



## CLINICAL RESEARCH

# Analgesic and hemodynamic effects of intravenous infusion of magnesium sulphate versus dexmedetomidine in patients undergoing bilateral inguinal hernial surgeries under spinal anesthesia: a randomized controlled study

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### KEYWORDS

Magnesium sulphate;  
Dexmedetomidine;  
Spinal anesthesia;  
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### Abstract

**Background:** Spinal anesthesia is commonly employed during inguinal hernial surgeries. Its short duration may, however, be considered a limitation, especially for bilateral hernial repair. The aim of this research is to investigate the analgesic and hemodynamic effects of intravenous infusion of both MgSO<sub>4</sub> and dexmedetomidine on patients undergoing bilateral inguinal hernia surgeries under spinal anesthesia.

**Methods:** This study was a prospective, randomized, double-blinded controlled trial. It included 60 male patients who had been scheduled for bilateral elective inguinal hernia surgery under spinal anesthesia at Kasr Al-Aini hospital. Patients were randomly allocated to one of three groups (n = 20 each) to receive 50 mL of 0.9% saline intravenous infusion of either dexmedetomidine 0.5 µg.kg<sup>-1</sup>. h<sup>-1</sup> (Group D) or magnesium sulphate 15 mg.kg<sup>-1</sup>. h<sup>-1</sup> (Group M) or normal saline (Group S). The primary outcome of this study was set as the total duration of analgesia. Secondary outcomes were set as the onset and duration of sensory and motor blockade, perioperative hemodynamics, and the total 24-hour postoperative morphine consumption.

**Results:** Durations of sensory and motor blockades as well as durations of analgesia were all significantly longer among patients in Group D (mean 2.2, 3.5, 5.8 hours respectively) and Group M (mean 2.2, 3.3, 5.2 hours respectively), in comparison to Group S (mean 1.5, 2.7, 3.9 hours respectively). No significant differences were found in systolic or diastolic arterial blood pressure, heart rate oxygen saturation, cardiac output, or stroke volume among the study groups. Seven patients in Group D and four patients in Groups M and S developed hypotension.

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**Conclusion:** Intravenous infusion of either dexmedetomidine or MgSO<sub>4</sub> with spinal anesthesia effectively improves the quality of spinal anesthesia and prolongs the duration of postoperative analgesia and decreases the 24-hour postoperative morphine consumption. Results also demonstrated that the use of dexmedetomidine resulted in a slightly longer duration of analgesia, whilst the use of MgSO<sub>4</sub> resulted in slightly better hemodynamic stability.

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## Introduction

Inguinal hernial repair is one of the most commonly performed surgical procedures. It may be conducted under general, regional, or local anesthesia.<sup>1</sup> Spinal anesthesia is commonly employed during inguinal hernial repair because of its simplicity, ease of administration, and absence of the side effects associated with general anesthesia.<sup>2</sup> Its short duration may, however, be considered a limitation, especially for bilateral hernial repair, which requires longer intraoperative time and potent postoperative analgesia. Therefore, many adjuvants (e.g., ketamine, opioids, clonidine, neostigmine, and epinephrine) are being used to prolong the duration of postoperative analgesia after spinal anesthesia. However, all these adjuvants have many side effects and results of studies that have examined their efficacy have not been conclusive.<sup>3</sup>

Magnesium sulphate (MgSO<sub>4</sub>) acts on both adrenergic nerve terminals and the adrenal gland by blocking the release of catecholamines. Previous studies have demonstrated that an intravenous infusion of MgSO<sub>4</sub> during spinal anesthesia had prolonged the durations of both sensory and motor blocks as well as postoperative analgesia.<sup>4-6</sup> Notably, MgSO<sub>4</sub> was reported to have had only a minor effect on the hemodynamic status of patients when used as adjunct to general anesthesia.<sup>7,8</sup> Prior to this study, no other study had reported the hemodynamic effect of intravenous infusion of MgSO<sub>4</sub> with spinal anesthesia.

Dexmedetomidine is an alpha-2 adrenergic receptor agonist with a higher  $\alpha_2/\alpha_1$  selectivity, allowing it to promote analgesic and anesthetic effects. Many studies have investigated the use of dexmedetomidine as an adjuvant to local anesthetics and its use through intravenous infusion during spinal and epidural anesthesia. Results indicated that the use of dexmedetomidine had potentiated motor and sensory blockade of local anesthetics, enhanced sedation, and prolonged the duration of postoperative analgesia.<sup>9-12</sup> Results of studies that have examined the hemodynamic effects of dexmedetomidine when used along with spinal anesthesia are conflicting, and thus inconclusive.<sup>13-15</sup>

The aim of this study was to investigate the analgesic and hemodynamic effects of the intravenous infusion of both MgSO<sub>4</sub> and dexmedetomidine on patients undergoing bilateral inguinal hernia surgeries under spinal anesthesia.

