

Study the Effect of Intravenous Infusion of Dexamethasone versus Magnesium Sulphate on Incidence and severity of Post Dural Puncture Headache in Parturient Undergoing Caesarean Section

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ABSTRACT

Background: Cerebrospinal fluid (CSF) leaks from the subarachnoid space, causing the CSF volume and pressure to drop which exerts traction on the intracranial pain-sensitive structures and leads to post-dural puncture headache (PDPH). **Objective:** Modulation of PDPH in parturient undergoing cesarean section using intravenous infusion of dexamethasone versus magnesium sulfate. **Subjects and Methods:** Prospective, randomized, controlled, double-blind, clinical study included 72 pregnant women undergoing spinal anesthesia for elective cesarean sections and were allocated into three groups at random. 24 patients per group: **Group C:** patient received 100ml IV infusions of normal saline over 20 minutes after clamping of the umbilical cord, **Group D:** patient received dexamethasone 0.1 mg/kg IV infusion diluted in normal saline with a total volume of 100 ml over 20 minutes beyond clamping of the umbilical cord, **Group M:** cases received 50mg/kg magnesium sulfate IV infusion diluted in normal saline with total volume 100ml over 20minutes beyond umbilical cord clamping. Incidence and severity of PDPH were recorded at 6,12,24,36,48,60&72 postoperatively. **Results:** In comparison to the control group dexamethasone significantly reduce the incidence of PDPH. Both dexamethasone and magnesium sulfate significantly lowered the severity of PDPH in comparison to the control group without any significant difference between the two groups without side effects.

Conclusion: It has been demonstrated using intravenous dexamethasone in pregnant women who have undergone cesarean section with spinal anesthesia reduces the frequency and severity of PDPH. While intravenous magnesium sulfate just reduces the intensity of headache with no adverse effects.

Keywords: Dexamethasone, Magnesium Sulphate, Post Dural Puncture Headache.

INTRODUCTION

A common side effect of spinal anesthesia is post-dural puncture headache (PDPH). The prevalence of PDPH following neuraxial procedure ranges from 6 to 36% ⁽¹⁾. The incidence of dural puncture varies depending on a variety of parameters, including age, gender, the kind and size of the needle, the type of procedure, and the number of tries ⁽²⁾.

The headache is usually intense and throbbing, starting from the front of the head and radiating to the occiput, it gets worse when you sit or rise ⁽³⁾. The standard diagnostic criteria for PDPH include the positional nature and dramatic alleviation after resuming the supine position ⁽⁴⁾. Following intraspinal puncture, CSF loss and a decrease in intracranial pressure are connected to PDPH. The usefulness of intravenous infusion of dexamethasone and magnesium sulfate in avoiding PDPH was demonstrated in certain double-blind and placebo-controlled studies ^(6,7).

Corticosteroids' suppressive effect on the synthesis of inflammatory mediators in immune cells at the puncture site may play a role in the prevention of PDPH as these mediators will be released less frequently into CSF and subsequently decrease the number of stimulated pain receptors in CNS ⁽⁸⁾.

Although the precise mechanism is uncertain, magnesium sulfate's ability to function as a non-competitive antagonist of (NMDA)receptors among peripheral tissues as well as the central nervous system

explains the analgesic effects ⁽⁹⁾. It also affects how much intracellular calcium is present ⁽¹⁰⁾.

SUBJECTS AND METHODS

At 6 months duration from January to June 2022, we conducted our prospective, randomized, controlled, double-blind, clinical study. Using a computer-generated randomization table, 72 expectant mothers undergoing elective cesarean sections were divided into three equal groups at random.

Inclusion criteria:

Acceptance of the participant who was admitted to the hospital for a planned cesarean section with spinal anesthesia, ASA physical status II, the age ranged from 21 to 40, and Body Mass Index (BMI) ranged from 25 to 30 kg/m².

Exclusion criteria:

uncontrolled hypertensive or diabetic, absolute contraindication to spinal anesthesia, history of headache or adverse reactions to study drugs, woman who had taken any form of pain medication in the 24 hours before surgery, more than one attempt for spinal anesthesia, severe intraoperative hypotension [when systolic blood pressure (SBP) is lowered more than 25% from baseline] or required more intraoperative vasopressor drugs than expected.

Preoperative preparation:

All cases were visited before surgery, the goal of the study and the anesthetic procedure was explained in

detail, and informed written consent was obtained. Full history was taken, full laboratory investigations were obtained and clinical examination of vital signs, cardiac, chest condition, examination of airway and back. Any contraindications were excluded. All cases were kept nil orally before the operation (eight hours for fatty meals, six hours for light meals, and two hours for clear fluid).

