Comparative study between intrathecal dexmedetomidine and intrathecal magnesium sulfate in prevention of post spinal shivering in uroscopic surgery. (RCT)

CURRENT STATUS: ACCEPTED

BMC Anesthesiology  ▪  BMC series

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Abstract

Background: Hypothermia and shivering are associated common complications after spinal anesthesia especially in uroscopic procedures when large amounts of cold intraluminal irrigating fluids are used. Magnesium sulphate and dexmedetomidine are the most effective adjuvants with least side effects. Our aim of the study is to compare the effect of intrathecal dexmedetomidine versus intrathecal magnesium sulfate in prevention of post spinal shivering. Methods: This prospective randomized, double-blinded controlled study was conducted at Kasr El-Aini Hospital on 105 patients scheduled for uroscopic surgeries. patients were randomly allocated into three groups using computerized generated random tables, Group C (n=35) received 2.5 ml hyperbaric bupivacaine 0.5% (12.5 mg) +0.5 ml normal saline, Group M (n=35) received 2.5 ml hyperbaric bupivacaine 0.5% (12.5 mg) +25 mg magnesium sulfate in 0.5 ml saline and Group D (n=35) received 2.5 ml hyperbaric bupivacaine 0.5% (12.5mg) + 5 μg dexmedetomidine in 0.5 ml saline. Primary outcomes were the incidence and intensity of shivering. Secondary outcomes were incidence of hypothermia (Temp < 36° C), sedation, the use of meperidine to control shivering and complications, bradycardia, nausea and vomiting. Results: C group showed statistically significant higher number of total patients who developed shivering (21), patients who developed grade IV shivering (20) and patients who needed meperidine (21) to treat shivering than M group (8,5,5) and D group (5,3,6) which were comparable to each other. Time needed to give meperidine after giving the block was similar in the three groups. Hypothermia didn’t occur in any patient in the three groups. The three groups were comparable regarding occurrence of nausea, vomiting, bradycardia & hypotension. All patients of C group, 32 patients in M group and 33 patients in D group had sedation score of 2. 3 patients in M group and 2 patients in D group had a sedation score of 3. Conclusions: intrathecal injection of dexmedetomidine and magnesium sulfate were both effective in reducing the incidence of post spinal shivering. So, we encourage the use of magnesium sulphate being more physiological, readily available in most operating theatres and much cheaper than dexmedetomidine. Clinical trial registration ID: PACTR201801003001727, on January 2018.

Background
For short procedures like uroscopic surgeries, spinal anesthesia (SA) is a very reliable and convenient technique especially procedures in which patient consciousness is important to detect intraoperative complications such as TURP syndrome (1). However, hypothermia and shivering are associated with common complications after SA especially in such procedures if large amounts of cold intraluminal irrigating fluids are used (2). SA impairs thermoregulation, inhibits the tonic vasoconstriction, and causes redistribution of core heat from the trunk to the peripheral tissue (3). Shivering interferes with proper monitoring and it is associated with several adverse effects as it increases circulating catecholamine, heart rate, cardiac output, minute ventilation, patient’s oxygen consumption, metabolic CO$_2$ production, lactic acid level, intraocular and intra cranial pressure, postoperative pain from surgical incision stretching (4).

Various opioid and non-opioid agents have been used for shivering prevention like meperidine, ketamine, tramadol, clonidine but they have many side effects or their results were not conclusive (5).

Dexmedetomidine is a highly selective alpha-2- adrenoreceptor agonist with potent effects on the central nervous system decreasing the sympathetic tone (5). It has been effectively used intravenously in several studies for treatment (6-10) and for prevention (11-14) of shivering following SA without any major adverse effect. Few trials examined intrathecal dexmedetomidine in postspinal shivering prevention (5, 15).

Magnesium sulfate (Mg SO$_4$) which is an inorganic salt has been shown to suppress postoperative shivering suggesting that the agent reduces the shivering threshold (16). It has a good safety profile as there are no side effects related to the intrathecal use of the drug with no significant changes in hemodynamic parameter (17). Mg SO$_4$ has been effectively examined in many trials intravenously (2, 18-20) and in few trials intrathecally (3) to control shivering.