The primary outcome of this study was the duration of analgesia achieved by the use of MgSO<sub>4</sub> or dexmedetomidine. Secondary outcomes were the onset and duration of

sensory and motor blockade and the various perioperative hemodynamics (heart rate, blood pressure, stroke volume, and cardiac output).

## Methods

After acquiring approval of the Ethics Committee of Cairo University Hospital (N-112-2017), protocol registration in the Pan African Clinical Trial Registry PACTR202003463247180, and obtaining patients' informed written consents, this prospective randomized, double-blinded randomized controlled study was conducted at Kasr Al-Aini Hospital in the surgical operating theatres following the guidelines of the Consolidated Standards for Reporting Trials (CONSORT). A total of 60 patients scheduled for bilateral elective inguinal hernia surgeries were enrolled. Inclusion criteria were as follows: male patients between 20 and 60 years of age with American Society of Anesthesiologists (ASA) physical status I or II, with uncomplicated bilateral inguinal hernias. Exclusion criteria were as follows: patients who refused to participate in the study; patients with impaired mental status; patients suffering from coagulation disorders; patients with histories of allergic reactions to local anesthetics; patients suffering from severe cardiac, respiratory, hepatic, renal, or neuropsychiatric disorders; and patients with histories of chronic use/abuse of sedatives, narcotics, and of alcohol, or other drug abuse.

Sixty male patients who were scheduled to undergo bilateral inguinal hernial repairs under spinal anesthesia were randomly allocated to one of three groups (n = 20 in each group) to receive intravenous infusions of either dexmedetomidine (Group D), MgSO<sub>4</sub> (Group M), or normal saline (Group S).

Randomization was achieved using computer generated numbers. Details were concealed in serially numbered sealed opaque envelopes. Details of the series were unknown to the investigators and group assignments were kept in a set of sealed envelopes, each bearing only the case number on the outside. Prior to each surgery, a numbered envelope was opened by a nurse. The card inside indicated the group to which the patient would be assigned.

Upon arrival at the surgical theatre, demographic data (age, gender, weight, and height) of patients were recorded, and ECGs and non-invasive blood pressure measurements were conducted. A pulse oximeter was then attached in order to record the baseline heart rate (HR), systolic arte-

rial blood pressure (SAP), diastolic arterial blood pressure (DAP), and arterial oxygen saturation (SPO<sub>2</sub>).

Electrical cardiometries (ICON® Cardiotonic, Osyka; Berlin, Germany) were used to monitor each patient's cardiac output (CO) and stroke volume (SV). Four electrodes were applied on the patient's bare skin (on the left neck below the ear, directly above the midpoint of the left clavicle, along the left mid-axillary line at the level of the xiphoid process, and two inches caudal to the third electrode).

An intravenous access with an 18G cannula was established and avasive blood pressure measurements were conducted. A pulse oximeter was then attached in order to record the baseline heart rate (HR), systolic arterial blood pressure (SAP), diastolic arterial blood pressure (DAP), and arterial oxygen saturation (SPO<sub>2</sub>).

Electrical cardiometries (ICON® Cardiotonic, Osyka; Berlin, Germany) were used to monitor each patient's cardiac output (CO) and stroke volume (SV). Four electrodes were applied on the patient's bare skin (on the left neck below the ear, directly above the midpoint of the left clavicle, along the left mid-axillary line at the level of the xiphoid process, and two inches caudal to the third electrode).

An intravenous access with an 18G cannula was established and preloading with a 500 mL of lactated Ringer's solution preload was started; no premedication was given.

Drug infusion was initiated directly before spinal anesthesia. Group M patients received MgSO<sub>4</sub> in a dosage of 50 mL of 0.9% saline infused at a rate of 15 mg.kg<sup>-1</sup>.h<sup>-1</sup>. Group D patients received dexmedetomidine in 50 mL of 0.9% saline solution infused at a rate of 0.5 µg.kg<sup>-1</sup>.h<sup>-1</sup>. Group S patients received 50 mL of 0.9% saline solution. Drug infusion continued until the end of the surgery.

