/kg/hr), and (M3=20mg/kg/hr). and group S received normal saline. Due to a drop in blood pressure and severe bradycardia in the M3 group, we had to stop the infusion, so the M3 group was excluded from the study, and 60 patients from the M1, M2, and S groups were studied.

Results: The M2 group experienced a decrease in bleeding volume, intraoperative fentanyl consumption, and postoperative pain score compared to the M1 and S groups.

Conclusion: In this study, we showed that the administration of magnesium sulfate during surgery can have positive and protective effects on the quality of anesthesia and the postoperative period. The recommended dose of magnesium was 15 mg/kg/hr because it has the lowest amount of narcotic consumption during the operation and the lowest amount of narcotic and analgesic consumption after the operation, and on the other hand, it has good hemodynamic stability. At the same time, doses higher than 15 mg/kg/hr are not recommended due to the drop in HR and MAP.

Introduction

Fusion operation in the spine is a gold standard treatment method for treatment of many kinds of musculoskeletal disorders in the spine area. This procedure aims to stabilize the spine by limiting motion between unstable vertebrae. Fusion involves connecting one or more vertebrae using a bone graft assisted by stabilizing implants such as screws, rods, and intervertebral cages [1]. Grafts can be positioned between the vertebral bodies, replacing the disc, or placed in the posterior aspect of the vertebrae. Following the surgery,

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the fused vertebrae behave as a single unit, eliminating relative movement. This surgical approach addresses conditions like vertebral fractures, spinal deformities, degeneration of intervertebral discs, tumors, spinal cord injuries, and abnormalities within the vertebrae or discs [2]. Magnesium is an essential cation crucial for human homeostasis, activating approximately 300 enzyme pathways involved primarily in energy metabolism [3-4]. Although the precise analgesic mechanism of magnesium remains unclear, its action on calcium channels and N-Methyl-D-aspartate (NMDA) receptors is believed to be significant [5-6]. NMDA receptors facilitate excitatory synapse transmission and play a key role in central sensitization, particularly in post-surgical pain syndromes. Therefore, NMDA antagonists may prevent heightened nociceptive sensitivity [7-8]. Additionally, magnesium may reduce catecholamine release, subsequently mitigating the response of environmental nociceptors to surgical stress. For decades, magnesium has been utilized to alleviate postoperative pain. The first randomized controlled trial (RCT) investigating magnesium as an adjunct analgesic emerged in 1996, confirming its effectiveness in reducing the need for analgesics during and after surgical procedures [9-11]. Numerous studies have demonstrated that magnesium administration significantly decreases fentanyl requirements in both preoperative and postoperative periods [12-13]. Spine surgery poses unique challenges due to the necessity for stable hemodynamics and a dry surgical field, alongside the positioning of patients during the procedure, which complicates anesthesia management [14-15]. Several clinical studies indicate that magnesium sulfate infusion during general anesthesia lessens the demand for intraoperative anesthetics and postoperative analgesics. However, some researchers argue that magnesium's impact on postoperative pain may be minimal. Limited research has explored the effects of magnesium sulfate during regional anesthesia. One study found that administering 8 mg/kg of intravenous magnesium sulfate resulted in significantly less postoperative pain at intervals of one, three, six, and twelve hours compared to a placebo group. Furthermore, morphine requirements in the first 24 hours post-surgery were reduced [16]. Despite its limited penetration of the blood-brain barrier (BBB), intrathecal administration of fentanyl (25 mcg) combined with magnesium sulfate (50 mg) has been shown to prolong analgesia more effectively than fentanyl alone, likely due to magnesium's enhancement of narcotics' analgesic effects on both central and peripheral mechanisms [17]. In 2007, a systematic review suggested that postoperative magnesium might not significantly influence pain intensity or analgesic needs, highlighting the necessity for additional research as potential analgesic benefits still exist [9]. Beyond pain management, magnesium sulfate is the preferred treatment for controlling and preventing seizures in eclampsia and pre-eclampsia [18-19], while also offering effects such as vasodilation and increased cardiac output through systemic vascular resistance (SVR) reduction [20-21].