Our aim of the study is to evaluate and to compare the effect of intrathecal dexmedetomidine versus intrathecal magnesium sulfate in prevention of post spinal shivering.

Primary outcomes were incidence and intensity of shivering. Secondary outcomes were incidence of
pethidine use, hemodynamics and incidence of complications i.e hypotension, bradycardia and sedation.

Methods
After approval of the Ethics Committee of Cairo university hospital (12015006), protocol registration in in Pan African Clinical Trial Registry (PACTR) (clinical trial registration ID: PACTR201801003001727) and obtaining informed written consent from each patient, this prospective randomized, double-blinded randomized controlled study was conducted at Kasr El-Aini Hospital in urosurgical operating theatre on 105 patients scheduled for uroscopic surgeries. Included patients were those aged between 20-60 years old and classified by the American Society of Anesthesiologist (ASA) physical status as class I or class II. Exclusion criteria were patient’s refusal, coagulopathy, and history of allergic reactions to local anesthetics and severe cardiac, respiratory, hepatic or renal disease.

In the operating room, after the skin was infiltrated with 2% Lidocaine; venous access was done with a 18 gauge cannula and a preload of 500 ml lactated ringer solution was infused and no premedication was given. Monitoring by five lead ECG, pulse oximetry and non-invasive arterial blood pressure (NABP) was done. Baseline systolic and diastolic arterial blood pressure (SBP and DBP), heart rate (HR) and arterial oxygen saturation (PSO\textsubscript{2}) were recorded. Spinal block was done while the patient was sitting and leaning forward at L4–L5 interspace or L3-L4 with a 22-gauge spinal needle after sterilization by povidone iodine and infiltration of the skin at the site of lumbar puncture with 2 cm of lidocaine 1%.

Patients were randomly allocated into three equal groups using computerized generated random tables and the random numbers were concealed in closed opaque envelopes, Group C (n=35) received 2.5 ml hyperbaric bupivacaine 0.5% (12.5 mg) +0.5 ml normal saline, Group M (n=35) received 2.5 ml hyperbaric bupivacaine 0.5% (12.5 mg) +25 mg magnesium sulfate in 0.5 ml saline and Group D (n=35) received 2.5 ml hyperbaric bupivacaine 0.5% (12.5mg) + 5 μg dexmedetomidine in 0.5 ml saline. The specific intrathecal drugs solutions were prepared and injected by a non-involved anesthesiologist

The anesthesiologists involved in patients’ observation and data collection were blinded to the
Onsets and duration of motor and sensory block were assessed by Bromage scale and pinprick test respectively. Level of the block was assessed to make sure it was between T10-T8, blocks above T8 and failed blocks were excluded. One layer of surgical drapes was placed over the patient, the room temperature was kept at 24°C and all irrigating and IV fluids were pre-warmed. No warming device was used. The incidence and intensity of shivering were assessed by a blinded observer immediately after block, every 5 minutes for the first 15 minutes, then every 10 minutes for two hours after the block using Crossley and Mahajan scale (21) (0 = no shivering, 1 = piloerection or peripheral vasoconstriction but no visible shivering, 2 = muscular activity in only one muscle group, 3 = muscular activity in more than one muscle group but not generalized shivering, 4 = shivering involve the whole body). 25 mg of IV meperidine was given on reaching grade 3 shivering. Core temperature was monitored using a tympanic probe before block, immediately after block and every 15 minutes for two hours after the block. Hypothermia and active warming were considered if core temperature reached 36°C. HR, BP and SPO2 were recorded every 5 minutes for the first 15 minutes, then every 10 minutes for two hours after the block.

Sedation was observed and recorded every 30 minutes for two hours or till giving IV pethidine using the Ramsay sedation scale (22), in which 1 = patient was anxious, agitated or restless; 2 = patient was co-operative, oriented, and tranquil; 3 = patient responded to commands only; 4 = patient exhibited a brisk response to light glabellar tap or loud auditory stimulus; 5 = patient exhibited a sluggish response to light glabellar tap or loud auditory stimulus; and 6 = patient exhibited no response.

