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Research Article

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Efficacy of Prophylactic Mg Infusion for Reducing Shivering and Extend the Duration of Analgesia Caesarean Section with Spinal Anesthesia

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Abstract

Background: *Magnesium sulphate ($MgSO_4$) infusion started before surgery in spinal anesthesia reduces the analgesic requirement and shivering. In this study, it was aimed to investigate the effects of magnesium sulphate infusion during spinal anesthesia and postoperative first 24 hours on block time, sedation and postoperative analgesic consumption.*

Methods: *10 mg / kg bolus and 500 mg / hour magnesium sulphate and serum were administered to Group M for 24 hours. Group R received only Ringer Lactate i.v infusion. Group R and Group M received 10 mlt / kg Ringer's lactate for intraoperative. In the first 24 hours: shivering, the first pain sensation, motor block withdrawal period and analgesic requirement of the groups were evaluated, as well as a 6-hour sedative and visual analog scores.*

Results: *A significant decrease in total analgesic consumption was detected in the magnesium infusion group for 6-hour (Tenoxicam: Group M: 50 ± 20 mg, Group R: 80 ± 20 mg for 24 hours, p: 0.001). At the same time, visual analogue scores decreased over all periods. There was no difference between motor block regression and sedation scores.*
Conclusion: It was concluded that magnesium sulfate infusion was a safe drug to reduce analgesic consumption for spinal blockade and to reduce shivering without affecting daily activities.

Introduction

The most common used anesthetic technique for cesarean section (CS) is spinal anesthesia (SA) because of its advantages [1]. However; complications such as hypotension, bradycardia, nausea and shivering are very common. Shivering is one of the most frequent and disturbing complication associated with SA, with an occurrence rate of 45–85% [2]. The spinal block causes vasodilatation, which leads to redistribution of heat from central to the peripheral compartments. It also decreases shivering threshold, thereby reducing the patient's ability to maintain the core body temperature [3,4]. However, the exact mechanism of this is not clear. Shivering may affects monitoring of the electrocardiogram, blood pressure and oxygen saturation [5]. It may also increase oxygen consumption, lactic acidosis and carbon dioxide production, as well as causing distress to parturients with a low cardiac pulmonary reserve and a high metabolism [3,6]. The pain and shivering may increase the severity of each other. In this regard, prevention and treatment of shivering and postoperative pain is an important aspect of patient care during SA for CS, resulting in better postoperative outcomes and a reduced incidence of post-surgical complications [7].

At present, a number of pharmacological methods are used to treat shivering [8]. Many medications have been investigated for their ability to control postoperative shivering, including meperidine and tramadol [9]. However, these medications may have adverse effects on the baby if administered to parturients prior to delivery [8,10]. Various pharmacological agents including opioids, N-methyl D-aspartate receptor antagonists, magnesium sulphate, and α2-agonists have been investigated for treatment of post-spinal shivering [8, 9]. However, these medications may have adverse effects on the baby if administered to parturients prior to delivery [8,10].

$MgSO_4$ (Magnesium Sulphate) infusion reduces analgesic requirement and sedation requirement. Magnesium ion (Mg^{+2}) is the second most abundant in intracellular fluid. It is involved as a cofactor for many enzyme functions. Neurochemical impulse plays an important role in transmission and muscle excitability. The mechanism of action is not fully known. Magnesium may suppress neuromuscular burst by inhibiting acetylcholine release at the myoclonic junction. It may also have depressive effects on the smooth muscles, as well as the central nervous system [11,12]. The aim of the present study was to investigate whether 10 mg/kg bolus than 500 mg/h of intravenous infusion administered Mg affects the incidence and severity of shivering and to evaluate the efficacy Mg a prophylactic agent for the prevention of shivering in patients undergoing caesarean section during SA.

Materials and Methods

This randomized, double-blinded trial performed at the anesthetic clinic of Zekai Tahir Burak Training and Research Hospital during November 2017 to April 2018, after obtaining approval from the institutional ethical committee and written informed consent from

all the participants.Eighty parturient females (19 to 38 years of age) belonging to the American Society of Anesthesiologists (ASA) Grade I/II who were scheduled for elective cesarean section under spinal anesthesia were enrolled in the study. The patients were randomly allocated to two groups (group R and group M; n=40 per group). In Group M, 10 mg/kg bolus and 500 mg/h magnesium sulphate were administered in equal volume for 24 hours. In Group R, only 10 ml / h of Ringer Lactate infusion was administered intravenously until the end of surgery. During the first 24 hours, the first pain sensation, motor block lifting duration and analgesic requirement, as well as sedation and visual analogue scores taken every 24 hours, were evaluated.

