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Evaluation of the Effects of Magnesium Sulfate on Prevention of Post-dural-Puncture Headache in Elective Cesarean in Kamali Hospital

Banafsheh Mashak [1], Seyyed Mohsen Pouryaghobi [1], Mehdi Rezaee [2], Samira Saee Rad [3], Mina Ataei [4*], Aida Borzabadi [5]

[1] Assistant Professor of Anesthesioligy, Alborz University of Medical Sciences, Karaj, IRAN
[2] Department of Anesthesioligy, Alborz University of Medical Sciences, Karaj, IRAN
[3] Medical Geneticist, Saee rad genetic laboratory, Karaj, Alborz, IRAN
[4] Assistant Professor, Infertility Fellowship, Obstetrics and Gynecology, Social Determinants of Health Research Center, Alborz University of Medical Sciences, Karaj, IRAN
[5] Student Research Committee, Alborz University of Medical Science, Karaj, IRAN
***Corresponding Author:** Ataee.mina@yahoo.com

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ABSTRACT

Introduction: One of the most common complications of spinal anesthesia in elective cesarean is a headache, known commonly as post-dural-puncture headache (PDPH). Various methods are mainly recommended such as resting and the use of non-opioid analgesics, caffeine, and codeine, but none of them has been fully effective in its treatment. Hence, this study was conducted to evaluate the effect of magnesium sulfate on the prevention of post-dural-puncture headache in the elective cesarean.

Method: a total of 68 patients candidate for elective cesarean and admitted to Kamali Hospital were selected using convenient sampling and they were randomly divided into two groups. One group received magnesium and other group received saline. Subjects of case group received magnesium at the dose of 50 mg / kg as bolus and the subjects of control group received normal saline at the same dose as bolus. The incidence of headache and its severity 12, 24, 36, 48 , 60 and 72 hours after surgery were measured in both case and control groups.

Results: The mean age of patients in the magnesium sulfate group was 27.94 years with a standard deviation of 5.18 and the mean age of patients in the normal saline group was 29.35 years with a standard deviation of 5.97. The mean body mass index (BMI) in the magnesium sulfate group was 26.34 with a standard deviation of 4.03 and the mean body mass index (BMI) in the normal saline group was 27.15 with a standard deviation of 2.47. Post-dural-puncture headache severity was lower in the case group than that in the control group at all times ($P < 0.05$).

Conclusion: The results of this study revealed that intravenous administration of magnesium sulfate before elective cesarean in patients undergoing spinal anesthesia significantly decreases the severity of post-dural-puncture headache (PDPH).

Keywords: cesarean, spinal anesthesia, PDPH, magnesium sulfate

INTRODUCTION

Spinal anesthesia is considered as an anesthesia method in outpatient surgeries and it is used highly in many surgeries daily. Spinal anesthesia is done easily and it has fast effects and controls the pain as muscles are loose in surgery. However, it is followed by consequences. Two major complications of anesthesia are headache and low back pain. Post-dural-puncture headache is a common problem among young women candidate for cesarean, while the use of needles with little diameters has reduced its prevalence (1). One of the most common complications following spinal injection in elective cesarean is headache, referred as post-dural puncture headache (PDPH). Brain and spinal cord are surrounded by the CSF and this kind of injection can cause a small leakage of cerebrospinal fluid, which this level of leakage is not risky. However, when the leakage to dural space is high, it will reduce the pressure of the fluid around the brain and finally it will cause headache (2,3). Generally, symptoms of the complication emerge few hours after the dural puncture and last up to 7 days later (4-6). Risk factors for this type of headache include immediate discontinuation of caffeine using, history of previous headaches, dehydration, age, size of spinal needle diameter, and the number of dural punctures and history of previous headache following spinal injection (5). Due to the shortened hospitalization of women after cesarean section, it might occur after the discharge of mothers or it might be a cause for delay in discharge of women from the hospital (6-9).