The group-specific intravenous drug solutions were prepared and injected by an anesthesiologist who was not involved in the study. The anesthesiologists involved in patient observation and data collection were blinded to the treatment group to which each patient was assigned, as were the patients.

Spinal anesthesia was administered at the L3–L4 intervertebral space in the sitting position using 25G Quincke's needle, after ensuring free flow of cerebrospinal fluid. Three milliliters of hyperbaric bupivacaine 0.5% (15 mg) was administered intrathecally to patients of all three groups.

The Bromage scale was used to assess onset and duration of motor block, whereas the pinprick test was used to assess sensory block. The level of the blockade was assessed to ensure that it was between T10–T8; blocks higher than T8 and failed blocks were excluded. Two segment regression was used to assess the duration of sensory blockade. Surgery commenced only after achieving a sensory block of T8 and a Bromage score of 3.

Hypotension was defined as a fall in systolic blood arterial blood pressure less 20% of baseline readings. It was treated with the injection of incremental doses of 3 mg intravenous ephedrine. Bradycardia was defined as a fall in HR to less than 50 beats/min and was treated with intravenous 0.01–0.02 mg.kg<sup>-1</sup> of atropine. Drops in cardiac output or stroke volume greater than 20% of baseline levels were treated with fluid boluses of 250 mL crystalloids (0.9% NaCl) which could be repeated until cardiac output/stroke volume had reached normal levels. Desaturation was defined

as a SPO<sub>2</sub> level of less than 90% and was treated using a face mask with O<sub>2</sub> flow of 4 L.min<sup>-1</sup>.

BP, HR, SPO<sub>2</sub>, SV, and CO were recorded preoperative as baseline readings, at 15 minutes intraoperatively and every 30 minutes thereafter until the end of surgery. Subsequently, readings were recorded every hour postoperatively until the first call for analgesia.

A visual analogue scale was used to assess pain postoperatively. For a pain intensity ≥ 3, rescue analgesia was provided in the form of 3 mg boluses of intravenous (IV) morphine which could be repeated every 10 minutes until pain intensity fell below three. A maximum dose of 0.5 mg.kg<sup>-1</sup>.24 h<sup>-1</sup> of morphine was allowed. Duration of analgesia was defined as the time from the subarachnoid block to a visual analogue scale pain intensity ≥ 3. Total consumption of morphine during the first postoperative 24 hours was recorded.

Intraoperative and postoperative complications (hypotension, bradycardia, desaturation, nausea, vomiting, shivering, and excessive sedation at a Ramsay sedation scale value of 5 or 6) were assessed and recorded. Nausea and vomiting were treated with 10 mg of metoclopramide.

The primary outcome was set as the total duration of analgesia. Secondary outcomes were set as the onset and duration of sensory and motor blockade, perioperative hemodynamics (heart rate, blood pressure, stroke volume, and cardiac output), and the total 24-hour postoperative morphine consumption.

### Sample size

The primary outcome of the current study was the achieved duration of analgesia. A previous study<sup>3</sup> reported a duration of analgesia with the use of MgSO<sub>4</sub> to have averaged 262 (±21) minutes. In this study, proper patient sample sizes needed to detect a mean difference of 10% (26 minutes) between study groups was computed using MedCalc. This was done after taking a study power of 95% and alpha error of 0.05. A minimum number of 54 patients (18 per group) were found to be needed for study results to be of value. The number was increased to 22 patients per group to compensate possible dropouts.

### Statistical analysis

Data were tabulated on Microsoft Office Excel 2010 for Windows spreadsheet. Data were then processed and statistically analyzed using the Statistical Package for the Social Sciences software program, version 20 (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.).

Quantitative variables were presented as means ± standard deviations for normally distributed data or as medians and interquartile ranges for non-normally distributed, and qualitative variables were reported as frequencies and percentages. Genders and ASA grades were presented as numbers and percentages. Ages, heights, weights, total morphine doses, onsets and durations of sensory and motor blockade were presented as means and standard deviations, while results of assessments conducted using the Ramsay sedation scale were presented as medians and interquartile ranges. Normality of distribution of quantitative data was

**Table 1** Demographic data and duration of surgery.

	Group D (n = 20)	Group M (n = 20)	Group S (n = 20)	p-value
Age (years)	40.3 ± 6.38	37.8 ± 7.48	39.2 ± 6.79	0.934
ASA(I/II)	12/8	14/6	11/9	0.85
Weight (kg)	74.6 ± 6.69	75.8 ± 3.37	76.4 ± 2.7	0.815
Height (cm)	168.1 ± 4.8	168.3 ± 5.8	168.5 ± 4.2	0.995
Body Mass Index (Kg.m <sup>-2</sup> )	26.4 ± 1.5	26.8 ± 2.2	25.6 ± 5.7	0.924
Duration of surgery (min)	109.4 ± 2.3	114.5 ± 1.7	114.6 ± 2.1	0.942

Group D, Dexmedetomidine Group; Group M, Magnesium Sulphate Group; Group S, Saline Group.