Prevalence of severe cardiovascular complications, preoperative >38°C or <35°C temperatures, contraindications to regional anesthesia, preeclampsia, diabetes mellitus, significant peripartum haemorrhage or the existence of an absolute or relative contraindication for the application of the spinal technique, locomotor neuromuscular disease, bleeding tendency or spinal local skin infection in the anesthetic area of the patients we were excluded of the study. In a previous study, intraoperative shivering was reported not to be associated with intraoperative temperature [13]. Because intraoperative room temperature and infusion fluid temperature were controlled and the intraoperative temperature was maintened constant during the study. The temperature of the operating room was kept at 23-25 ° C and 50-60% humidity. The lactated Ringer solution was heated to 37°C in a heating cabinet and administered intravenously at 10 mL / kg throughout the operation. All patients were under standard monitoring.

CSE was performed in the sit position at the L3-L4 lumbar vertebral interspace, with 12.5 mg 0.5% hyperbaric bupivacaine by a spinal needle [Atracaun 26G x88mm]. Mg at the onset of the before C/S operation 10 mg/kg bolus Mg was administered, followed immediately by 500 mg/h Mg infusion (i.v).

Sensory and motor assessments were performed at 1 min intervals using pinprick testing and the modified Bromage score, respectively. Surgery began when adequate anesthesia to the T6 dermatome was achieved [14]. The duration of surgery (from initial skin incision to the last stitch) were recorded, as were hemodynamic changes and the amount of irrigation fluid used during the procedure. Side effects, including hypotension, nausea, were also recorded. The Apgar Score at 1 and 5 min after birth of baby was recorded [15]. All hypotensive episodes were treated by crystalloid infusion if necessary, with intravenous ephedrine (5-15 mg). Spinal anesthesia hemodynamic parameters and sensory and motor block were measured at 5., 10., 15., 20., 30., 60., 90., 120. and 150. minutes. Sensory block was evaluated with pin prick method and motor block with Bromage score (Table 1). Assessment for sensory and motor block was continued in 30 minute intervals until full regression of blockade. Side effects such as nausea, vomiting, hypotension, bradycardia, and itching were recorded. Bradycardia was defined as slowing heart rate of more than 30% of individual baseline or less than 60 beats per minute. Atropine 0.5 mg per dose was administered to treat bradycardia. Similarly, hypotension was considered when the mean arterial pressure (MAP) decreased to more than 30% of baseline or less than 60 mmHg. Hypotension was treated with intravenous doses of ephedrine. Shivering was graded with a scale similar to that validated by Crossley and Mahajan [14]. Grades were as follows: 0 no shivering; 1 piloerection or peripheral vasoconstriction with no visible shivering; 2 muscular activity in one muscle group; 3 muscular activity in > one muscle group, but not generalized shivering; and 4 shivering involving the whole body. When shivering grade was ≥3, patients were treated with an i.v bolus of meperidine (25mg).

Table 1: Description of the Bromage Score

Grade	Criteria	Degree of Block (%)
I	Free movement of legs and feet	Nothing (0)
II	Just able to flex knees with free movement of feet	Partial (Group M:30, GroupR:35)
III	Unable to flex knees, but with free movement of feet	Almost complete (Group M:20, GroupR:25)
IV	Unable to move legs or feet	Complete (Group M:50, GroupR:40)

Statistical analysis

A power analysis was performed using a power threshold of 90% and an α-value of 0.05. Data are presented as the mean ± standard deviation for continuous data and frequency for non-parametric data. Differences between demographic anesthetic and surgical characteristics of patients were assessed using an independent t-test. Fisher's exact test was used to analyze categorical variables. The normal distribution of quantitative variables was assessed with Kolmogorov-Smirnov test. To compare quantitative variables in the 2 groups, ANOVA or Kruskal-Wallis test were used, as appropriate. Qualitative variables were compared with chi square test. Significance level was determined as $p < 0.05$. Data were analyzed using statistical package for social sciences software (SPSS Company, Chicago, IL) Version 23.

