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Effect Of Pre-Emptive Magnesium Sulfate In Pain Relief After Elective Cesarean Sections

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ABSTRACT

One of the most important things concerning surgeries is pain and its consequences on the patient and his general condition. So, we have to decrease pain following surgeries as much as we can to achieve optimum pain relief for the patients passing surgeries. A lot of studies and researches have been focused on the usage of magnesium sulfate ($MgSo_4$) preoperatively to assess its effect in decreasing pain postoperatively to elective cesarean sections. To assess the analgesic efficacy in decreasing pain post-operatively by a preoperative single dose of intravenous magnesium sulfate in patients undergoing elective cesarean sections by the usage of two pain scales. A sixty pregnant women who underwent elective cesarean section were randomly separated into two groups. Before the induction of the anesthesia, the magnesium sulfate group (group A) received magnesium sulfate 50 mg/kg intraveneously (i.v) in bolus dose in 100 ml isotonic saline. The control group(group B) received the same volume of isotonic saline 0.9%(100ml). The pain score was taken at rest and movement for up to 12 hours post-operatively. There were no statistical differences regarding patients characteristics. Magnesium sulfate was very effective(statistically highly significant) in decreasing pain according to visual analogue scale and overall the four readings that detected in this clinical research and also the numeric pain scale showed that magnesium sulfate group was very effective (statistically highly effective) in three readings and effective (in the last reading). Pre-operative magnesium sulfate causes a significant reduction in pain intensity elective cesarean section.

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INTRODUCTION

Magnesium is considered as an important cation which represents the most common cation intracellularly after potassium and also represents the fourth most common body cation (Jahnen-Dechent and Ketteler, 2012). More specific roles of magnesium include the proper functioning of the Na+_K+ exchange pump which is responsible for the generation of the electrical gradient across cell membranes. Magnesium has a crucial role in the regulation of calcium movement into the cells of smooth muscle, so it has a pivotal role as it responsible for the cardiac contractile strength maintenance, in addition, its role in the maintenance of vascular tone peripherally (Romani, 2011). Magnesium is a physiologic blocker for calcium channel and it is considered as an antagonist for N-methyl-D-aspartate (NMDA) receptor in a non-competitive manner (Olivares *et al.*, 2012). The average-sized adult contains approximately 24 gram of magnesium, a little more than half of it is accumulated within a bone, while plasma magnesium represents less than 1%, that limits the value of using plasma levels as an indicator for the levels of magnesium in total body (Gupta and Gupta, 2018). So, serum becomes the most representative test for magnesium status and the most reliable test for the evaluation of magnesium levels that confer its importance in clinical medicine particularly to assess acute changes in magnesium status rapidly (Elin, 2010).

The serum concentration of magnesium in healthy individuals maintained closely within the physiological range with values ranged in adult serum from 0.65-1.05 mmol/L for total concentrations magnesium and 0.55–0.75 mmol/L for ionized magnesium (Tietz, 1990) or 0.7 -1.0 mmol/L for total serum magnesium and 0.4 -0.6 mmol/L for ionized serum magnesium (Maj-Zurawska, 1994).

Urinary magnesium excretion is considered as another approach for magnesium status assessment. Due to the fact that renal magnesium excretion subjected to circadian rhythm, a 24-h urine specimen should be collected for the accurate assessment of magnesium excretion and absorption which is valuable for the assessment of magnesium wasted by kidneys due to medications or as a result to a certain physiological status. The results obtained can provide information about the etiology in which high excretion of magnesium in urine can indicate a wasting of magnesium from the renal system while the low value may indicate that there was an inadequate intake or absorption of magnesium (Elin, 1988).

Magnesium sulfate (MgSO4) considered as central nervous system depressant and anticonvulsant. It acts on several sites such as myoneural junction and its administration cause a reduction in hyperreflexia as a result of acetylcholine release inhibition at the neuromuscular junction, reduce the acetylcholine sensitivity at motor endplate and reduce muscle membrane excitability. It is also considered as a mild vasodilator which causes a reduction in the hyperactivity of uterus that leads to an increase in the uterine blood flow Additionally, MgSO4 act as a vasodilator at liver and renal beds that improve their function (Euser and Cipolla, 2009). The administration of Magnesium sulfate intravenously showed an immediate anticonvulsant action that lasts for approximately of 30 minutes whereas the administration via intramuscular rout showed an onset of action for about one hour but last for 3-4 hours (Santi *et al.*, 1994).

Cesarean section (S/C) is a surgical procedure in which one or more incisions are made through the abdomen if the mother (laparotomy) and her uterus (hysterotomy) for the delivery of one or more babies. Ferdinand Adolf Kehrer which is a considered as the first gynecologist that performed a modern Cesarean section (Ritter, 2012).