Any dural leakage can lead to PDPH and this headache can be spontaneous or due to medical interventions. This headache can occur up to 24 hours after spinal. The rate of this headache is highest among people aged 18-30 years and lowest among children younger than 13 and people older than 60 years (10,11). Its rate is also more in people with low BMI than that in obese people. Rest, treatment with fluid, caffeine, synthetic form of adrenocorticotropic, sumatriptan, injection of Dextran and saline 9% in spinal space, blood patch and morphine injection are among the treatments investigated (12-15).

Magnesium is the second intracellular cation in terms of rate and it is required for activity of most of the enzyme systems. It also plays a major role in the neuro-chemical transmission muscle stimulation (16, 17). Magnesium sulfate reduces muscle contraction and blocks peripheral neuromuscular transmission by reducing the release of acetylcholine at the neuromuscular junctions. It also has analgesic effect by blocking NMDA receptors (18-22). The positive effect of the intravenous magnesium sulfate in reducing migraine headaches has been proven in several studies and it has been shown that unlike other drugs prohibited during pregnancy, it is an appropriate drug (23,24). CACNA1A is one of the known genes in the molecular pathway of magnesium sulfate. It is the first gene known in familial migraine (25-28). Given the incidence of mental and psychological problems as well as the increased hospital costs in patients with this complication and the lack of definite prevention methods for these types of headaches and the results of previous studies on the effect of magnesium sulfate on migraine headache treatment, the present study was conducted with the aim of evaluating the effect of magnesium sulfate on the prevention of post-dural-puncture headache in elective cesarean section surgery in Kamali Hospital (29-32).

METHODOLOGY

The present study was conducted in vitro. After obtaining the consent of the subjects and giving adequate information for patients, 68 candidates candidate for elective cesarean section were selected using convenient sampling method and were randomly divided into two groups. Exclusion criteria included known allergy to one of the drugs studied, severe kidney, liver, and heart failure, severe obesity BMI> 35, neuromuscular diseases, lumbar disc disease, history of neuropathy, use of opioid or painkiller 3 days before study, consumption of calcium channel blockers, problem in spinal block and spinal anesthesia more than two times in pre-operation visit. Subjects of case group received magnesium at dose of 50 mg / kg as bolus and the subjects of the control group received normal saline at same dose as bolus. The incidence of headache and its severity 12 hours, 24 hours, 36 hours, 48 hours, 60 hours and 72 hours after surgery were measured in both case and control groups. Required information will be collected according to project objectives by using a questionnaire that includes demographic information and recording events related to the project. Pain ruler will be used to measure pain severity. In order to determine the severity of pain in people, VAS method is commonly used. For this purpose, the individual is asked to specify the severity of pain in a part of the affected body by selecting a number between 1 and 10 or selecting one of the options of no pain, mild pain, average pain, severe pain, the most severe pain. Chi-square and Wilcoxon tests with a significance level of less than 0.05 are used for data analysis. Statistical analysis is performed using SPSS 22 software.

Table 1. Frequency of VAS score at hour 12 in the magnesium sulfate group based on age

score	N (%)	Age mean (SD)	P value
0	(64.7%) 22	(5.02) 27.82	0.687
2	(8.8%) 3	(7.09) 26.33	
3	(8.8%) 3	(2.89) 32.67	
4	(5.9%) 2	(7.07) 29.00	
5	(8.8%) 3	(6.51) 26.67	
7	(2.9%) 1	(-) 23.00	

Table 2. Frequency of VAS score at hour 12 in the magnesium sulfate group based on BMI

score	N (%)	BMI mean (SD)	P value
0	(64.7%) 22	(3.80) 25.55	0.469
2	(8.8%) 3	(7.10) 27.20	
3	(8.8%) 3	(3.03) 25.50	
4	(5.9%) 2	(6.08) 28.60	
5	(8.8%) 3	(1.42) 30.07	
7	(2.9%) 1	(-) 28.10	

RESULTS

The VAS score at the end of 12 hours in the magnesium sulfate group based on age (**Table 1**) showed that there was no significant difference in the chi-square test (P value = 0.687).

VAS score at hour 12 in the magnesium sulfate group based on BMI (**Table 2**) showed that there was no significant difference in the chi-square test (P value 0.469).