Patients were monitored for complications. Hypotension (20% decreases in SBP from the baseline) was treated by increments of 3 mg of ephedrine and 200 ml of lactated ringer, bradycardia (HR < 50) was treated by a bolus of 0.01-0.02 mg/kg of atropine. Nausea and vomiting treated with 10 mg metoclopramide.

Postoperatively, patients were transferred to PACU, monitored and covered with one layer of cotton sheet. PACU temperature was kept at 25°C.
Primary outcomes were the incidence and intensity of shivering. Secondary outcomes were incidence of hypothermia, sedation, the use of pethidine to control shivering and complications as hypotension, bradycardia, nausea and vomiting.

**Statistical analysis:**

**Sample size:**

Power analysis was performed using Chi square test for independent samples on frequency of patients complaining of intra-operative and early postoperative shivering because it was the main outcome variable in the present study. Previous studies showed that the frequency of patients with perioperative shivering was about 50% in patients undergoing elective minor lower abdominal operations under spinal anaesthesia and 20% in patients receiving dexmedetomidine (15). Taking power 0.8 and alpha error 0.025, a minimum sample size of 35 patients was calculated for each group.

**Method of analysis:**

Data was entered on the computer using "Microsoft Office Excel Software" program (2010) for windows. Data was then transferred to the Statistical Package of Social Science Software program, version 20 (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.), to be statistically analyzed.

Data was presented using range, mean, standard deviation for quantitative variables and frequency and percentage for qualitative ones.

Gender and ASA were presented as number and percentage. Age, height, weight, sensory and motor onset and duration are presented as mean and standard deviation. Shivering incidence and grades, need of meperdine and complications are presented as number and percentage.

The Kolmogorov-Smirnov test was used to verify the normality of distribution. Quantitative data were described using mean, standard deviation. Significance of the obtained results was judged at the 5% level. Chi-square test was used for categorical variables, to compare between different groups. F-test (ANOVA) was used for normally distributed quantitative variables, to compare between the three groups, and Post Hoc test (Tukey) for pairwise comparisons.
Results
One hundred and eighteen patients scheduled for uroscopic surgeries were enrolled in this study, 8 patients didn’t meet inclusion criteria and 5 patients were excluded from the study due to failure to achieve block within 15 min. Types of the performed surgeries were 41 cystoscopy, 17 transurethral resection of prostate (TURP), 27 ureteroscopy and 20 urethroscopy and these surgeries were comparable between the three groups.

All patients were comparable regarding demographic data including age, weight, height, sex, duration of surgery and ASA classification (table 1).

All patients in the three group were comparable regarding SBP and DBP (figure 2), HR and SpO₂ (figure 3) throughout all the recorded times.

Onset and duration of Sensory and motor block showed statistically significant difference between the three groups. D group showed the shortest onset and M group showed the longest onset (p<0.001) (table 1).

Tympanic temperature was above 36° C in all patients at all times and no patient needed active warming. (figure 4).

C group showed statistically significant higher number of total patients who developed shivering, patients who developed grade IV shivering and patients who needed meperidine to treat shivering than M group and D group which were comparable to each other (table 2,3).

Time needed to give meperidine after giving the block was similar in the three groups.

The three groups were comparable regarding occurrence of nausea, vomiting, bradycardia & hypotension. All patients of C group, 32 patients in M group and 33 patients in D group had sedation score of 2. 3 patients in M group and 2 patients in D group had a sedation score of 3 (table 4).

Discussion
Besides its well-known advantages, SA has an additional one in uroscopic surgeries especially procedures that need intraluminal fluids irrigation such as TURP, as it allows early detection of complications as TURP syndrome in conscious patients (1). However, SA is not a complication free technique; Shivering is one of the common complications of spinal anesthesia with an incidence reach
40-60% of patients undergoing spinal anesthesia (5). Though, shivering is a protective mechanism to preserve body heat but it causes patient discomfort and pain and it may be dangerous in patients with impaired cardiovascular reserve or a limited respiratory capacity as shivering increases circulating catecholamine, heart rate, cardiac output, minute ventilation, patient’s oxygen consumption, metabolic CO₂ production and lactic acid level. It also increases intraocular and intracranial pressure, postoperative pain from surgical incision stretching. Shivering also may interfere with the monitoring of patients by causing artifacts of the ECG, blood pressure, and pulse oximetry (4). Also shivering in high grades -III & IV- may cause some difficulties to the surgeon and increase the operative time.