Patients And Method

Study Design And Setting

This study is a prospective, randomized, double-blinded clinical trial. The study was conducted in the elective operation theatres in Madinat Al-imamain Al-kadumian (Al kadhimia teaching hospital previously) medical centre in Baghdad, Iraq, from the 2^{nd} of January 2016 to 15^{th} of February 2017.

Approval was obtained from the Arabic commission for medical specialization as well as written informed consent from all the patients.

In this study, 60 patients were a candidate to elective cesarean section surgery; patients were divided into two equal groups. One group received magnesium sulfate 50mg/kg in 100ml of isotonic saline pre-emptive 30 minutes before the operation and over 15 minutes and the other group received 100 ml of isotonic saline only also 30 minutes before the surgery and over 15minutes.

The inclusion criteria

1. Elective operations
2. ASA class two
3. Age 18 -40 years
4. Weight between 50 and 100 kilograms
5. Length of the operation between 30 and 60 minutes

The exclusion criteria

1. Cases with an allergy to the medications used in the study
2. Patients with hepatic dysfunction
3. Patients with renal dysfunction
4. Patients with cardiovascular dysfunction
5. Patients with neurological disorders
6. Patients with opioid or analgesic abuse
7. Patients receiving chronic treatment with magnesium or calcium channel blockers
8. Patient with severe hypotension(MAP <30%) to base line MAP reading
9. The patient refusal

Anesthetic protocol

Anesthetic induction and maintenance were the same for all patients. They were randomly allocated to the magnesium sulfate group or control group which is without magnesium sulfate.

1. IV induction with propofol anesthetic dose 2-2.5 mg/kg
2. halothane 0.5- 0.7 MAC
3. Fentanyl 1 microgram per kilogram (after delivery of the baby)
4. I.V fluid(10-15ml/kg) of isotonic normal saline 0.9%
5. Atracurium 0.25 mg/kg (when the effect of suxamethonium terminated)
6. suxamethonium 1.5mg/kg
7. antidote used with neostigmine 2.5 mg with atropine 1 mg

Study Procedure

Before induction of anesthesia, name, age, gender, patient identification number, weight and initial vital signs all were recorded.

Magnesium sulfate ampoules and according to the weight of the patient has been given as 50 mg /kg to be given diluted in 100 ml of normal saline given to the patient through 15 minutes. The other group received the same volume of isotonic saline over the same duration .no premedication used for the patients.

The anesthesia was induced with medications mentioned previously, then cuffed endotracheal tube was performed by direct laryngoscopy. the maintenance of the operation was by using halothane 0.5-0.7 MAC

MAP(mean arterial pressure), pulse rate was recorded as the following, preinduction,preintubation, post-intubation,10 minutes later, POCU (postoperative care unit, two hours, 4 hours,12 hours).

ECG and spo2 also used for further monitoring of the patient.

After the operation, the patients were transferred to the recovery room and the consciousness score was evaluated every 10 minutes until ready for discharge from the recovery room. Analgesia was administered in the form of tramadol 100mg and diclofenac sodium 75 mg. Pain scores at rest were evaluated using a 0-10 cm visual analogue scale (VAS, starting from 0; no pain, to 10; worst pain imaginable). The VAS score was recorded at emergence from anesthesia and at 2, 4, and 12 hours after the surgery. The numeric pain scale was used also along with VAS. The dosage and timing of analgesia were recorded immediately after consciousness(all the patients received the same dose of tramadol and diclofenac sodium).

Data Analysis

Data were analyzed using the SPSS® 21 (Statistical Package for Social Sciences) statistical software. Categorical data described as count and percentage. While numerical data were described as mean and standard deviation. Independent sample t-test used for comparison between magnesium sulfate group and control group in pain intensity according to visual analogue scale and numeric pain scale. A P-value of less than 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

This study included 60 patients, 30 for each group. One patient has been excluded from the study (in the magnesium sulfate group). Because this patient had hypotension (MAP difference is more than 30% to that of baseline MAP) but this patient was excluded from the cases but replaced with another suitable case, so the number of magnesium sulfate group still 30. Thus, 60 patients were analyzed, 30 patients in each group, as illustrated in a Table 1.

There are no statistical differences between all variables with p-value more than 0.05 as illustrated in a Table 2.