Intraoperative:

Monitors were attached to the patient and basal readings were recorded at that time. An 18 gauge cannula was secured and preloading with 15 ml/kg crystalloid IV fluid was started. All patients received subarachnoid block in the sitting position and paramedian approach using a 22-gauge Quincke spinal needle at L3-L4 or L4-L5 intervertebral space. The spinal needle advanced at an angle of about 45° toward the midline till CSF flow is obtained then 12.5mg of hyperbaric bupivacaine 0.5% with 25 mcg fentanyl were injected and the needle was extracted. The parturient was immediately placed in a supine position with a 15-degree left tilt and a slight pad elevating the head and neck of the patient. An oxygen face mask with 3 L/min flow was applied to the parturient. Then, the fluid deficit was administered. Pin-brick test and modified Bromage scale were used to assess the effectiveness of the sensory and motor blocks, respectively(12). After the assessment, the surgeon was allowed to proceed.

During the surgery: vital signs were recorded every 5 minutes during the first 25 minutes then every 10 minutes till the end of surgery. Hypotension which was a 20% decrease from the basal systolic blood pressure reading was treated by increasing intravenous fluid and increments of 6mg of IV ephedrine which may be repeated if needed. Bradycardia (heart rate below 55 beats per minute) was treated with 1mg of IV atropine. following delivery and cord clamping, Syntocinon® 10 IU/ml infusion was given, and the patients were randomly split into 3 equal groups:

Group C (n=24): patient received 100 ml IV infusion of normal saline (control group).

Group D (n=24): patient received dexamethasone 0.1 mg/kg IV infusion diluted in normal saline with a total volume of 100 ml.

Group M (n=24): patient received 50 mg/kg magnesium sulfate IV infusion diluted in normal saline with a total volume of 100ml.

Either normal saline or the study drugs diluted in normal saline were produced in identical bottles by a nurse anesthetist. After the infant was born and the umbilical cord was clamped, all drugs were administered intravenously in doses of 100 ml each for 20 minutes. The group randomization was unknown to the patients and the researcher who collects all the data.

Postoperative:

Transfer of the patient to the post-anesthesia care unit (PACU). For an hour, vital signs were recorded in the PACU every 15 minutes. After being evaluated

using the Alderete score (13), the patient was then transferred to the ward.

Headache was observed and recorded using pain assessment on a 0-10 cm line [Visual analog scale (VAS) 0 = no pain, 1-3 = mild pain, 4-6 = moderate pain 7-10 = severe pain](14).

VAS readings were recorded at (6,12,24,36,48,60,72) hours post-operative. Patients were considered to have fully responded if they did not experience PDPH for the full 72 hours. If the patient complained of headache with VAS ≥ 3 , conventional methods (lying flat in the bed, fluid replacement IV and/or orally up to 3000ml daily, Diclofenac(rescue analgesia) 50 mg every 8 hours was administered orally and caffeine 300 mg orally once daily) were applied and the first time to require analgesia was recorded. When the headache was resistant to conventional methods the patient was transferred to the pain clinic for further management. Using a 5-point Likert scale, patient satisfaction was evaluated. (15).

Sample size:

Assuming the frequency of mild PDPH was 25% versus 62.5% in the dexamethasone group versus the control group(16), so the sample size was calculated to be 72 cases, 24 cases in each group using open Epi program at 80% power and 95% CI.

Ethical consent:

Approval of the study was obtained from Zagazig University Academic and Ethical Committee [IRB approval number is (8058)]. Every patient signed an informed written consent for the acceptance of participation in the study. This work has been carried out following the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis:

The statistical package for the social sciences, SPSS, version 26, was used to analyze the data. Quantitative variables' means, standard deviations, or median and interquartile range were used to characterize them, depending on the kind of data. To compare categorical variables, the Monte Carlo test, and the chi-square test were applied where necessary. Categorical variables were presented as percentages and numbers using their absolute frequencies. Levene (homogeneity of variances) and Kolmogorov-Smirnov (distribution-type) tests were used to evaluate hypotheses for use in parametric testing. The Kruskal-Wallis test (for data that are not regularly distributed) and the one-way ANOVA test (for data that are normally distributed) were employed to compare quantitative data between more than two groups. When p is used for comparing two groups, both the pairwise comparison and the posthoc Tukey HSD test were employed. $P < 0.05$. was used as the statistical significance level. If $p \leq 0.001$, a highly significant difference was evident.

RESULTS

The flow chart of the study showed in (Figure 1).