Data of age, weight, height, body mass index, and duration of surgery are presented as mean ± SD. ASA classification presented as numbers.

\*Denotes statistically significant difference between three groups.

†Denotes statistically significant difference with control group.

\*\*Denotes statistically significant difference between MgSO<sub>4</sub> and dexmedetomidine groups.

tested using the Kolmogorov-Smirnov test. Categorical data were compared using either the Chi-Square or Fisher's Exact tests. *F*-tests (ANOVA) were used to compare the normally distributed quantitative variables between the three groups. Comparisons between baseline values and subsequent values of BP, HR, SPO<sub>2</sub>, SV, and CO within the same group (pair-wise group comparison) were performed using the repeated measures ANOVA model followed by the Bonferroni test as a post-hoc test. For all statistical comparisons, a *p*-value < 0.05 was considered significant.

## Results

Seventy-six male patients were screened for possible enrollment in this study; 12 patients did not meet the inclusion criteria, and 3 patients were excluded due to spinal block levels higher than T8. Another patient was excluded due to failure to achieve spinal block within 15 minutes. Sixty patients (20 for each group) were included in the randomization process. All patients were comparable with regards to their demographic data, age, weight, height, BMI, duration of surgery, and ASA classifications (Table 1).

Duration of analgesia was significantly longer among patients in Group D (mean: 5.8 hours) and Group M (mean: 5.2 hours) compared with patients in Group S (mean: 3.9 hours). The differences in duration of analgesia between patients in Group D and Group M were statistically insignificant (Table 2).

Similarly, durations of sensory and motor blockade were significantly longer among patients in Group D (means: 2.2, 3.5 hours, respectively) and Group M (means: 2.2, 3.3 hours, respectively) compared with patients in Group S (means: 1.5, 2.7 respectively). Again, differences between Groups D and M were insignificant. Overall, there was no statistically significant difference in the timing of onset of sensory and motor blockade among the three groups (Table 2).

In addition, total postoperative 24-hour morphine requirements were significantly higher in group S (12.8 mg) compared with group D (8.7 mg) and group M (9.5 mg), with insignificant differences between patients in groups D and M (Table 2).

No statistically significant differences were found between the study groups with regards to their SAPs (Figure

1) and DAPs, HRs (Figure 2), or SpO<sub>2</sub>. Of all patients, seven in Group D and four in both Groups M and S developed hypotension. Incremental doses of ephedrine were administered in each incident of hypotension, and in all cases the arterial blood pressure was normalized.

There were no significant differences between any of the study groups with regards to cardiac output (CO) or stroke volume (SV), either during the intraoperative or postoperative periods (Figures 3 and 4). The immediate postoperative sedation scored with the Ramsay Sedation Scale was significantly higher in Group D compared with Groups M and S with a median 2 and interquartile range of (2–4) in Group D, 1 (1–2) in Group M and 1 (1–2) in Group S. The average regression time for scores of the Ramsay sedation scale in Group D was 2 hours. No cases of excessive sedation (Ramsay sedation scale of 5 or 6) were recorded (Table 2).

Three cases in each of Groups D and S experienced nausea, compared with two cases in Group M. No cases of vomiting were observed among the three study groups. Two cases in each of Groups D and M experienced shivering compared with four cases in Group S. None of these differences were found to be statistically significant.

## Discussion

Spinal anesthesia is considered safe and efficient for many surgical procedures. It reduces instances of deep venous thrombosis, pulmonary embolism, requirements for blood transfusion, pneumonia, and respiratory depression. However, the duration of sedation it provides is considered as a limiting factor for many surgical procedures.<sup>16</sup>

Magnesium sulphate (MgSO<sub>4</sub>), a non-competitive antagonist of N-Methyl-D aspartate (NMDA) receptors, is one of the most used drugs in various fields of anesthesiology with a good safety profile. It acts by causing reinforcement of local anesthetic action on peripheral nerves. It also acts as a calcium antagonist that prevents transmission of pain impulses by preventing calcium influx into the cells.<sup>3-5</sup> This antagonism is responsible for the perioperative analgesia associated with the administration of MgSO<sub>4</sub>.