Methods

In this clinical trial study, after obtaining the approval of the ethics committee, 80 patients who were candidates for posterior spinal fusion surgery and who met the inclusion criteria were included in the study. The patients were divided into four groups, including M1, M2, M3, and S group (the control group), who received the same volume of placebo (normal saline). Each patient was given a sealed envelope containing the information of the study group and the control group. It was given and opened by a specified nurse in the operating room. The patients were blinded to the study group or placebo, but the anesthesiologist in the operating room was aware of the type of drug received. The study drugs were prepared and prescribed by the anesthesiologist. The patients and other members of the research group were not aware of the intervention group. A pre-operative visit was performed for all patients. First, the patients were pre-oxygenated with 100% oxygen for 3 minutes with a mask. The premedication was the same in all groups in the form of midazolam 0.02 mg/kg, fentanylmic. lidocaine 3-5 mg/kg, lidocaine 1-1.5 mg/kg, and propofol 1.5-2 mg/kg for induction of anesthesia and atracurium 0.5 mg/kg. To maintain anesthesia propofol infusion, 50% oxygen and air with the goal of BIS=40-50 and maintaining hemodynamic variables. It was used at the base level of±%25. During the operation, supplementary doses of atracurium relaxant were used if necessary. A relaxant injection was performed with TOF monitoring.

Also, titrated doses of fentanyl were given based on the patient's heart rate and blood pressure (in the range of 75% to 125% of baseline). Full standard monitoring, including SPO2, BIS, IBP, NIBP, and TOF was established for all patients, and an arterial line was also installed. 15 minutes before the start of anesthesia, a bolus dose of 50 mg/kg of intravenous magnesium sulfate was given within 15 minutes, and an infusion of doses of 10, 15, and 20 hr/mg/kg continued until the end of the procedure, and group S was given a bolus dose of the same volume of normal saline over a period of 15 minutes and continued until the end of the procedure. Due to a drop in blood pressure and severe bradycardia in the M3 group, we had to stop the infusion, so the M3 group was excluded from the study, and 60 patients from the M1, M2, and S groups were studied. All patients in this study were operated on by one surgeon. The patients did not have neuromonitoring during the operation. Group M received a bolus dose of 50 mg/kg intravenous magnesium sulfate within 15 minutes, 15 minutes before the start of anesthesia, and group S received a bolus dose of the same volume of normal saline for 15 minutes, and the infusion continued until the end of the surgery.

The vital signs of the patients and the amount of bleeding during the operation were recorded based on the weighing of gases and the amount of blood in the suction with the deduction of the amount of liquid used for washing and the intensity of pain based on NRS at 1, 2, 6, 12, and 24 hours.

In the case of NRS=4-6, Ketorolac 30 mg intravenous ampoule was prescribed (the manufacturer of Ketorolac is Exir), in the case of NRS=7-10, pethidine 25 mg intravenous ampoule was prescribed. The amount of painkiller consumption was reported in each patient. According to the patient's condition, a decision was made regarding the placement of a central venous line. All patients of this study were subjected to posterior spinal fusion by a surgeon with general anesthesia and prone position. Patients did not have intraoperative neuromonitoring. At the end of the procedure, the amount of alcohol and narcotic consumption was recorded. Before the operation, the level of magnesium base was measured. The collected data are entered into the computer by EPI6 and SPSS statistical software and are analyzed. The tests used in the statistical analysis will be t, chi square, ANOVA and Wallis Kruskal.

Target population

This study involved a double-blind, randomized clinical trial conducted on 60 patients classified as ASA class 1 and 2, aged between 18 and 65 years. The target population consisted of patients scheduled for elective posterior spinal fusion (PSF) surgery involving 2-3 tubes, referred to Loghman Hakim Hospital.

Case study

The cohort included patients deemed suitable for elective spine surgery, who were to undergo the procedure under general anesthesia, accompanied by muscle relaxation and ventilation via a mechanical ventilator at Loghman Hakim Hospital.