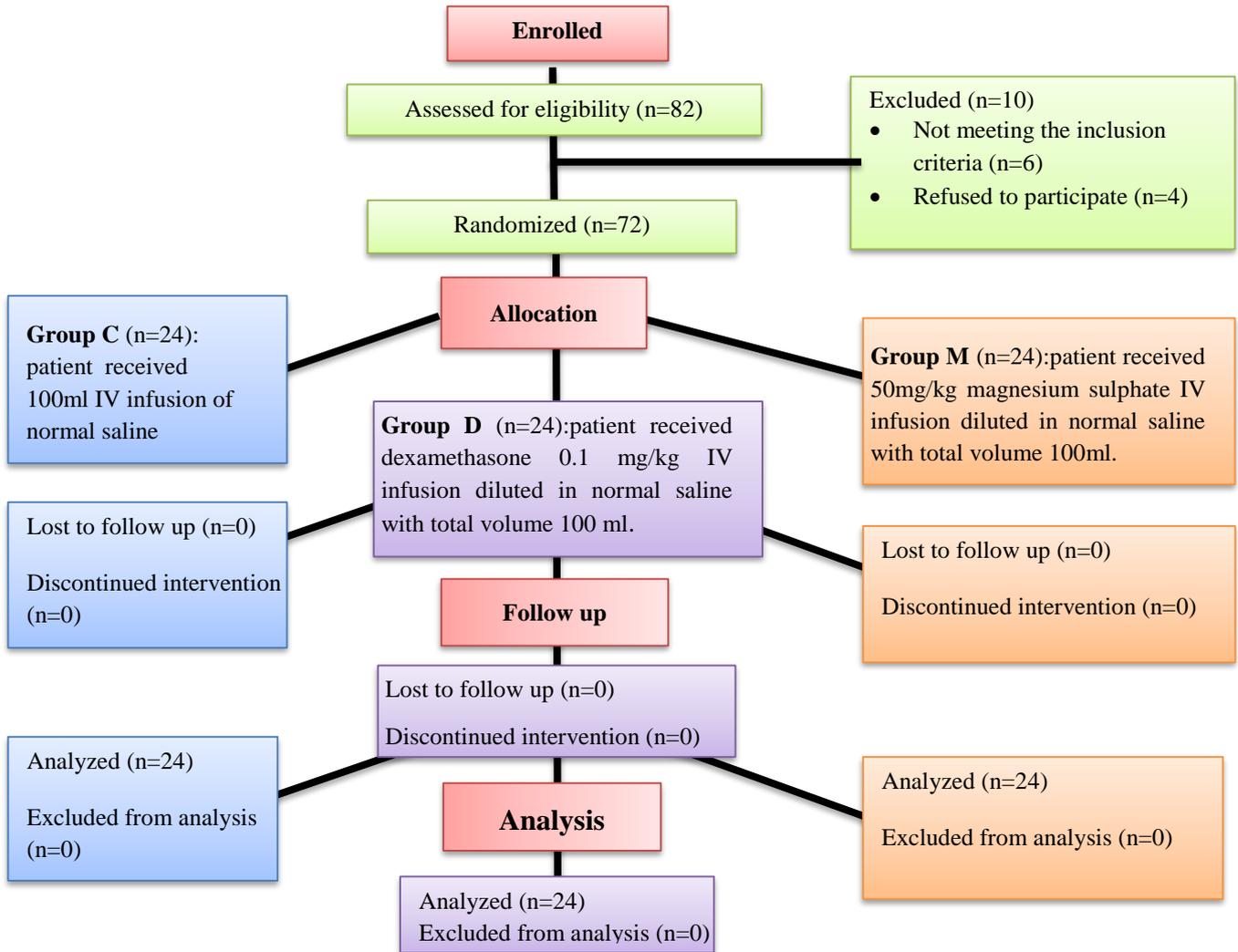


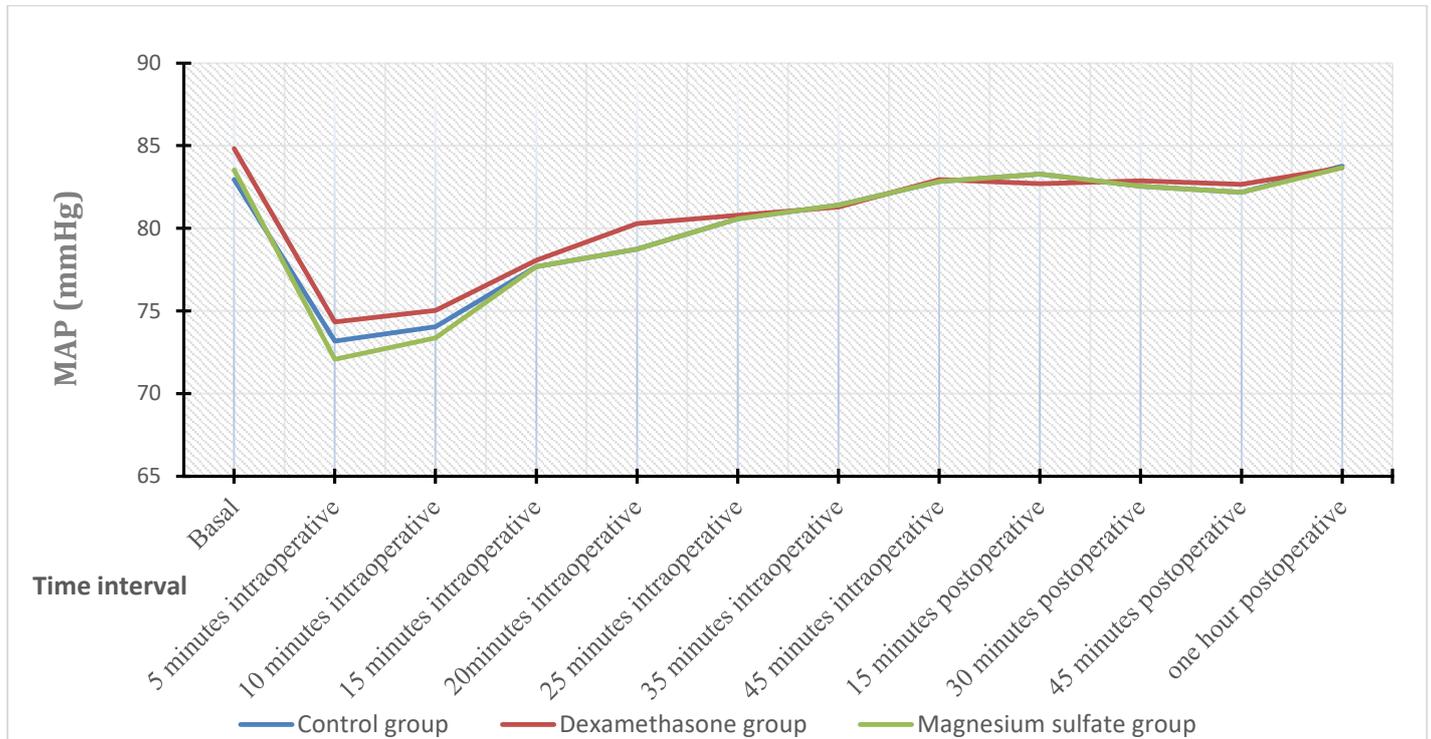
Figure (1): Flow chart of the study.