The hemodynamic effect of MgSO<sub>4</sub> is believed to be due to different mechanisms, first by blocking the release of catecholamines from the adrenergic nerve terminals and



**Table 2** Spinal block characteristics and Ramsay sedation scale.

	Group D (n = 20)	Group M (n = 20)	Group S (n = 20)	p-value
Onset sensory (min)	4.6 ± 1.69	5.1 ± 2.27	5.9 ± 1.62	0.097
Duration sensory (h)	2.2 ± 0.57 <sup>b</sup>	2.2 ± 0.53 <sup>b</sup>	1.5 ± 0.40	< 0.001 <sup>a</sup>
Onset motor (min)	4.6 ± 1.28	4.0 ± 2.34	5.4 ± 2.25	0.209
Duration motor (h)	3.5 ± 0.78 <sup>b</sup>	3.3 ± 0.54 <sup>b</sup>	2.7 ± 0.50	0.001 <sup>a</sup>
Duration analgesia (h)	5.8 ± 1.30 <sup>b</sup>	5.2 ± 1.44 <sup>b</sup>	3.9 ± 1.03	< 0.001 <sup>a</sup>
Morphine (mg)	8.7 ± 1.92 <sup>b</sup>	9.5 ± 2.44 <sup>b</sup>	12.8 ± 2.36	< 0.001 <sup>a</sup>
Immediate postoperative Ramsay sedation scale	1 (2–4) <sup>b,c</sup>	1 (1–2)	1 (1–2)	< 0.001 <sup>a</sup>

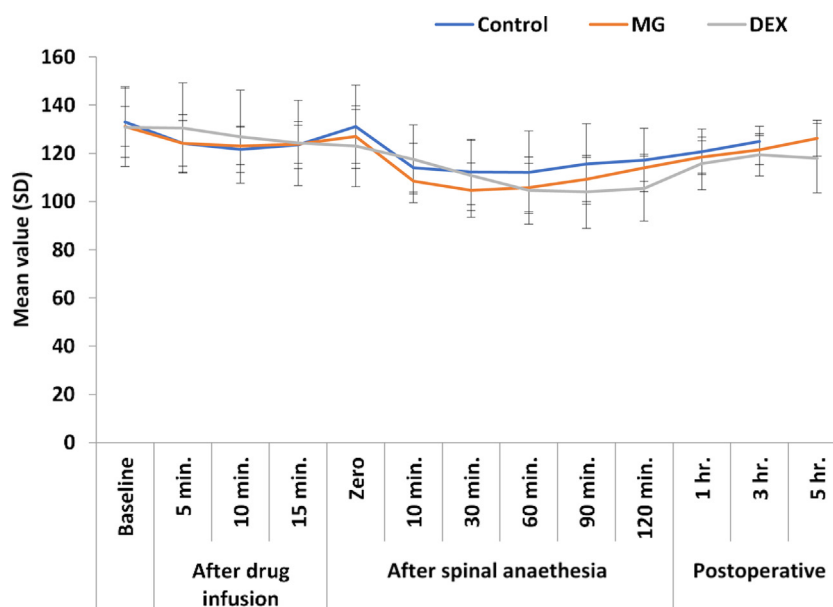
Group D, Dexmedetomidine Group; Group M, Magnesium Sulphate Group; Group S, Saline Group.

Data are presented as mean ± SD. Ramsay sedation scale is presented as median (interquartile range).

<sup>a</sup> Denotes statistically significant difference between three groups.

<sup>b</sup> Denotes statistically significant difference with control group.

<sup>c</sup> Denotes statistically significant difference between MgSO<sub>4</sub> and dexmedetomidine groups.