Results

A total of 80 parturients were included in this study and two groups were randomized (n = 40). No significant differences in patient characteristics, including age, body mass index, gestational week and operation duration were observed between groups (Table 2). The frequency of nausea and hypotension (systolic pressure, <90 mmHg) and the use of ephedrine were not different between the two groups. There was no statistical difference in the mean arterial blood pressure, tympanic temperature, and ephedrine consumption in the two groups. Group R also had more 24-hour consumption of tenoxicam ($p < 0.05$). The number of patients undergoing shivering in Group R was statistically significantly higher. Therefore, more meperidine was used in Group R ($p < 0.05$). Group R had a higher percentage of nausea and vomiting, but there was no statistically significant difference (Table 3, Table 4).

Table 2: Demographic and operative data in the two studied groups

Patient characteristics	Group R (n=40)	Group M (n=40)	p value
Age (years)	27.0±10	26.0± 12	<0.42
Body mass index (kg/m^2)	28.6±3.5	27.5±3.3	<0.12
Gestational age (weeks)	38.3±1.0	38.9±1.1	<0.45
Operation duration (min)	60.0±13.6	60.0±12	<0.22
Heart rate (bpm)	84.3±11.5	81.9±15.3	<0.24
SpO_2 (%)	99±2	99±3	<0.23
APGAR 5.min	8.8±1.2	8.6±1.5	<0.22
APGAR 10. min	10±0.0	10±0.0	<0.24

Data are presented as the Mean ± Standard Deviation.
SpO_2: Peripheral capillary oxygen saturation.

Table 3: Vital signs and clinical data in the two studied groups

Variable	Group R (n=40)	Group M (n=40)	p value
MAP_0 0.min	95±10	94±8	<0.15
MAP_1 5.min	92±8	90±10	<0.46
MAP_2 10.min	73±10	74±8	<0.32
MAP_4 20.min	85±10	86±8	<0.29
MAP_5 30.min	86±7	84±6	<0.12
MAP_5 postoperatif	88±11	88±9	<0.23
T_0 ^{0}C (Just before induction of spinal anesthesia)	36.7±0.2	37±0.3	<0.31
T_1 ^{0}C (Just after delivery of the baby)	36.5±0.3	36.5±0.5	<0.25
T_2 ^{0}C (At the end of the surgery)	36.4±0.5	36.3±0.5	<0.56
T_3 ^{0}C (In the wake-up room)	36.3±0.5	36.4±0.5	<0.32

Data are presented as the Mean ± Standard Deviation.
MAP = Mean Arterial Blood Pressure (mmHg), T = Tympanic temperature.

Table 4: Duration of Recovery from Sensory and Motor Block, and the Rate of Complications in Two Groups

Variable	Group R (n=40)	Group M (n=40)	p value
Recovery from sensory block, min	130 ± 18	136 ± 15	0.725
Recovery from motor block, min	115± 20	114 ± 18	0.605
Atropine administration (mg)	5 (10%)	5(10%)	0.709
Ephedrine administration (mg)	15 (30%)	12 (20%)	0.812
Nausea (n)	9(22.5%)	7 (17.5%)	0.065
Vomiting (n)	6 (15)	4 (10%)	0.93
Total analgesic consumption (mg/24 h) tenoxicam	80 ± 20 *	50 ± 20 mg	0.001
Analgesic use rate (24 hours)	28(70 %)	20 (50%)	
Preoperative magnesium (mg /dl)	1.92 ± 0.2	1.99 ± 0.2	0.625
Postoperative magnesium (mg /dl)	2.04± 0.3	2.65 ± 0.5* *	0.04
Incidence of shivering at any time	15/40(37.5%)*	9/40(22.5%)	<0.005
Median and range of shivering	2 (1–4)*	1 (0–4)	<0.004
Incidence of maximum shivering at any time (%)	11/40 (27.5%)*	-5	<0.002
Poatoeratif meperidin i.v. 25 (mg)	5 patients	1 patient	<0.001
Block level (Thoracic segment = T)	T6 (4–6)	T 6 (4–6)	<0.56

Data represented as median range or numbers and percentages (%).
* Statistically significant difference between groups; ($p < 0.05$).