VAS score at hour 12 in the magnesium sulfate group based on education level (**Table 3**) showed that there was no significant difference in the chi-square test (P value= 0.111).

Then, normal saline group was examined. VAS score at hour 12 based age in **Table 4** showed that there was no significant difference in chi-square test (P value=0.622).

Table 3. Frequency of VAS score at hour 12 in the magnesium sulfate group based on education level

score	N (%)	illiterate	Below diploma	diploma	academic	P value
0	(64.7%) 22	(4.5%) 1	(45.5%) 10	(45.5%) 10	(4.5%) 1	0.111
2	(8.8%) 3	(0%) 0	(100%) 3	(0%) 0	(0%) 0	
3	(8.8%) 3	(66.7%) 2	(33.3%) 1	(0%) 0	(0%) 0	
4	(5.9%) 2	(0%) 0	(0%) 0	(100%) 2	(0%) 0	
5	(8.8%) 3	(0%) 0	(33.3%) 1	(66.7%) 2	(0%) 0	
7	(2.9%) 1	(0%) 0	(100%) 1	(0%) 0	(0%) 0	

Table 4. Frequency of VAS score at hour 12 in normal saline group based on age

score	N (%)	Age mean (SD)	P value
0	(14.7%) 5	(6.69) 30.20	0.622
1	(2.9%) 1	(-) 37.00	
2	(17.6%) 6	(2.88) 31.50	
3	(35.3%) 12	(5.98) 27.92	
4	(29.4%) 10	(7.04) 28.60	

Table 5. Frequency of VAS score at hour 12 in normal saline group based on BMI

score	N (%)	BMI mean (SD)	P value
0	(14.7%) 5	(1.29) 26.20	0.810
1	(2.9%) 1	(-) 26.30	
2	(17.6%) 6	(2.23) 26.52	
3	(35.3%) 12	(3.12) 27.65	
4	(29.4%) 10	(2.40) 27.51	

Table 7. Comparison of mean age and BMI in two groups

	Mean (SD)		
Variable	Magnesium sulfate group	Normal saline group	P value
age	(5.18) 27.94	(5.97) 29.35	0.285
BMI	(4.03) 26.34	(2.47) 27.15	0.289

Table 8. Comparison of patients' education level in two groups

	N (%)		
Variable	Magnesium sulfate group	Normal saline group	P value
illiterate	(8.8%) 3	(0%) 0	0.135
Below diploma	(47.1%) 16	(41.2%) 14	
diploma	(41.2%) 14	(55.9%) 19	
Academic	(2.9%) 1	(2.9%) 1	

Table 9. Comparison of mean VAS scores between the two groups at different times

	Mean (SD)		
Mean score	Magnesium sulfate group	Normal saline group	P value
Hour 12	(2.02) 1.32	(1.34) 2.61	0.004
Hour 24	(1.88) 1.17	(1.32) 2.58	0.002
Hour 36	(1.35) 0.55	(1.66) 2.11	0.002
Hour 48	(0.78) 0.23	(1.64) 1.97	0.000
Hour 60	(0.51) 0.08	(1.71) 1.73	0.000
Hour 72	(0.17) 0.02	(1.71) 1.73	0.000

VAS score at hour 12 in the normal saline group according to BMI (**Table 5**) showed that there was no significant difference in the chi-square test (P value = 0.810).

VAS score at hour 12 in the normal saline group based on education level (**Table 6**) showed that there was no significant difference in the chi-square test (P value = 0.531).

Then, age and body mass index of patients were compared in two groups (**Table 7**). Paired t- test showed no significant difference between them.

Then, the education level of the patients in the two groups was compared (**Table 8**). Wilcoxon test showed no significant difference between them.

Then, the mean VAS scores of patients were compared at hours 12, 24, 36, 48, 60 and 72 after surgery in the two groups (**Table 9**). Wilcoxon test showed a significant difference between the two groups in this regard (P value < 0.05).