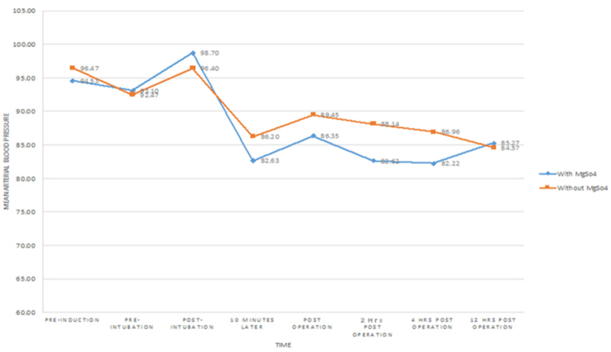

Figure 1: showing MAP changes

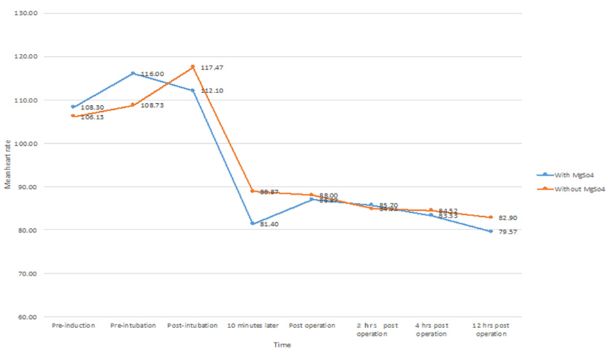

Figure 2: showing HR changes

Table 1: Description of the studied groups

Randomized (n=60)	
Magnesium sulfate group	Control group
(n=30) received 50mg/kg Mgso4 Pre-emptively (in 100 ml 0.9% N/S)	(n=30) received 100 ml 0.9 % N/S
Lost to follow up no= 0 Discontinued intervention(n=0)	Lost to follow up(n=0) discontinued intervention(n=0)
Analyzed (n=30)	Analyzed (n=30)

Table 2: Patient Characteristics in all studied groups

	Study groups		P-value
	Without $MgSo_4$	With $MgSo_4$	
Age (years)	27.63±5.09	25.73±5.43	0.181NS
Weight (kg)	73.55±8.81	68.9±14.32	0.140NS
Duration of surgery (minutes)	43.67±8.9	47.67±6.12	0.052NS

NS: statistically non-significant (p>0.05).

Table 3: Mean arterial pressure changes (MAP)

MAP	With $MgSo_4$	Without $MgSo_4$	p-value
Pre-induction	94.53±9.52	96.47±10.19	0.451NS
Pre-intubation	93.10±12.67	92.47±12.34	0.845NS
Post-intubation	98.70±8.10	96.40±21.11	0.580NS
10 minutes later	82.63±6.14	86.20±12.52	0.167NS
Post-operation	86.35±7.55	89.45±8.64	0.144NS
2-hour post-operation	82.62±6.06	88.14±8.55	0.039*
4 hrs post-operation	82.22±6.44	86.96±7.22	0.010*
12 hrs post-operation	85.27±6.91	84.57±7.13	0.706NS
P-value	<0.001**	<0.001**	

NS: statistically not significant (p>0.05).
*: Statistically significant (p≤0.05)
**: Statistically highly significant (p≤0.001)

Table 4: Heart rate changes

HR	With $MgSo_4$	Without $MgSo_4$	p-value
Pre-induction	108.30±13.79	106.13±18.63	0.611 NS
Pre-intubation	116.00±10.44	108.73±11.98	0.015*
Post-intubation	112.10±14.36	117.47±16.82	0.080 NS
10 minutes later	81.40±9.35	88.87±11.71	0.008*
Post-operation	86.97±6.94	88.00±9.17	0.624 NS
2 hours post-operation	85.70±4.62	84.93±7.44	0.634 NS
4 hrs post-operation	83.33±4.99	84.52±8.37	0.510 NS
12 hrs post-operation	79.57±5.12	82.90±9.26	0.091 NS
P-value	<0.001**	<0.001**	

NS:statistically not significant (p>0.05).
*:Statistically significant (p≤0.05)
**:Statistically highly significant (p≤0.001)

Table 5: Pain intensity by using VAS (visual analogue scale)

VAS	With $MgSo_4$	Without $MgSo_4$	p-value
POCU	5.27±1.53	7.13±1.33	0.001**
2 hrs post-operation	4.37±1.16	5.80±1.24	0.001**
4 hrs post-operation	3.00±0.98	4.53±1.38	0.001**
12 hrs post-operation	2.27±0.45	3.23±1.43	0.001**
P-value	<0.001**	<0.001**	

**:Statistically highly significant ($p \leq 0.001$)

Table 6: Pain intensity by using Numeric pain scale

Numeric Pain scale	With $MgSo_4$	Without $MgSo_4$	p-value
POCU	5.40±1.50	7.20±1.32	0.001**
2 hrs post-operation	4.47±0.94	5.80±1.27	0.001**
4 hrs post-operation	3.03±0.96	4.57±1.33	0.001**
12 hrs post-operation	2.43±0.50	3.17±1.26	0.004*
P-value	<0.001**	<0.001**	

