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Effect of intravenous magnesium sulphate infusion during spinal anasesthesia on postoperative pain following caesarean section

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Abstract
Caesarean section is the most widely performed obstetric procedure, Post-operative pain is one of the greatest concerns after caesarean delivery. Currently, opioids are commonly used for relief of post-operative pain but the usage of opioids is associated with many undesirable side effect
Thereafter, there are needs for alternative analgesic drugs to reduce the amount and side effects of opioids such as magnesium sulphate.
Objective: This study aims to evaluate the effect of intravenous infusion of magnesium sulphate during spinal anesthesia on post-operative analgesia and post-operative analgesic requirements in patients undergoing elective caesarean section.
Methods: Total number involved in this study are sixty adult patients scheduled for elective cesarean section under spinal anaethesia, their ages ranged from 21 to 40 years.
Spinal anesthesia was performed at L3-4 or L4-5 interspace. After Dural puncture with a 25 G Quincke needle, hyperbaric bupivacaine 0.5% solution 12.5 mg with fentanyl 25 microgram (µg) was injected
Group (A): 30 Patients received magnesium sulphate 50 mg/kg for 20 min after spinal anesthesia and then 8 mg/kg/h by continuous IV infusion by syringe pump until end or surgery.
Group (B): 30 Patients received the same volume of isotonic saline over the same period.
Results: The time for first need of analgesia was significantly shorter in group II than group I in patients who require ketolac supplements.
Total dose of analgesic consumption in the 24-hour postoperative period was significantly higher in group II than in group I. (P=0.010)
There was no statistically significant difference between the two studied groups regarding perioperative side effects as nausea, vomiting, hypotension, bradycardia and shivering.
Conclusion
1. The addition of intravenous magnesium sulphate during spinal anaesthesia significantly improves pain scores and provides prolonged postoperative analgesia in caesarean section procedures.
2. The addition of intravenous magnesium sulphate during spinal anaesthesia provides stable hemodynamics without significant side effects.
3. The addition of intravenous magnesium sulphate during spinal anaesthesia provides no significant effects on the APGAR score.

Keywords: pain, magnesium sulphate, visual analogue scale, cesarean section

Introduction
Currently opioids are commonly used for relief of post-operative pain after caesarean section, either by intrathecal administration prior to section or post-operative parentral administration but the usage of opioids is associated with many undesirable side effects such as drowsiness, nausea, vomiting, hypotension, itching and respiratory depression [1]
Magnesium is an abundant cation in the body which is essential to numerous physiological activities. Magnesium sulphate is an established treatment of pre-eclampsia, acuteasthma and tachyarrythmias. Magnesium is a non-competitive N-methyl-D-aspartate receptor antagonistand inhibits voltage gated calcium channels.
There are reports about the role of intravenous magnesium sulphate in reducing intra- and post-operative analgesic requirements even high doses of intravenous magnesium sulphate such as those used in treatment of pre-eclampsia undergo minimal transfer across the blood brain barrier [2]
Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage [3]
Magnesium (Mg) is the 4th most abundant mineral in the body, after Sodium, Potassium and Calcium. It is the 2nd most abundant intracellular cation after Potassium. It is a physiological antagonist of Calcium at different voltage-gated channels. It activates about 300 enzymes in the body, many of which involve energy production. ATP is fully functional when chelated to Mg. Mg regulates Calcium entry into the cells [4]
Magnesium is a Ca^{2+} antagonist. It competes with calcium to inhibit vasoconstriction. It blocks the NMDA receptor thus decreasing intracellular calcium. Magnesium inhibits Ryanodine receptors decreasing muscle contraction. Also directly inhibits catecholamine release from the adrenal medulla [5]

Patients and Methods

A total number of sixty adult patients scheduled for elective cesarean section under spinal anaethesia.

This study was carried out in Al Azhar university hospital (Assiut) from May 2019 to April 2020.