Hypothermia is a major risk for shivering, but there is no definite linear relationship between body temperature and appearance of shivering. Other major risk factors include aging, level of sensory block, and temperatures of the operating room and intravenous solutions (23).

The exact mechanisms that explains occurrence of shivering during SA haven’t been established yet. The possible mechanisms include disturbance of central thermoregulation, internal body heat redistribution, and loss of body heat to the environment (24). Regional and general anesthesia are known to impair the efficiency of hypothalamic thermoregulatory center causing different grades of hypothermia (25). During regional anesthesia, vasodilatation and redistribution of the core temperature is restricted to the lower body below the block, while vasoconstriction and shivering are restricted to the upper body as they are inhibited below the level of block due to sympathetic and somatic nerve block (26).

The neurotransmitter pathways of shivering are complex and different receptors are involved like opioids, α-2 adrenergic, serotonergic, and anti-cholinergic receptors. Different drugs that act on these receptors have been examined in different trials for the prevention or treatment of shivering that occurs after SA (4). These drugs include meperidine, fentanyl, clonidine, ketamine, and tramadol, and they have resulted in different degrees of efficacy and many associated side effects like hemodynamic instability, respiratory depression, nausea and vomiting (27).

Dexmedetomidine (5-15) and magnesium sulphate (2, 3, 17-20) proved efficacy and safety in
preventing and treating shivering following spinal anesthesia as equal as, or sometimes superior than, other adjuvants with less adverse effects. Few of these trials (3, 5, 15, 17) examined them intrathecally to prevent related shivering.

Dexmedetomidine is a highly selective alpha-2 adrenergic agonist known with its sedative effect in anesthesia & intensive care practice and it has ten times higher affinity for alpha-2 adrenoreceptor than clonidine (28). The response to activation of this alpha-2 receptors includes decrease sympathetic tone resulting in decrease in blood pressure and heart rate. Dexmedetomidine has been effectively examined in several studies for prevention and treatment of shivering following general or spinal anesthesia in a dose that doesn’t cause major sedation or hemodynamic instability, no respiratory depression, less nausia and vomiting (11). The exact mechanism of dexmedetomidine in shivering control is not clear and complex. The suggested mechanism is that dexmedetomidine and other alpha-2 agonists reduce shivering through inhibiting the central thermoregulatory control by restraining the neuronal conductance and through suppressing the vasoconstriction and shivering thresholds. These drugs which inhibit thermoregulatory vasoconstriction prevent shivering (29).

Magnesium (Mg$^{+2}$) is a naturally occurring non-competitive antagonist of N-methyl-D aspartate (NMDA) receptors with a good safety profile and neuroprotective properties during hypothermia (30). Anti-shivering effect of Mg SO4 has many theories, as it has been reported to reduce shivering through a central effect by reducing shivering threshold (16,31). Also blocking NMDA receptors decreases norepinephrine and 5-HT, which both play a role in thermoregulation control (32). Being a calcium antagonist, magnesium has a peripheral mild muscle relaxation effect which may reduce the gain of shivering (incremental shivering intensity with progressing hypothermia) (33). Magnesium also causes peripheral vasodilation that increases the cutaneous circulation leading to decreasing the incidence of shivering (34,35).

Based on those previous studies, we compared the effect of subarachnoid injection of dexmedetomidine and magnesium sulfate in prevention of shivering after spinal anesthesia in patients with uroscopic surgeries. The current study showed that both SA injection of dexmedetomidine 5μg and magnesium sulfate 25 mg have significantly reduced the incidence of post
spinal shivering. (5 patients (14.3%) developed shivering in D group, 8 patients (22.8%) in M group, and 21 patients (60%) in C group). Number of patients who develop shivering and needed meperdine administration was 5 patients (14.3%) in D group, 6 patients (17.4%) in M group, and 21 patients (60.0%) in C group.