Discussion

Magnesium was used as bolus infusion in our study. Further studies are required to see whether the incidence of shivering could be reduced further, by administering magnesium infusion following with the bolus in the postoperative period. In our study, magnesium was used as infusion following with the bolus. This study showed that magnesium sulphate infusion was effective in preventing shivering, and it reduced analgesic consumption, without any notable complications. Our study has shown that magnesium was effective in preventing shivering during SA. It also significantly reduced the total analgesic consumption without affecting the hemodynamics or causing any side-effects.

Shivering is a common and uncomfortable side effect associated with neuraxial anesthesia. Neuraxial techniques may block the activity of the sympathetic nervous system and reduce a patient's ability to regulate body temperature [16]. Additionally, it may inhibit thermoregulatory control centrally and lead to internal redistribution of heat from the core to the periphery [17,18]. In addition, the release of amniotic fluid from the mother's body may lead to heat loss [19]. Collectively, all of these factors may increase the incidence of shivering in parturients.

Shivering during and following caesarean section increases oxygen consumption and the burden on the heart and lungs, as well as reducing hepatorenal blood flow, influencing uterine contractions and extending the anesthesia recovery time [2,10,20]. Therefore, intraoperative and postoperative prevention of shivering in patients receiving spinal anesthesia is of important clinical significance [21]. Although shivering is a protective mechanism when the body is subjected to low temperatures, there is no definite linear relationship that exists between body temperature and the occurrence of shivering during CSE; shivering may also be observed in normothermic patients under spinal anesthesia, suggesting that mechanisms other than heat loss and subsequent decrease in core temperature contribute to the development of shivering [22]. These mechanisms may include uninhibited spinal reflexes, postoperative pain, decreased sympathetic activity, pyrogen release, adrenal suppression and respiratory alkalosis [23]. Shivering may therefore be considered both thermogenic and non-thermogenic [13,22]. As such, a variety of measures are widely used to prevent postoperative shivering [21,24].

A number of pharmacological methods for inhibiting shivering have been reported [25]. Numerous pharmacological interventions have been proposed for the treatment of postoperative shivering, however the ideal treatment has not yet been established [9]. Meperidine has been reported to be one of the most effective drugs used to treat post-anesthetic shivering [30]. In the present study, 20 mg meperidine was intravenously administered if the severity of shivering was above grade 2. The side effects of intravenous meperidine, including nausea, vomiting, pruritus, hypotension, bronchospasm, bradycardia and respiratory insufficiency, have been reported to be dose-related and may limit the application of this agent, particularly in parturients [31].

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Magnesium has many clinical applications in anesthesia and pain syndromes. Control of the sympathoadrenal response of endotracheal intubation, suppression of the blood during delivery, and anesthesia-balanced infusion during the resection of the pheochromocytoma were found to be beneficial in clinical practice [27,28]. It has been used for other anesthesia, such as preventing postoperative tremor [12,29]. Intrathecal administration in rats leads to spinal anesthesia and sedation without significant neurotoxicity [12,229]. The application of magnesium infusion during general anesthesia and the reduction of analgesic requirement during anesthetic or postoperative period is controversial. Some studies reported that magnesium sulphate anesthetic consumption [30] decreased analgesic requirement when applied pre-emptively and postoperatively [29,32]. Mg has been shown to reduce injurious behaviors in experimental peripheral nerve cuts [32]. In this study, the analgesic effects of magnesium sulphate infusion may be thought to be due to the calcium-sensitizing effect or NMDA [N-Methyl-D-aspartate] antagonist effect [12,33].

The abstiallodynic effect of intrathecal gabapentin in rat postoperative pain model, NMDA antagonists reduces magnesium chloride and ruthenium breakdown [11,29]. Pain is increased by the partial increase of the α2δ subunit of voltage-related calcium channels and magnesium is also associated with these receptors to reduce pain [32]. There are different approaches to magnesium infusion dosing and administration protocol in the studied studies. Seyhan et al. the efficacy of four doses of two different infusion doses of 10 and 20 mg / kg followed by a 40 mg / kg dose prior to the infusion intravenous infusion of 8 mg / kg followed by a preoperative 50 mg / kg dose, Bhatia et al. bolus and 15 mg / kg infusion were administered at the same dose [12,29,32,33]. In a study using similar doses, the duration of infusion was 6 h. In one study, 50 mg / kg magnesium was administered within 20 minutes immediately after induction of anesthesia [29].