Sampling method

The study employed a simple random sampling method utilizing a table of random numbers.

Sample size

Sample size determination was carried out using Krejcie and Morgan's table.

How to calculate the sample size

Based on preliminary research involving a total of 20 patients in each group, consultations with a statistician were also conducted to confirm the sample size.

Results

In this double-blind clinical trial, 60 patients targeted for posterior spinal fusion at Loghman Hakim Hospital were included. The participants were randomly allocated into three groups of 20, where the M groups received magnesium sulfate at varying doses (M1 = 10 mg/kg/hr, M2 = 15 mg/kg/hr), while the control group (S) was administered normal saline (Table 1). presents statistical data regarding the demographic characteristics of the study population (Table 2). Out of 60 patients, 32 (53.3%) were male and 28 (46.7%) were female (Figure 1). No statistically significant differences were observed in blood volume (BV), blood pressure, and heart rate across the groups ($P > 0.05$) (Figures 2, 3, 4). A statistically significant difference was identified in fentanyl consumption during surgery among the three groups ($P = 0.04$). The amount of isoflurane administered during the procedure was greater in group S compared to group M, with a larger amount found in group M1 relative to group M2 (Table 3). This indicates that higher magnesium doses significantly reduce the isoflurane requirement during surgery ($P = 0.04$). The analysis revealed a significant difference in intraoperative bleeding between the groups, with group S experiencing more bleeding than group M. Additionally, group M2 exhibited less bleeding compared to group M1 ($P = 0.03$) (Table 4). A statistically significant difference was also recorded concerning the duration from the cessation of medication to extubation. The recovery period in group M was longer than that in group S, with group M2 having a longer duration than M1 ($P = 0.03$). Significant differences were noted in pain scores measured via the Numeric Rating Scale (NRS). Pain levels in group S at 1, 2, 6, 12, and 24 hours post-operation were higher than those in group M, with scores in group M1 exceeding those in M2. A significance level of less than 0.05 was established for analysis (Table 5).

Table 1- Descriptive statistics of age

	Frequency	Percent	Valid Percent	Cumulative
Male	32	53.3	53.3	53.3
Female	28	46.7	46.7	100.0
Total	60	100.0	100.0	

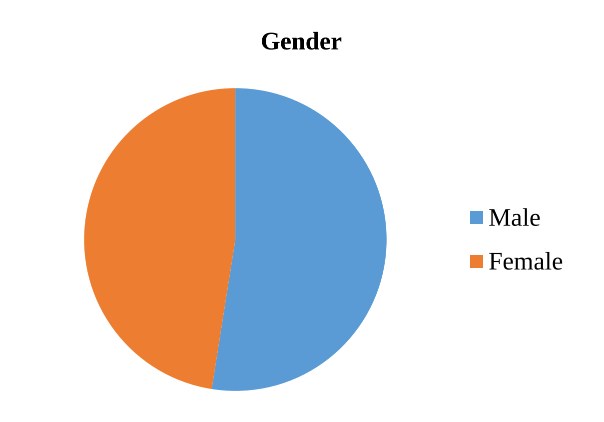

Figure 1- Descriptive statistics of gender

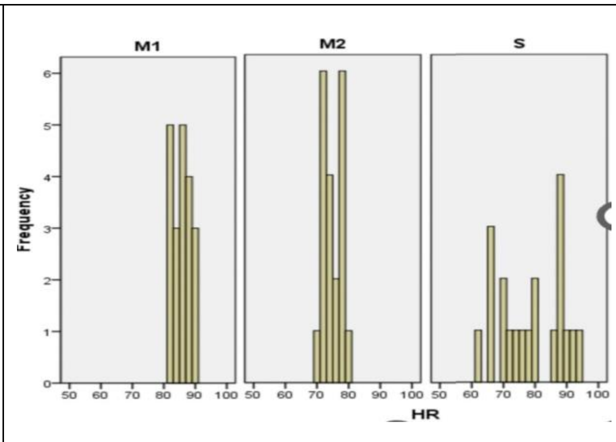

Figure 2- Differences were observed in heart rate (HR)