Similar to our study using the same intrathecal dexmedetomidine dose (5 μg), Ellakany et al (15) concluded that both intrathecal dexmedetomidine and meperidine effectively lowered the incidence of shivering following spinal anesthesia in patients undergoing lower abdominal surgeries, but meperidine was associated with more side effects like pruritus, nausea and vomiting. On sixty patients undergoing lower abdominal surgeries, Abdel Hamid et al. (36) concluded that adding dexmedetomidine 5 μg to intrathecal bupivacaine improved the characters of the spinal block with less postoperative analgesic requirements and less shivering incidence when compared to placebo with no sedation or other complications.

Moawad et al (5) studied the effect adding dexmedetomidine to intrathecal bupivacaine but in a larger dose, 10 μg, than that of our study 5 μg, and they found that it significantly decreased the incidence and degree of shivering in patients undergoing TURP.

Usta et al (12) and Bajwa et al (23) studied the prophylactic effect of intravenous dexmedetomidine on shivering in patients who had spinal and general anesthesia respectively. They found that perioperative dexmedetomidine infusion significantly decreased the incidence and intensity of shivering with no major adverse effects.

Botros et al. (14) compared the prophylactic effect of intravenously infused placebo, 1μg/kg of dexmedetomidine and 8 mg ondansetron on preventing postspinal shivering on 120 patients undergoing different lower body surgeries, and they found that both iv dexmedetomidine and ondansetron are equally effective in reducing the incidence of postspinal shivering compared to placebo.

Abdel-Ghaffar et al. (37) compared the clinical efficacy and side effects of three different doses of iv dexmedetomidine (0.5, 0.3 and 0.2 μg/kg) and iv meperdine 0.4 mg/kg on treating postspinal shivering in 120 patients. They found that dexmedetomidine 0.3μg/kg was the most appropriate in
treating shivering after spinal anesthesia effectively with the modest effect on hemodynamics and sedation.

Faiz et al study (3) concluded that Intrathecal injection of MgSO4 (25 mg) improved perioperative shivering in female patients undergoing elective caesarean section.

Ibrahim et al (19) studied the iv prophylactic and therapeutic effects of MgSO4 on spinal anesthesia induced shivering and proved it effective.

Gozdemir et al. (2) found that following spinal anesthesia, iv infusion of 80/kg mg Mg So4 over 30 minutes, followed by iv infusion at a rate of 2g/hr till the end of surgery is significantly effective in prevention of postspinal anesthesia shivering in patients undergoing TURP.

In Sachidananda et al study (20), prophylactic iv infusion of MgSO4 and tramadol effectively reduced shivering incidence during cesarean section under SA with a reduced shivering intensity with MgSO4.

There is no difference between the three groups in intraoperative hemodynamics. Regarding onset of sensory and motor block, D group had the fastest onset of sensory and motor block while M group had a delayed onset of sensory and motor block than D and M groups. This may be due to change in ph and baricity of bupivacaine due to addition of magnesium sulfate. Duration of both sensory and motor blocks of D group were longer than those of M group which were longer than those of C group.

Similar results were observed in two studies (38,39) which compared the intrathecal effect 10 μg dexmedetomidine and 50 mg Mg SO4 when added to bupivacaine targeting the characteristics of spinal block as primary out comes.

Limitations and recommendations:

The limitation was that we didn’t estimate the mean volume of the irrigating fluids in each group.

Besides, we recommend conducting further studies on both drugs with larger sample size and different doses.

Conclusion: We concluded that intrathecal injection of dexmedetomidine and magnesium sulfate with bupivacaine in spinal anesthesia were both effective in reducing the incidence of post spinal shivering. So, we encourage the use of magnesium sulphate being more physiological, readily available in most operating theatres and much cheaper than dexmedetomidine.
Abbreviations
SA: spinal anesthesia; TURP: transurethral resection of the prostate; CO₂: carbon dioxide; Mg SO₄:
Magnesium sulfate; ASA: American Society of Anesthesiologist; ECG: Electrocardiography; NABP: non-invasive arterial blood pressure; SBP: systolic arterial blood pressure; DBP: diastolic arterial blood pressure; HR: heart rate; PSO₂: arterial oxygen saturation; ° C: degree Celsius; IV: intravenous; PACU: postanesthesia care unit; Mg²⁺: Magnesium; NMDA: N-methyl-D-aspartate; μg: microgram.