**Figure 1** Baseline, intraoperative and postoperative Systolic arterial blood pressure. DEX, Dexmedetomidine group; Mg, Magnesium sulphate group; Control, Saline group.

the adrenal glands and producing vasodilatation by acting directly on blood vessels. Secondly, MgSO<sub>4</sub> is believed to act through calcium inhibition in the cell membrane and intracytoplasmic through activating membrane Ca-ATPase and Na-K-ATPase, which are normally involved in transmembrane ion exchange during depolarization and repolarization.<sup>17</sup>

Dexmedetomidine is a highly selective  $\alpha_2$ -adrenergic receptor agonist in the brain and spinal cord which induces hypnosis, sedation, and anxiolysis. It causes hyperpolarization of nerve tissue, produces analgesia, and enhances regional anesthesia by changing the trans-membrane ionic conductivity of the locus coeruleus in the brainstem. This sympatholytic effect causes a decrease in arterial blood pressure and heart rate by reducing norepinephrine release.<sup>18</sup>

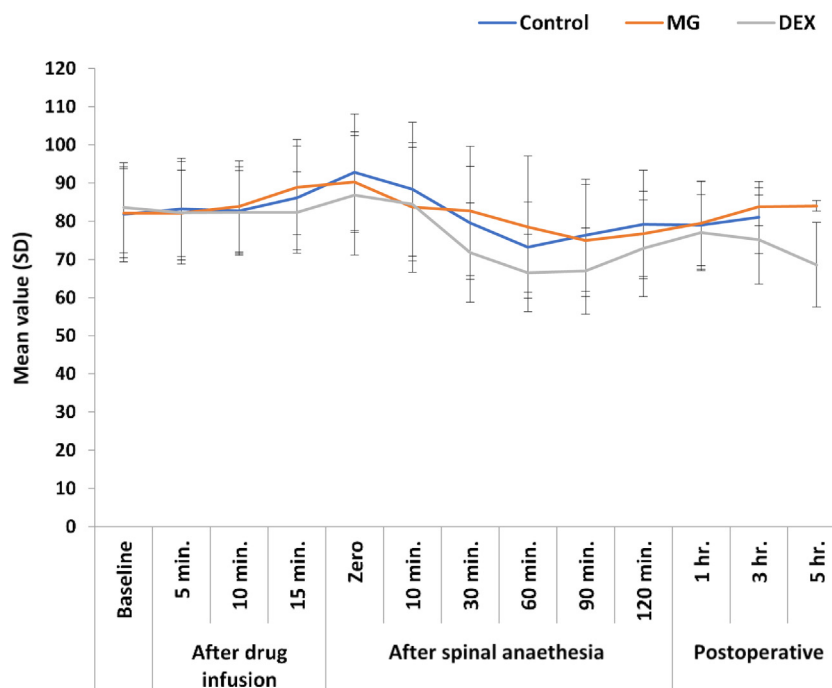
Our study demonstrated that intravenous infusion of either MgSO<sub>4</sub> or dexmedetomidine during spinal anesthesia had prolonged the duration of sensory and motor blockades,

duration of analgesia and had reduced the 24-hour postoperative morphine consumption with no effect on the onset of spinal anesthesia.

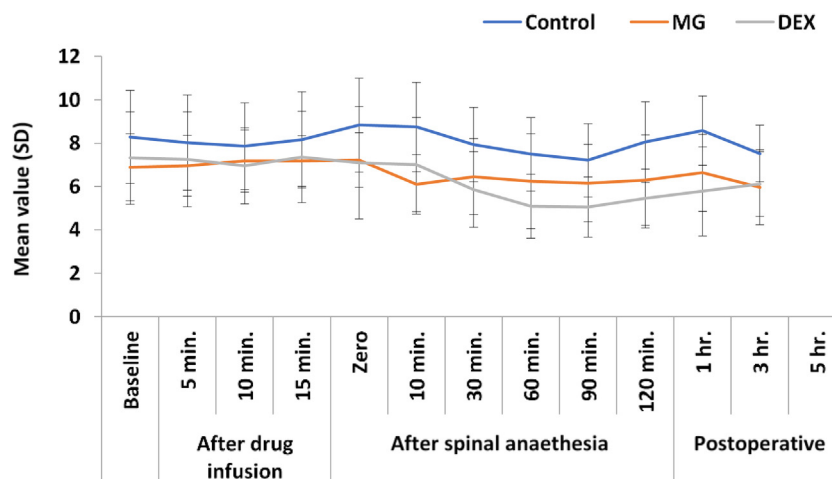
Previous studies have reported that the synergistic interaction between intravenous infusion of either dexmedetomidine<sup>15,19–22</sup> or MgSO<sub>4</sub><sup>3,23–25</sup> and local anesthetics during spinal anesthesia had reduced the time of onset of sensory and motor blockades. Reportedly, these synergistic interactions had also prolonged the duration of both sensory motor blockades and induced sedation.