As regards patients' characteristics (age, BMI, parity, gravidity, ASA & history) and duration of surgery among the examined groups, there were statistically insignificant differences ($p > 0.05$) (Table 1).

Table (1): Characteristics and duration of surgery among the studied groups

Parameter	Groups			Test	
	Control group (group C) (n=24)	Dexamethasone Group (group D) (n=24)	Magnesium Sulphate group (group M) (n=24)	F	P
	Mean ± SD	Mean ± SD	Mean ± SD		
Age (year)	27.38 ± 4.56	27.83 ± 4.79	27.67 ± 4.05	0.064	0.938
BMI (kg/m ²)	26.92 ± 1.47	27.0 ± 1.93	26.88 ± 1.68	0.033	0.967
	Median (IQR)	Median (IQR)	Median (IQR)	KW	P
Parity	1 (1 – 2)	2 (1 – 2)	2 (1 – 2)	1.02	0.6012
Gravidity	2 (1 – 2)	2 (1 – 2)	2 (1 – 3)	0.244	0.885
	n (%)	n (%)	n (%)	χ ²	P
ASA: II	24 (100%)	24 (100%)	24 (100%)	MC	>0.999
History:					
Free	24 (100%)	23 (95.8%)	23 (95.8%)		
Controlled DM	0 (0%)	0 (0%)	1 (4.2%)	MC	>0.999
Controlled HPN	0 (0%)	1 (4.2%)	0 (0%)		
	Mean ± SD	Mean ± SD	Mean ± SD	F	P
Duration of surgery (minute)	45.83 ± 1.49	45.46 ± 1.47	45.79 ± 1.28	0.502	0.607

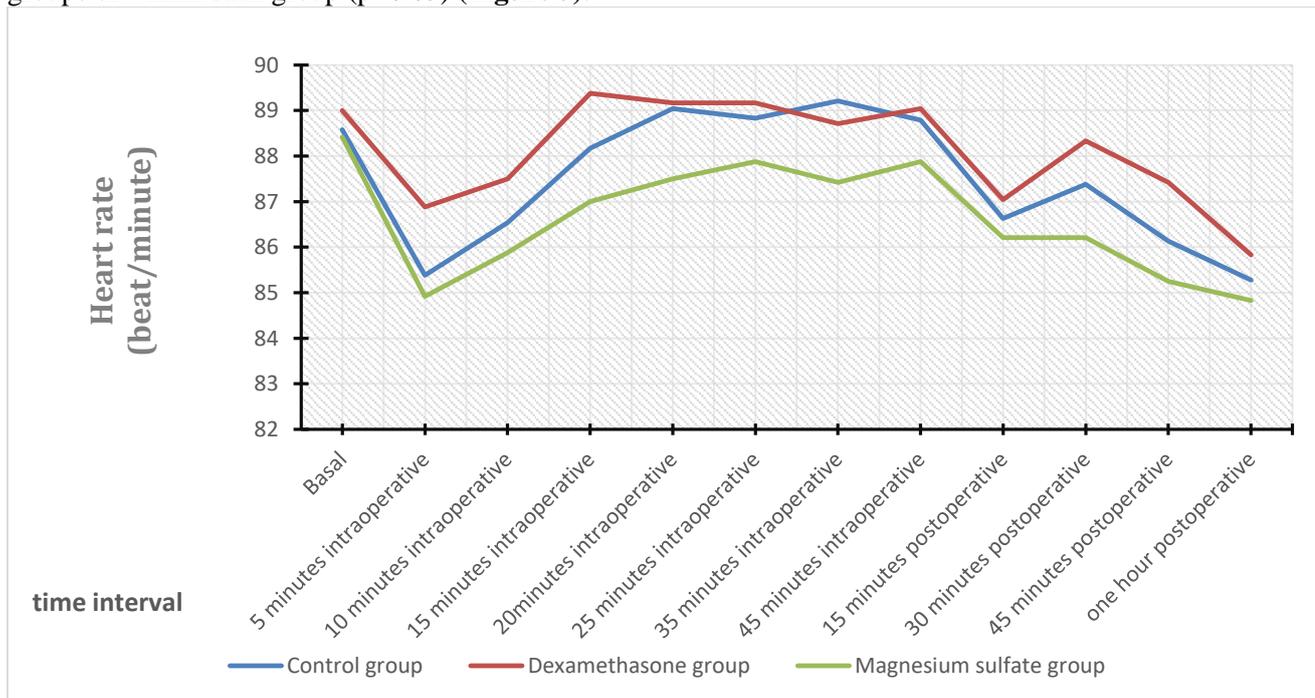
Data were expressed as mean \pm Standard Deviation (SD) or n number of patients and (%) percentage or median and IQR (interquartile range), ASA American Society of Anesthesiology, DM Diabetes Mellitus, HPN Hypertension, χ^2 Chi square test, MC Monte Carlo test, F One way ANOVA. There was a statistically highly significant decline in MAP within each group at 5 and 10 minutes after spinal anesthesia induction compared to baseline ($p > 0.001$), there was no significant difference in MAP between the examined groups intraoperatively or postoperatively ($p < 0.05$) (**Figure 2**).