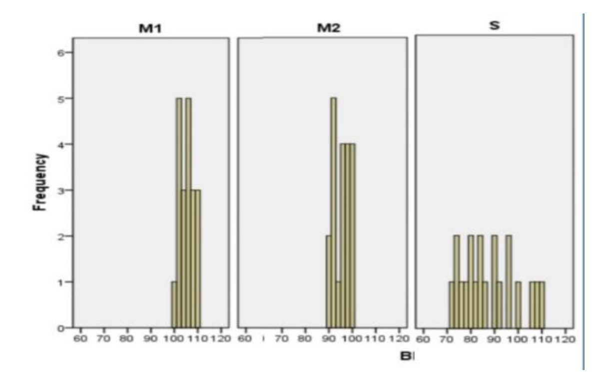

Figure 3- Differences were observed in blood pressure (BP)

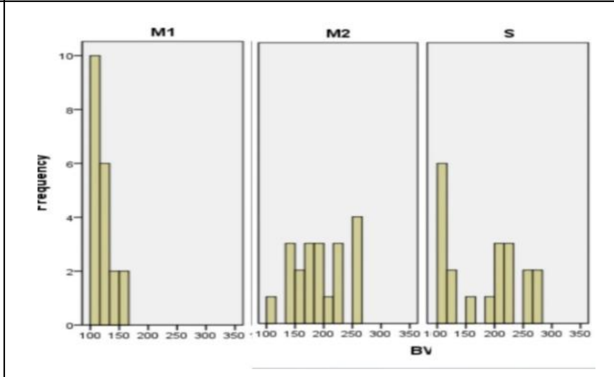

Figure 4- Differences were observed in blood volume (BV)

Table 2- Descriptive statistics of age

	N	Minimum	Maximum	Mean	Std. Deviation
Age	60	18	65	44.31	11.180
Valid N (listwise)	60				

Table 3- Distribution of the frequency of drug intake

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	M1	20	33.33	33.33	33.33
	M2	20	33.33	33.33	66.66
	S	20	33.33	33.33	100.0
	Total	60	100.0	100.0	

Table 4- Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
droge	60	1	3	2	1.125
age	60	18	65	44.31	11.180
HR	60	60	93	75.66	9.201
BP	60	70	110	91.65	11.744
BV	60	100	320	181.50	60.913
Valid N (listwise)	60				

Table 5- Statistics

		N	Mean	Std. Deviation
HR	M1	20	85.05	2.856
	M2	20	74.50	2.929
	S	20	87.32	10.232
MAP	M1	20	104.95	3.017
	M2	20	94.90	3.307
	S	20	109.33	11.741
BV	M1	20	192.80	43.343
	M2	20	180.05	64.584
	S	20	233.90	44.658
wakeup	M1	20	14.40	1.852
	M2	20	14.65	2.113
	S	20	10.02	3.150
Fentanyl	M1	20	218.5	33.307
Consumed	M2	20	209.7	26.482
	S	20	273.1	30.005
NRS1h	M1	20	3.50	.513
	M2	20	3.00	.000
	S	20	3.80	.410
NRS2h	M1	20	7.25	.786
	M2	20	6.35	.489
	S	20	7.35	.745
NRS6h	M1	20	5.45	.918
	M2	20	5.00	1.356
	S	20	4.45	.759
NRS12h	M1	20	4.70	.657
	M2	20	3.90	.447
	S	20	5.90	.641
NRS24h	M1	20	3.60	.598
	M2	20	3.10	.308
	S	20	4.00	.649

Discussion

Are different doses of magnesium sulfate effective on the amount of fentanyl used during spine surgery? In 2021, Silva et al. explored the analgesic effects of magnesium sulfate in patients undergoing surgery with intravenous general anesthesia. This prospective, double-blind trial involved 50 patients scheduled for abdominoplasty following bariatric surgery, who were divided into two groups to receive either remifentanil or magnesium sulfate for intraoperative analgesia. The findings indicated that magnesium sulfate is a safe and effective alternative for managing intraoperative pain, particularly when opioid use is contraindicated, aligning with the results of the current study. [22].