DISCUSSION

The results of the present study showed that the infusion of magnesium sulfate in patients undergoing cesarean section with spinal anesthesia reduced the incidence and severity of the headache (33). However, the mechanism of action of this effect is not known. However, it seems that interference with calcium channels and NMDA receptors to play an important role in this analgesic effect (34,35). Studies have shown that calcium channel blockers increase opioids analgesics in cancer patients treated with morphine (36). As the entry of calcium into cell releases neurotransmitters and other pain-causing cases, the analgesic effect of calcium channel blockers can be due to increased pain threshold due to interference with the entry of calcium into cell (37,38).

In addition, NMDA, which is an amino acid receptor and responsible for the transmission of stimuli through synapses and the junction of stimulating amino acids, such as glutamate and weakening molecules such as ketamine and magnesium, it can bind to an ion channel permeable to potassium and calcium. Magnesium inhibits the voltage-dependent flows through this receptor (39).

Accordingly, magnesium can have a preventive effect on pain before the onset of stimulation induced by surgery. Preventive analgesia can be useful for patient by preventing the formation of the central sensitization process or what occurs as a result of incision or inflammation or both of them. Many studies have shown that the need for analgesic drugs decreases with the administration of magnesium. The results of this study are similar to those of previous studies. However, most studies have focused on the effectiveness of magnesium in general anesthesia and few studies have been conducted to investigate its effect during spinal anesthesia.

Davoudi et al. (2012) carried out a research to investigate the effect of magnesium sulfate on the prevention of postoperative pain following spinal anesthesia in patients undergoing a cesarean section. In this research, 68 patients undergoing elective cesarean section were divided into two equal groups and one group received intravenous magnesium sulfate at a dose of 50 mg / kg as bolus and 10 mg / kg as a continuous infusion during surgery and the control group received normal saline at the same dose. The results revealed

Table 6. Frequency of VAS score at hour12 in normal saline group based on education level

score	N (%)	illiterate	Below diploma	diploma	academic	P value
0	(14.7%) 5	(0%) 0	(80%) 4	(20%) 1	(0%) 0	0.531
1	(2.9%) 1	(0%) 0	(0%) 0	(100%) 1	(0%) 0	
2	(17.6%) 6	(0%) 0	(50%) 3	(50%) 3	(0%) 0	
3	(35.3%) 12	(0%) 0	(33.3%) 4	(66.7%) 8	(0%) 0	
4	(29.4%) 10	(0%) 0	(30%) 3	(60%) 6	(10%) 1	

that intravenous injection of magnesium sulfate during cesarean section in patients undergoing spinal anesthesia reduced postoperative analgesic consumption and relieved postoperative pain (41).

The research conducted by Mavuromatti and Wolf also emphasized that magnesium sulfate as bolus and infusion reduces the need for analgesics and anesthesia drugs during surgery and improves the postoperative analgesia (7,12).

In another study conducted by Howang et al (2010), results showed that pain severity decreased following the administration of magnesium sulfate in patients undergoing spinal anesthesia. In this study, the severity of pain was higher in the magnesium-receiving group than that of the control group 4, 24, and 48 hours after the surgery (13,42). In the present study, the severity of pain was significantly lower in the magnesium sulfate group than that in the control group at all times. However, some studies suggest that magnesium administration near the surgery had little effect on the postoperative pain, while these studies have used low sample size (5,6). Kotler et al (2005) also conducted a study to compare magnesium of CSF fluid and plasma in patients who had post-dural-puncture headache and the patients without headache (43). The results of the study revealed no significant difference between CSF and plasma magnesium levels of the two groups (14). However, the results of most studies in this area confirm the effectiveness of magnesium sulfate in preventing and reducing the severity of pain after spinal anesthesia.

CONCLUSION

The results of this study showed that intravenous administration of magnesium sulfate before elective cesarean section in patients undergoing spinal anesthesia significantly decreases the severity of post-dural-puncture headache (PDPH). Conducting a research with a larger sample size and evaluating the effectiveness of magnesium sulfate on other complications after cesarean section with spinal anesthesia such as shivering, itching, hot flushes, and nausea and vomiting in patients and investigating the rate of complications of magnesium sulfate administration in this group can confirm and complete our research results on the selection of this drug in preventing consequences of spinal anesthesia.

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