Zarauza et al. 30 mg / kg bolus and 10 mg / kg infusion were applied for 20 hours postoperatively [34]. Kara et al. (30 mg / kg) followed by 500 mg / hour (approximately 7 mg / kg) infusion for 20 hours [34]. In a study was taken as an example for the infusion of dyspnea while limiting the duration of magnesium bolus dosing block [29,33]. Clinical observations related to magnesium sulfate infusion to reduce anesthetic and analgesic requirements are contradictory [11,32]. There are a number of studies that report that our work reduces the consumption of anesthetic and analgesic in parallel with the result. In patients undergoing arthroscopic knee surgery with total intravenous anesthesia, i.v. magnesium sulphate infusion decreased the analgesic requirement during the operation and in the postoperative period [32]. Total intravenous anesthesia significantly reduced the need for magnesium, propofol, remifentanil and vecuronium in patients undergoing elective spinal surgery [29]. Tramer et al. showed that magnesium sulphate infusion in patients undergoing abdominal hysterectomy under general anesthesia reduced PCA morphine consumption and improved sleeping comfort and comfort [35].

After abdominal hysterectomy, intravenous drugs such as fentanyl, ketamine, and magnesium sulphate have been used for pain relief and sensitivity and the effects on opioid consumption were investigated. Pain scores and morphine consumption were similar, and all drugs reduced spinal sensitivity after surgery [16,29]. In patients undergoing open cholecystectomy, the reduction of pain in the early postoperative period did not change the total morphine consumption [29]. In a recent study in which patients with radical retropubic prostatectomy were treated with magnesium infusion, postoperative tramadol consumption was significantly reduced [29,30]. Seyhan et al. found that two different doses of infusions were sufficient in low-dose studies to support inraoperative anesthetic consumption [32].

In a study in which preemptive magnesium sulphate administration was compared with remifentanil, magnesium provided better analgesia in postoperative period and better hemodynamic stability in perioperative period [11,12,29]. Furthermore, in a study conducted in a similar surgical group, it was shown that bolus and infusion in the perioperative period reduced the analgesic requirement without side effects [12,29]. In a study conducted in our clinic, postoperative magnesium sulphate infusion significantly reduced the postoperative analgesic requirement in patients who underwent spinal anesthesia [29,30]. Our previous study and our findings with this study are important in that the analgesic activity of magnesium is not only associated with general anesthetics or with similar mechanisms. On the other hand, during colorectal surgery, oral nifedipine, i.v. nimodipine and magnesium sulphate administration did not affect perioperative morphine consumption [30,33]. These unfavorable outcomes may be explained by the number of study groups, the route of administration, the type of calcium channel blocker given and the mechanism of pain. As such, during the operation i.v. showed that magnesium sulfate infusion did not have a positive effect on postoperative pain [29,30]. Non-steroidal anti-inflammatory drugs (NSAIDs) are used as an analgesic option for postoperative pain, however, many concerns about adverse effects of these drugs, such as gastrointestinal bleeding, acute renal failure and allergic reactions have limited their usage [36]. One other study, intra-operative MgSO4 is effective in postoperative pain and it reduces analgesic requirements, therefore, the need to consume NSAIDs postoperatively may be also decreased for 24 h.

In our study magnesium sulfate infusion was a safe drug to reduced the postoperative analgesic requirement in patients who underwent spinal anesthesia and to reduced shivering without affecting daily activities. Magnesium sulphate infusion reduced meperidine requirement and consumption in the postoperative period.

As a result, pre-emtif i.v administration of magnesium sulphate infusion resulted in reduced meperidine requirement and consumption in the postoperative period. Magnesium has been found to be safe and effective in the prevention and treatment of shivering after SA for pregnancies with C/S. There was no hemodynamic side effect of this drug and did not affect the rate of arterial oxygen saturation and body temperature. Magnesium is recommended to be used after spinal anesthesia because of the prevention of shivering and the reduction of analgesic consumption for 24 h.

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