*:Statistically significant ($p \leq 0.05$)
**:Statistically highly significant ($p \leq 0.001$)

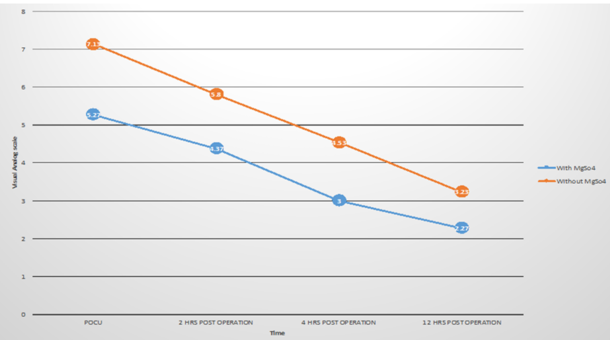

Figure 3: visual analogue scale(VAS)

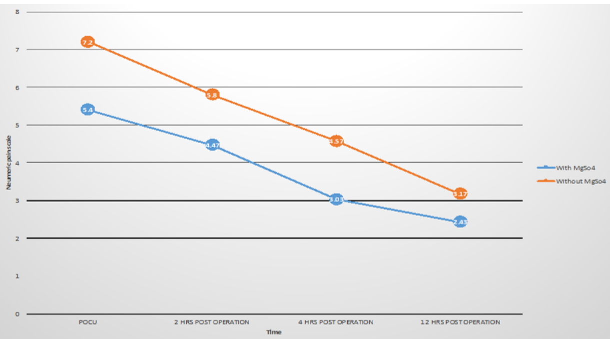

Figure 4: Numeric Pain Scale

The difference in MAP was statically significant in (2 and 4 hours readings) with a p-value less than 0.05 as demonstrated in a Table 3 and Figure 1.

Results listed I Table 4 and demonstrated in Figure 2 showed that the difference in HR was significant in the readings pre-intubation and (10 minutes post-intubation).

Table 5 and Figure 3 revealed that visual analogue scale (VAS) was highly significant in all readings

Table 6 showed that there was highly significant (p<0.001) differences in the following readings (POCU, 2 hours and 4 hours post-operatively) and it's statistically significant (p<0.05) in the reading (12 hours post-operatively) as shown in Figure 4.

Patient characteristic (age, weight) showing no significant difference between the two groups (magnesium sulfate group and control group) as seen in the table, the p-value for age and weight were 0.181 and 0.140 respectively and all of them more than 0.05. Similarly, the duration of operation showing p-value of 0.052. This insignificance could be mainly due to our selection criteria, which produced small ranges of patient characteristics in our study.

The aim of this study was to describe a clinical effect of magnesium on postoperative analgesia and we wished to administer a dose that was most likely to achieve an effect without adverse effects.

Mean arterial pressure (MAP) was significant as in the table in the readings (2 hours post-operation, 4 hours post-operation) with the p-values 0.039 and 0.010 respectively and this mainly related to the effect of Mgso4 on blood pressure (BP) as it acts as a calcium channel blocker.

Heart Rate (HR) was significant as in the table in the readings (pre-intubation and 10 minutes post-intubation) with the p-value 0.015 and 0.008, respectively. A previous study was conducted on 70 patients who underwent elective cesarean section and with the same protocol that we used to evaluate the analgesic effect of magnesium sulphate, it showed no statistical difference in HR between the groups (magnesium sulfate and control group) (Naghibi *et al.*, 2014).

VAS was highly significant in all the readings with the p-value 0.001 and Numeric Pain scale was highly significant in the (post-operative care unit, 2 hours post-operatively, 4 hours post-operatively) and it was significant in (12 hours post-operatively).

Few studies concur our results (Ryu *et al.*, 2006; Tan and Hu, 2006) however, two reports have suggested that mgso4 not decreasing the intensity of pain post-operatively (Paech *et al.*, 2006; Ko *et al.*, 2001).

Some studies suggested that magnesium sulfate infusion reduces the shivering threshold in humans, and I.V. magnesium sulfate has been reported previously to suppress post-anaesthetic shivering (Wadhwa *et al.*, 2005).

CONCLUSIONS

Pre-operative usage of 50mg/kg of magnesium sulfate showed a significant effect in the reduction of pain intensity in an elective cesarean section that scaled by using two pain scales, VAS and numeric pain scale, so magnesium sulfate can be used pre-operatively to reduce the intensity of pain after an elective cesarean section.

Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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