Data were expressed as mean

Figure (2): Mean arterial pressure (MAP) over time among the studied groups intraoperatively & postoperatively.

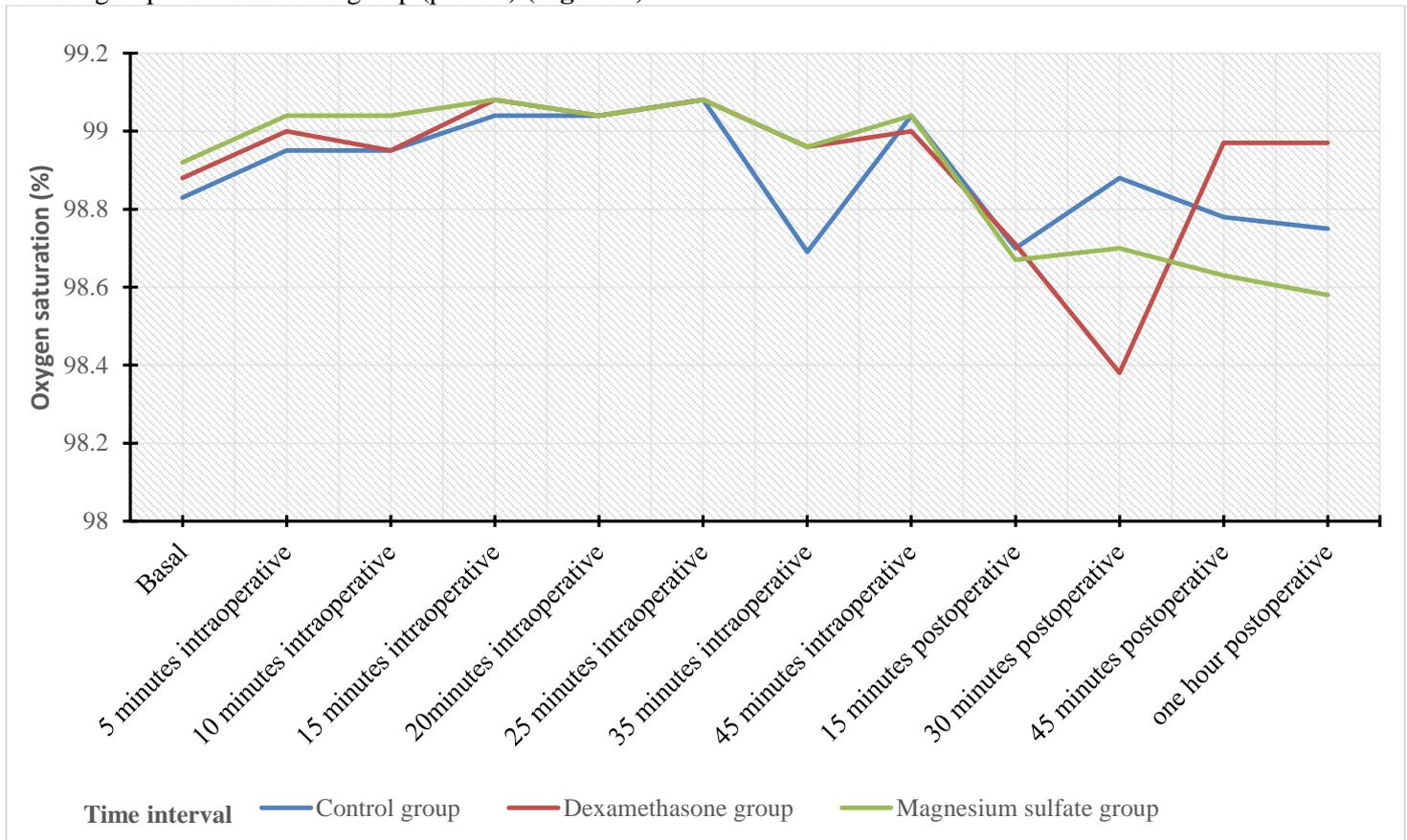
Heart rate did not show a statistically significant difference intraoperatively and postoperatively among the studied groups or within each group ($p > 0.05$) (**Figure 3**).