In 2010, Rahman Abbasi and colleagues examined the impact of a single gabapentin dose on the consumption of propofol and remifentanil in complete intravenous anesthesia. The study demonstrated that administering gabapentin prior to surgery significantly reduced the necessity for propofol and remifentanil in patients undergoing laparoscopic cholecystectomy, which supports the findings of the present research [23].

A 2021 study by Luiz Benevides et al. focused on patients undergoing abdominal hysterectomy with spinal anesthesia. In this randomized, double-blind trial involving 86 patients, those in the magnesium sulfate group received an initial dose of 50 mg/kg for 15 minutes, followed by 15 mg/kg for one hour until surgery concluded, while the control group received an equivalent volume of isotonic saline. Both groups were given 100 μg of intrathecal morphine, and all patients received dipyrone and ketoprofen during and after the procedure, along with dexamethasone administered only during surgery. Pain intensity, tramadol consumption, and side effects were assessed up to 24 hours postoperatively, concluding that magnesium sulfate significantly alleviated pain, consistent with the current study's results [24].

In 2020, Ebrahimi et al. conducted a study to evaluate the effects of magnesium sulfate on intraoperative bleeding in 80 patients aged 20 to 80 years, classified as ASA class 1 and 2. This double-blind study compared magnesium sulfate and saline groups. Although the visual analog scale (VAS) scores and morphine consumption were significantly lower in the magnesium sulfate group, it did not demonstrate a reduction in intraoperative bleeding, which is consistent with the findings of the present study [25].

Does magnesium sulfate injection reduce recovery time from anesthesia after spine surgery? A statistically significant difference was measured between the two groups in terms of the duration of waking up after stopping the drug until the time of waking up after stopping the drug until the time of waking up in the group of magnesium sulfate patients is more than the group of normal saline patients. A significance level of less than 0.05 was considered.

Does the injection of magnesium sulfate preserve the patient's hemodynamic stability during spine surgery? Another study was conducted by Srivastava and his colleagues in 2016 with the aim of comparing the effects of dexmedetomidine and magnesium sulfate in spine surgeries. 90 patients were randomly divided into three groups. Group D received a loading dose of dexmedetomidine of 1μg/kg over 15 minutes and a maintenance dose of 0.5μg/kg/h during surgery. Group M received a loading dose of magnesium sulfate of 50 mg/kg for 15 minutes and a maintenance dose of 15 mg/kg/h during surgery. Group C received a similar volume of normal saline. The results showed that dexmedetomidine is more effective than magnesium sulfate for maintaining hemodynamic stability in spine surgeries. Both of these drugs also reduce the need for anesthetics. Recovery from dexmedetomidine is as fast as the control group compared to magnesium sulfate, which was consistent with the results of the present study [26].

Conclusion

This study demonstrated that administering magnesium sulfate during surgery can positively influence anesthesia quality and the postoperative period. The recommended dosage of magnesium sulfate is 15 mg/kg/hr, as it was associated with the lowest narcotic consumption during surgery and reduced painkiller use afterward, while maintaining good hemodynamic stability. Higher doses exceeding 15 mg/kg/hr are not advised due to potential drops in heart rate and mean arterial pressure. Given the nature of posterior spinal fusion surgery and its associated postoperative pain, administering magnesium sulfate can significantly impact pain management. Patients receiving magnesium sulfate required lower doses of fentanyl during surgery. The advantages of intravenous magnesium sulfate infusion include reduced bleeding, fewer opioid-related side effects, and lower healthcare costs. This is particularly beneficial for patients with prolonged anesthesia. Managing bleeding volume is crucial, as it is linked to mortality, and administering higher magnesium sulfate doses during surgery can significantly mitigate this risk. Future studies should investigate the effects of magnesium sulfate administration during and prior to surgery across various patient populations and surgical types.

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