Patients

They were selected according to the following criteria

- age 21 to 40 years
- Undergo elective cesarean section under spinal anesthesia.
- ASA physical status I-II
- Singleton pregnancy.
- At least 36 weeks gestation.
- Length between 150 cm to 170 cm.

Exclusion criteria

- Contraindications for spinal anesthesia.
- Hypersensitivity to Magnesium.
- Myopathies.
- Chronic back pain patients.
- Opioid abusers.
- Patients on calcium channel blockers.
- Patients with varying degrees of heart block.
- Complicated pregnancy.

All patients had a pre-oparative visit that included

1. Preoperative history taking, physical examination and routine laboratory investigations (complete blood count, prothrombin time, urea, creatine and random blood sugar).
2. Patients were fasting for 6 hours.
3. Explanation of the usage of the visual analogue scale (VAS).

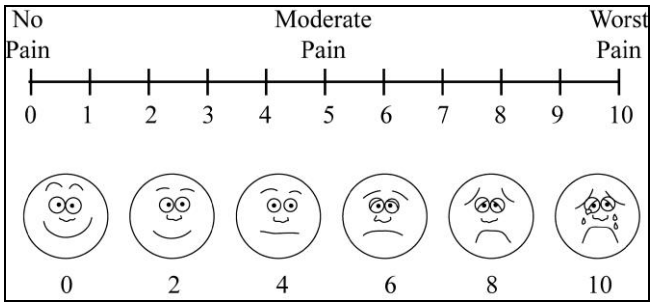

Fig 1: The visual analogue scale (VAS).

The visual analogue scale is usually presented as a 10 mm horizontal line on which the patient's pain intensity is represented by a point between the extremes of "no pain at all" and "worst pain imaginable" [6].

Groups

Using computer generated random table, patients were divided into two groups:

1. **Magnesium sulfate group (M group):** (30 patients)

Spinal anesthesia by 2.5 ml hyperbaric bupivacaine 0.5%.

Patients received magnesium sulfate (50 mg⁄kg) before the operation by intravenous infusion over 20 minutes, then (8 mg⁄kg⁄hour) in 50 ml syringe, started with the surgery and continued until the end of surgery.

2. **Control group (C group):** (30 patients)

Spinal anesthesia by 2.5 ml hyperbaric bupivacaine 0.5%.

Postoperative

Mean arterial blood pressure and heart rate. It was recorded every 30 minutes for the first two hours postoperatively, then every 4 hours for the first 24 hours.

- **Pain assessment**
- **The time interval** between spinal block to the first analgesic request.
- **Post-operative pain** was assessed using visual analogue scale every 30 minutes for the first two hours post-operatively, then every 4 hours for the first 24 hours.
- **Apgar score:** at 1st and 5th minutes.
- **Uterine Contractility:** assessed manually by the surgeon.
- Emergency resuscitation equipments and advanced cardiac support drugs will be available.

Results

This study was performed in Al-Azhar University Hospital on 60 adult patients scheduled for elective caesarean section under spinal subarachnoid block technique.It was successfully performed with no technical problems. Patients were categorized randomly into 2 groups group I ($MgSo_4$) and group II (Saline) 30 Patients each.

1. Hemodynamic data

a. Heart rate (in beats/ min)

Table 1: Heart rate pre-operative and intra-operative

Heart rate	Group I (n= 30)	Group II (n= 30)	P-value
	Mean ± SD	Mean ± SD	
Pre-operative	73.67 ± 10.21	78.73 ± 10.74	0.066
15 min	78.43 ± 10.89	74.73 ± 9.38	0.164
30 min	78.57 ± 12.56	76.60 ± 10.40	0.512
45 min	76.60 ± 10.08	79.77 ± 8.26	0.188
60 min	74.63 ± 8.68	74.60 ± 11.06	0.990
75 min	79.27 ± 9.38	80.17 ± 9.56	0.714
90 min	78.80 ± 10.13	79.90 ± 10.18	0.676
105 min	74.87 ± 10.09	78.40 ± 9.83	0.175
120 min	77.03 ± 10.46	78.13 ± 12.48	0.713