Data were expressed as mean

Figure (3): Heart rate over time among the studied groups.

Oxygen saturation did not show a statistically significant difference intraoperatively and postoperatively among the studied groups or within each group ($p>0.05$) (**Figure 4**).



Data were expressed as mean

Figure (4): Oxygen saturation over time among the studied groups

At 6 hours and 12 hours, the incidence of headache did not statistically different across the groups that were assessed ($p>0.05$). At 24, 36, 48, 60, and 72 hours, it was shown that the incidence of headache in the control group was statistically significantly greater than that in the dexamethasone group ($p<0.05$) when comparing each pair of groups separately. While there was no difference between the magnesium sulfate group and the control or dexamethasone groups ($p>0.05$) (**Table 2**).

Table (2): Comparison between the studied groups regarding the incidence of post-dural puncture headache over time

Headache	Groups			Test	
	Group C (n=24) n (%)	Group D (n=24) n (%)	Group M (n=24) n (%)	χ^2	P
6 hours	4 (16.7%)	0 (0%)	2 (8.3%)	4.161	0.154
12 hours	6 (25%)	2 (8.3%)	3 (8.3%)	2.543	0.353
	P_1 0.254	P_2 1.00	P_3 0.461		
24 hours	8 (33.3%)	2 (8.3%)	3 (12.5%)	5.19	0.099
	P_1 0.033*	P_2 1.00	P_3 0.086		
36 hours	8 (33.3%)	2 (8.3%)	4 (16.7%)	4.637	0.111
	P_1 0.033*	P_2 0.666	P_3 0.182		
48 hours	8 (33.3%)	2 (8.3%)	4 (16.7%)	4.637	0.111
	P_1 0.033*	P_2 0.666	P_3 0.182		
60 hours	8 (33.3%)	2 (8.3%)	4 (16.7%)	4.637	0.111
	P_1 0.033*	P_2 0.666	P_3 0.182		
72 hours	8 (33.3%)	2 (8.3%)	4 (16.7%)	4.637	0.111
	P_1 0.033*	P_2 0.666	P_3 0.182		

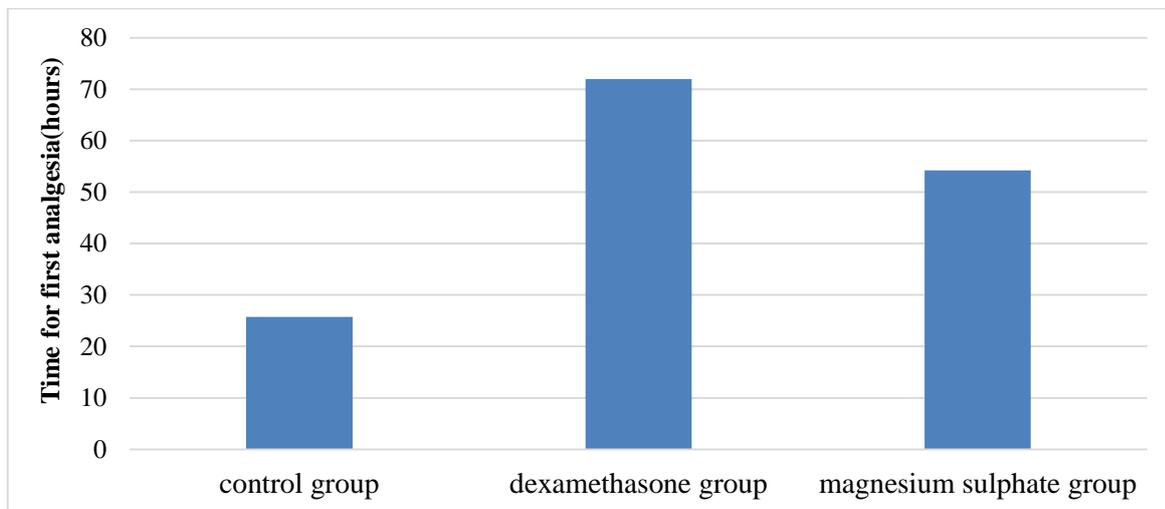
Data were expressed as n number of patients and percentage (%), χ^2 Chi-square test, $p < 0.05^*$ is a statistically significant difference, p1 difference between Dexamethasone group and control group, p2 difference between Magnesium sulfate group and Dexamethasone group, p3 difference between Magnesium Sulphate and control groups. Regarding VAS scores at 12, 24, 36, 48, 60, and 72 hours after surgery significant statistical disparities existed between the groups that were being assessed ($p < 0.05$) while at 6 hours this significance was not found ($p > 0.05$). Dexamethasone and control groups showed a statistically significant difference, as well as magnesium and control groups, but dexamethasone and magnesium sulfate groups did not show a statistically significant difference (**Table 3**).