Ebru Tarıkçı Kılıça et al reported mostly similar findings to those of the present study. They did however find that dexmedetomidine did not reduce analgesic requirements. This dissimilar finding may be attributable to the lower dose of 0.2  $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$  of dexmedetomidine used by them.<sup>26</sup>

In our study, seven patients in the dexmedetomidine group and four patients in both the control and MgSO<sub>4</sub> groups developed hypotension immediately after spinal



**Figure 2** Baseline, intraoperative and postoperative heart rate. DEX, Dexmedetomidine group; Mg, Magnesium sulphate group; Control, Saline group.



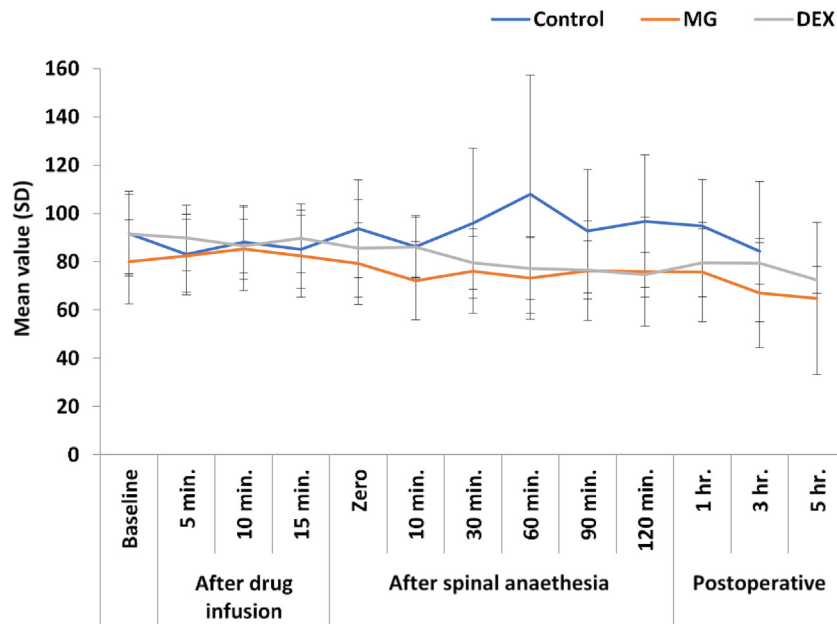
**Figure 3** Baseline, intraoperative and postoperative Cardiac output data. DEX, Dexmedetomidine group; Mg, Magnesium sulphate group; Control, Saline group.

anesthesia. Arterial blood pressure was normalized using a single incremental dose of ephedrine in each incident. These hypotensive attacks were not accompanied by any changes in cardiac output or stroke volume. We believe that this minor hemodynamic change was due to the effect of spinal anesthesia rather than the effect of the infusion drugs.

Santpur MU et al<sup>12</sup> reported a decrease in heart rate without a significant decrease in blood pressure following the infusion of dexmedetomidine. This bradycardia may be due to their administration of dexmedetomidine in a bolus then maintenance regimen ( $1 \mu\text{g}\cdot\text{kg}^{-1}$  over 20 min followed by  $0.5 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ ).

In the study performed by Ebru Tarıkçı Kılıça et al,<sup>26</sup> they found that the infusion of dexmedetomidine had induced hypotension and bradycardia without any noticeable effect on oxygen saturation. This was despite their usage of a lower dose of dexmedetomidine ( $0.2 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ ) than the dose used in the present study ( $0.5 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ ).

So Hui Yun et al<sup>21</sup> conducted a study to assess the hemodynamic changes and the extent of sedation and analgesia after the administration of dexmedetomidine to elderly patients undergoing total knee arthroplasty under spinal anesthesia. They recommended an intravenous infusion dose of  $0.4\text{--}0.8 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$  without the use of a loading dose. They found that patients who had received dexmedetomi-



**Figure 4** Baseline, intraoperative and postoperative Stroke volume data. DEX, Dexmedetomidine group; Mg, Magnesium sulphate group; Control, Saline group.

dine required lesser postoperative doses of opioids with a prolongation of duration of analgesia by about 3.5-hours with no significant changes in blood pressure or oxygen saturation. Bradycardia, however, was more common among patients who had received dexmedetomidine.

It appears that the key to the avoidance of the possible negative hemodynamic effects of dexmedetomidine is to administer it as a continuous intravenous infusion of low dose regimen rather than the administration of a high bolus dose of the drug.<sup>15</sup>

Akansha Agrawal et al<sup>3</sup> administered intravenous  $MgSO_4$  in bolus doses of  $50 \text{ mg.kg}^{-1}$  preoperatively to surgical patients, followed by  $15 \text{ mg.kg}^{-1}.\text{h}^{-1}$  during spinal anaesthesia. They did not report any significant side effects such as hypotension, bradycardia, nausea, vomiting, or significant oxygen desaturation.