Result of table (1)

There was no statistically significant difference between the two studied groups regarding heart rate at all times of measurement except at 90 min and 4 hrs postoperatively where p value were 0.016* and 0.001* respectively.

b. Respiratory rate (RR) (breaths /min)

Table 2: Respiratory rate pre-operative and intra-operative

RR	Group I (n= 30)	Group II (n= 30)	P-value
	Mean ± SD	Mean ± SD	
Pre-operative	13.43 ± 1.77	12.83 ± 1.70	0.187
15 min	12.50 ± 1.96	12.73 ± 1.70	0.624
30min	12.00 ± 2.30	12.77 ± 1.52	0.134
45 min	10.87 ± 2.13	12.83 ± 1.64	0.000*
60 min	10.93 ± 2.00	13.07 ± 2.07	0.000*
75 min	11.57 ± 2.25	11.93 ± 1.23	0.437
90 min	11.80 ± 1.32	12.17 ± 0.99	0.229
105 min	11.80 ± 1.06	12.40 ± 0.93	0.024*
120 min	12.50 ± 1.31	12.30 ± 1.47	0.579

Results of table (2)

No statistical significant difference was observed as regard

RR between the two groups at all times of measurement except at 45, 60,105 min intra-operatively where p value were <0.001, 0.001 and 0.024*respectively.

c. Oxygen saturation (SpO_2%)

Table 3: SPO_2 pre-operative and intra-operative

SPO_2	Group I (n= 30)	Group II (n= 30)	P-value
	Mean ± SD	Mean ± SD	
Pre-operative	97.90 ± 1.52	97.73 ± 1.82	0.701
15 min	97.57 ± 1.81	95.87 ± 7.52	0.234
30min	97.10 ± 1.77	95.40 ± 7.34	0.222
45 min	97.27 ± 1.78	97.27 ± 1.98	1.000
60 min	97.60 ± 1.54	97.33 ± 1.88	0.551
75 min	97.23 ± 1.59	96.90 ± 1.45	0.399
90 min	97.20 ± 1.69	97.33 ± 1.81	0.769
105 min	97.67 ± 1.56	97.13 ± 1.72	0.213
120 min	97.73 ± 1.66	97.03 ± 1.73	0.115

Results of table (3)
There was no significant change in SpO_2% throughout the times of measurement intraoperatively.
There was no statistically significant difference between the two studied groups as regard SpO_2 throughout the times of measurement intraoperatively ($p > 0.05$).

2. Pain Assessment
A. Visual analogue scale (VAS)

Table 4: Visual analogue scale of the studied groups

VAS	Group I (n= 30)	Group II (n= 30)	P-value
	Median (Range)	Median (Range)	
30 min.	0.0 (0.0-1.0)	0.0 (0.0-2.0)	0.150
60 min.	0.0 (0.0-1.0)	0.0 (0.0-2.0)	0.281
90 min.	0.0 (0.0-1.0)	1.0 (0.0-2.0)	0.005*
2 hrs	0.0 (0.0-3.0)	2.0 (0.0-3.0)	0.000*
4 hrs	1.5 (0.0-4.0)	2.5 (1.0-6.0)	0.002*
8 hrs	2.0 (0.0-6.0)	2.5 (1.0-6.0)	0.080
12 hrs	2.0 (0.0-5.0)	3.0 (1.0-6.0)	0.001*
16 hrs	1.5 (0.0-4.0)	2.0 (1.0-5.0)	0.011*
20hrs	1.0 (0.0-6.0)	2.0 (1.0-3.0)	0.002*
24 hrs	1.0 (0.0-2.0)	1.0 (0.0-3.0)	0.000*

Results of table (4)
The mean VAS was significantly higher in group II than in group I at 90 min, 2, 4, 12,16, 20, 24 hrs were p value were 0.005, 0.000, 0.002, 0.001, 0.011, 0.002, 0.000 respectively.