Table (3): Comparison between severity of post-dural puncture headache by VAS score over time among the studied groups

VAS	Groups			Test	
	Group C n=24	Group D n=24	Group M n=24	KW	p-Value
	Median (IQR)	Median (IQR)	Median (IQR)		
6 hours	3.5 (3 - 4)	0	1.5 (1 - 2)		0.057
12 hours	4 (3 - 5)	1.5 (1 - 2)	2 (1 - 2)	7.803	0.02*
	P ₁ 0.042*	P ₂ 0.739	P ₃ 0.018*		
24 hours	4.5 (3 - 5.5)	1.5 (1 - 2)	2 (1 - 2)	8.828	0.012*
	P ₁ 0.034*	P ₂ 0.739	P ₃ 0.013*		
36 hours	4 (3 - 5.5)	1.5 (1 - 2)	2 (1.5 - 2)	8.577	0.014*
	P ₁ 0.047*	P ₂ 0.576	P ₃ 0.012*		
48 hours	3.5 (3 - 5)	1 (1 - 1)	1.5 (1 - 2)	9.466	0.009*
	P ₁ 0.033*	P ₂ 0.264	P ₃ 0.009*		
60 hours	3 (2 - 4)	1 (1 - 1)	1.5 (1 - 2)	8.321	0.016*
	P ₁ 0.033*	P ₂ 0.264	P ₃ 0.021*		
72 hours	2 (2 - 2.5)	1 (1 - 1)	1 (1 - 1.5)	9.03	0.011*
	P ₁ 0.033*	P ₂ 0.48	P ₃ 0.013*		

Data were expressed as median and IQR(interquartile range), VAS Visual Analogue Scale, F one way ANOVA test, $p < 0.05^*$ is a statistically significant difference, p1 difference between Dexamethasone group and control group, p2 difference between Magnesium sulfate group and Dexamethasone group, p3 difference between Magnesium Sulfate and control groups

The duration of the initial analgesic request varied statistically significantly between the research groups. The difference was statistically significant between the magnesium sulfate group and the control group and also between the dexamethasone and control groups. Although the dexamethasone group's first request for analgesia lasted longer than the magnesium sulfate group's, the difference was not statistically significant. (**Figure 5**).



Data were expressed as mean

Figure (5): Comparison of the first time to request postoperative analgesia among the studied groups

Patient satisfaction scores across the groups show a statistically significant difference. Dexamethasone and control groups show statistically significant variation while the magnesium sulfate group and the dexamethasone or control groups did not differ significantly (Figure 6).

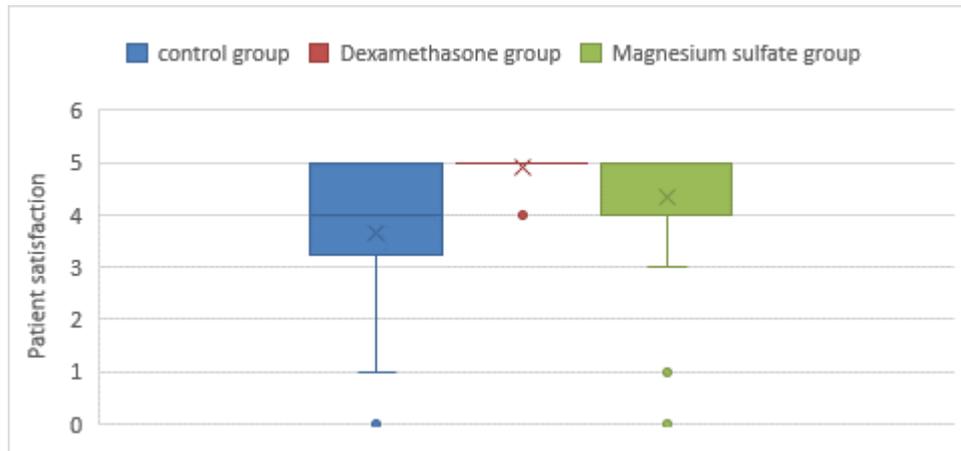


Figure (6): Comparison of patient satisfaction among the studied groups.

There were no side effects (sedation, nausea, vomiting, hypotension, flushing, sweating, poor reflexes) occurred in the studied groups at any time intraoperative or postoperative for 72 hours.

DISCUSSION

The findings of the present study showed that within each group the MAP dropped statistically compared to basal after spinal anesthesia then returning to normal range after delivery of the baby. This may occur because spinal anesthesia induces a sympathetic block which decreases systemic vascular resistance, venous return, and hence maternal cardiac output. In addition, progesterone's vasodilator impact may contribute to this problem (17,18).

Following delivery, MAP increases as a result of the uterine contractions-induced autotransfusion of blood and the relaxation of aortic compression, increasing the cardiac output by 60 to 80 percent (19).