Similarly, Prerana N. Shah et al<sup>23</sup> used 250 mg intravenous bolus doses of  $MgSO_4$  followed by 500 mg infusions during spinal anaesthesia. They similarly did not report any significant hemodynamically related side effects of bolus administration of  $MgSO_4$ .

In the present study, neither the use of dexmedetomidine nor of  $MgSO_4$  had led to any significant effects such as hypotension, bradycardia, peripheral oxygen desaturation, nausea, vomiting, or shivering.

We did not record any significant adverse changes to respiratory pattern (determined by the absence of tachypnea), nor to levels of oxygen saturation in our three study groups. This may be due to the use of low doses of infusion regimens rather than multiple intravenous boluses.

Moreover, no case of over sedation was observed in the three study groups. Still, scores of the Ramsay Sedation Scale were found to be higher in the dexmedetomidine group (median 2 and interquartile range of [2-4]) compared with both the  $MgSO_4$  (median 1 [1-2]) and control groups (median 1 [1-2]).

The sedative effect of dexmedetomidine has been examined in several previous studies. This sedative effect may be attributable to a combination of decreased afferent neural input to the reticular activating system and a direct effect of local anesthetics used during spinal anaesthesia.<sup>15,19-22</sup>

Zohar E., et al<sup>16</sup> studied the effect of different regimens of dexmedetomidine on the values of the sedation score. They administered a  $0.5 \mu\text{g.kg}^{-1}$  bolus over 15 minutes immediately after spinal anaesthesia to a patient of one group,  $0.5 \mu\text{g.kg}^{-1}.\text{h}^{-1}$  infusion until the end of surgery to a second group, and both the bolus and infusion to a third group. In all their study groups, RSS scores of 3 were constantly recorded post-surgically despite the different regimens and different doses of dexmedetomidine used. The maintenance dose of dexmedetomidine was suggested by the authors to prolong the period of anaesthesia and achieve satisfactory sedation.

In a number of previous studies, the use of both dexmedetomidine and  $MgSO_4$  led to effective prevention and management of spinal anaesthesia-induced shivering.<sup>27,28</sup>

The mechanism of action by which dexmedetomidine exerts its anti-shivering effect after spinal anaesthesia may be through inhibition of central thermoregulatory control through restraining neuronal conductance as well as suppressing vasoconstriction and shivering thresholds.<sup>28</sup>

On the other hand, the anti-shivering effects of  $MgSO_4$  have been postulated to be due to both central and peripheral mechanisms. Centrally,  $MgSO_4$  is believed to reduce the shivering threshold.  $MgSO_4$  is an NMDA receptor blocker that causes a decrease in the release of norepinephrine and 5-HT. Peripherally,  $MgSO_4$  is a mild muscle relaxant which, through calcium antagonism, causes peripheral vasodilatation.<sup>28</sup>

One important limitation of this study is not having specifically investigated the effects of dexmedetomidine or  $MgSO_4$  on postoperative bowel function or duration of postoperative hospital stay. Nevertheless, it's worth noting that most patients who had taken part in this study

were discharged only a day after surgery. The exact time of resumption of bowel function per each group was, however, not recorded.

## Conclusions

Results of this study demonstrated that intravenous infusion of either dexmedetomidine or MgSO<sub>4</sub> with spinal anesthesia would effectively improve the quality of spinal anesthesia, prolong the duration of postoperative analgesia, and decrease the 24-hour postoperative morphine consumption. The use of dexmedetomidine resulted in a slightly longer duration of analgesia, whilst the use of MgSO<sub>4</sub> resulted in slightly better hemodynamic stability.

## Clinical trial registration

Pan African Clinical Trial Registry PACTR202003463247180 ([www.pactr.org](http://www.pactr.org)).

## Funding

No funding was obtained aside from the resources available at the Cairo University Hospital.

## Availability of data and material

Data were made available to the corresponding author after submitting an appropriate request and obtaining permission from Cairo University.

## Ethics approval and consent to participate

Cairo University Hospital Research Committee n<sup>o</sup> N-112-2017. Before inclusion of patients, written informed consents were obtained.

## Conflicts of interest

The authors declare no conflicts of interest.

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