B. Time for the first need for postoperative analgesia and total dose of analgesic consumption (in milligrams of ketolac) in the 24-hour postoperative period

Table 5: First analgesic request and total ketolac consumption

	Group I (n= 30)	Group II (n= 30)	P-value
	Mean ± SD	Mean ± SD	
Firstanalgesic request	12.00 ± 5.33	7.17 ± 3.73	0.005*
Total ketolac consumption	35.00 ± 12.91	33.33 ± 12.04	0.721

Results of table (5)
- Total dose of analgesic consumption in the 24 hours postoperatively period ranged from 0.0-30.0mg with the mean value of 33.33 ± 12.04mg. Seven patients in group I consumed 15 mg ketolac and 5 patients consumed 30 mg ketolac while Fourteen patients in group II consumed 15 mg ketolac and 8 patients consumed 30 mg ketolac.
- The time for first need of analgesia was significantly shorter in group II than group I for the patients who required ketolac supplements. (p = 0.005).
- Total dose of analgesic consumption in the 24-hour postoperative period was significantly higher in group II than in group I (P = 0.721).

3. Comparison between the two studied groups according to APGAR score after 1st and 5 minutes:

Table 6: APGAR score

APGAR score	Group I (n= 30)	Group II (n= 30)	P-value
	Mean ± SD	Mean ± SD	
APGAR score 1m	5.60 ± 2.04	6.37 ± 1.94	0.141
APGAR score 5m	8.67 ± 1.12	9.00 ± 0.98	0.226

Results of table (6)
APGAR (1min)
No significant difference as regards the APGAR score in 1 min between the two groups (p = 0.141).

APGAR (5 min)
No significant difference as regards the APGAR score in 5 min between the two groups (p = 0.226).

4. Comparison between the two studied groups according uterine contractility (assessed manually by surgeon)

Table 7: Uterine contractility

Uterine contractility	Group I (n= 30)		Group II (n= 30)		P-value
	No.	%	No.	%	
Contracted	25	83.3	26	86.7	0.718
Relaxed	5	16.7	4	13.3	

Results of table (7)
In group I (83.3%) uterus was contracted, while in group II (86.7%) uterus was contracted. This revealed no significance difference between the two groups. (p = 0.718).

Discussion
Delivery by caesarean section is becoming more frequent and is one of the most common operative procedures worldwide; caesarean section is an alternative to having normal vaginal birth. It may be performed because of maternal or foetal problems that arise during labour or on maternal request [7].
Many methods are used in controlling post caesarean delivery pain and choosing the proper method is challenging. The systemic administration of opioids is used but high doses are associated with many side effects like nausea, vomiting and respiratory depression. Systemic administration of non-steroidal anti-inflammatory drugs alone is insufficient to effectively treat post caesarean section pain [8].
Also Kara *et al*. [9] studied the effect of I.V. magnesium sulphate on perioperative pain (a bolus of 30 mg/ kg then 0.5 g/ h infusion for the next 20 h) on 24 patients undergoing elective hysterectomy under spinal anaesthesia. They found that intravenous magnesium showed no significant hypotension due to prehydration with fluids and the magnesium bolus dose was infused over 15 min. Also,

Seyhan *et al*. [10] did not observe hypotensive episodes requiring ephedrine treatment even in the higher rate group.

Conclusion

1. The addition of intravenous magnesium sulphate during spinal anaesthesia significantly improves pain scores and provides prolonged postoperative analgesia in caesarean section procedures.
2. The addition of intravenous magnesium sulphate during spinal anaesthesia provides stable hemodynamics without significant side effects.
3. The addition of intravenous magnesium sulphate during spinal anaesthesia provides no significant effects on the APGAR score.

Compliance with Ethical Standards

Conflict of interest

-The authors declare that they have no conflict of interest.
-An approval of Al-Azhar Assuit faculty of medicine ethical committee was obtained before the start of this study, the aim of the study was explained to each participator before collection of data, verbal and written consent was obtained from those who agree to participate in the study.
- Privacy of the data was assured.

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