Neither dexamethasone nor magnesium sulfate infusion significantly affects maternal hemodynamics. This is consistent with the studies conducted by Shokrpour *et al.* (20) who found that dexamethasone had no significant effect on maternal hemodynamics when compared to ondansetron in preventing spinal anesthesia-induced headache in pregnant women for an elective cesarean section, spinal anesthesia, and Mireskandari *et al.* (21) who found that magnesium sulfate did not significantly affect the maternal hemodynamics when compared to placebo for post-operative cesarean pain.

The current research found that PDPH was more prevalent in the control group than in the other two groups. This difference was statistically significant for the dexamethasone and control groups, but it was not for the magnesium sulfate and control groups.

A similar study done by Okpala *et al.* (16)

demonstrated that the administration of dexamethasone 8 mg once intravenously reduced the incidence of PDPH compared to the placebo group.

Following Shokrpour *et al.* (20) who compared ondansetron and a placebo, they found that the use of dexamethasone lowers the frequency of PDPH following spinal anesthesia for elective cesarean delivery. Moreover, another study showed that dexamethasone was effective in reducing the rate of PDPH following spinal anesthesia compared to placebo (22).

On the other hand, Yousefshahi *et al.* (23) found that intraoperative intravenous dexamethasone usage was associated with a small increase in the overall incidence of PDPH. The difference between this study and ours is due to the fact that the spinal anesthesia was administered by several anesthetists of various cadres and proficiency. The inclusion of women who had several needle punctures could potentially account for the disparate results.

Shakhsemampour *et al.* (24) in their research on expectant mothers having cesarean sections under spinal anesthesia, noted that 2 ml of dexamethasone injection was unable to significantly reduce the incidence and severity of PDPH. As opposed to their study, which had a follow-up period of just 48 hours, ours had a follow-up period of 72 hours.

In research by Mashak *et al.* (7), it was discovered that the magnesium group, which included pregnant women scheduled for elective cesarean sections under spinal anesthesia, had a lower incidence of PDPH than the placebo group. Magnesium sulfate reduced the incidence of PDPH when compared to a

placebo in the current trial, but this impact was statistically insignificant.

Pregnant women who underwent cesarean sections under spinal anesthesia were the subject of research by **Banach et al.** (25) in the first 24 hours following surgery, caffeine, caffeine plus magnesium, caffeine plus magnesium plus aminophylline, and placebo were administered to the four groups of patients. The caffeine + magnesium group had the lowest PDPH rate, PDPH incidence did not differ across the groups in a statistically meaningful way, nevertheless. The significant difference between this experiment and ours is that all intervention drugs, including magnesium, were taken with caffeine, and the effect of magnesium on its own was not evaluated.

Nikooseresht et al. (26) conducted a study on expectant women under spinal anesthesia who were scheduled for cesarean sections and reported that taking 300 mg of magnesium before surgery dramatically reduced the occurrence and severity of PDPH. Our study differed from theirs in that we used a smaller sample size, whereas they used a larger sample size, which increased the likelihood that the significance would be noted. Additionally, we administered intravenous magnesium intraoperatively following childbirth while they administered oral magnesium sulfate before surgery.

The results of the study showed that the dexamethasone group's PDPH was less severe than those of the other groups. This is in line with the findings of **Okpala et al.** (16), who discovered a substantial decrease in headache intensity in the dexamethasone group compared to the control group.

Anbarlouei et al. (6) examined the effects of spinal anesthesia during a cesarean section on headache relief with intravenous dexamethasone and hydrocortisone. They discovered that intravenous dexamethasone reduced headache severity more effectively than the control group. Comparing intravenous dexamethasone to control and ondansetron groups, researchers found that dexamethasone was more successful in reducing headache intensity (20).

Magnesium sulfate considerably reduces the severity of PDPH as compared to the control group, according to the current study. This was supported by **Mashak et al.** (7), who found that pregnant women receiving magnesium sulfate had lower headache intensity compared to placebo during spinal anesthesia for cesarean sections. Another study revealed a greater reduction in headache severity in patients who took oral magnesium sachet than the patients who received starch powder (26).

Our results showed that dexamethasone was delayed the first time for analgesia requirement which agreed with **Thangaswamy et al.** (27) who used an 8 mg dosage of dexamethasone in their experiment and found that this dose delay was the first time for painkillers after surgery.

According to **Shamim et al.** (28) who gave magnesium sulfate in the same amount and discovered that this dose delayed patients' need for pain medication after surgery, our investigation indicated that magnesium sulfate delayed the initial time for analgesia need compared to the control group.

The current study found no evidence of any dexamethasone-related side effects. This was in agreement with **Naghbi & Hamidi** (29) whose study employed the same amount of dexamethasone without reporting any adverse effects.

According to **Mireskandari et al.** (21), who utilized the same dosage of magnesium sulfate in their trial with no side effects reported, there were no adverse effects of magnesium sulfate in the current study.

CONCLUSION

Based on the results of the current study, we can conclude that in patients having spinal anesthesia for elective cesarean delivery, intravenous dexamethasone decreased the incidence of PDPH compared to that intravenous magnesium sulfate. While both medications lessened the severity of PDPH in comparison to the control group and no adverse effects were reported.

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