Declarations
Acknowledgements: We would like to thank our professors and colleagues of anesthesia department, Cairo University for their help and support.
Funding: This research was done in Cairo university hospitals using the equipment and resources available.
Availability of data and material: The data that support the findings of this study are available from Cairo university hospitals; however, they are not publicly available. Data are however available from the authors upon reasonable request after permission of Cairo university.
Authors' contributions: MW was responsible for the conception of the idea. BA, HO, MH shared in design of the study, analysis of the data, and writing the manuscript. WA, MM, AE shared in data collection. BA, MH, HO, WA, PH, MH, AE, DK, MM, AH, PZ and MW shared in writing and revising the manuscript. All authors had read, revised and approved the final manuscript.
Ethics approval and consent to participate: ethics approval from Cairo university hospitals research committee- department of anesthesia was obtained (N-12015006). Written informed consents were obtained from participants before inclusion.
Consent for publication: Not applicable
Competing interests: The authors declare that they have no competing interests.

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Tables
Table (1): Demographic data.
|                          | C Group (n = 35) | M Group (n = 35) | D Group (n = 35) | p     | P1     | P2     | P3     |
|--------------------------|------------------|------------------|------------------|-------|--------|--------|--------|
| Gender (No &%)           |                  |                  |                  |       |        |        |        |
| Male                     | 28 (80.0)        | 26 (74.3)        | 29 (82.9)        | 0.669 | 0.569  | 0.759  | 0.382  |
| Female                   | 7 (20)           | 9 (25.7)         | 6 (17.1)         |       |        |        |        |
| Age (years)              | 50.29 ± 8.87     | 49.03 ± 8.83     | 49.23 ± 10.51    | 0.836 | 0.579  | 0.640  | 0.930  |
| Height (cm)              | 173.71 ± 5.60    | 174.29 ± 5.02    | 173.86 ± 5.83    | 0.903 | 0.644  | 0.914  | 0.745  |
| Weight (kg)              | 83.43 ± 7.93     | 82.29 ± 9.34     | 82.71 ± 10.24    | 0.872 | 0.605  | 0.747  | 0.846  |
| ASA classification       |                  |                  |                  |       |        |        |        |
| I                        | 17 (48.6)        | 17 (48.6)        | 15 (42.9)        | 0.858 | 0.858  | 0.631  | 0.631  |
| II                       | 18 (51.4)        | 18 (51.4)        | 20 (57.1)        |       |        |        |        |
| Duration of surgery (min)| 105.03±11.59     | 103.17±7.83      | 101.60±9.01      | 0.331 | 0.420  | 0.138  | 0.495  |
| Sensory Block onset      | 4.20 ± 0.63      | 6.69 ± 0.90      | 3.40 ± 0.50      | <0.001* | <0.001* | <0.001* | <0.001* |
| (time to reach T10)      |                  |                  |                  |       |        |        |        |
| Motor block onset        | 4.97 ± 0.71      | 8.03 ± 0.79      | 3.80 ± 0.76      | <0.001* | <0.001* | <0.001* | <0.001* |
| (time to reach bromage 4)|                  |                  |                  |       |        |        |        |
| Motor block duration     | 157.00±13.07     | 193.71±17.63     | 206.57±22.06     | <0.001* | <0.001* | <0.001* | 0.003* |
| Sensory block duration   | 198.14±18.67     | 243.43±23.22     | 301.57±39.44     | <0.001* | <0.001* | <0.001* | <0.001* |
| Intraoperative venous     | 971.43±16.10     | 997.14±16.85     | 1002.86±263.45   | 0.652 | .448   | 0.503  | .914   |
| fluids                   |                  |                  |                  |       |        |        |        |
| No of patients           | 15               | 13               | 13               |       |        |        |        |
| had cystoscopy (41)      |                  |                  |                  |       |        |        |        |
| No of patients           | 8                | 10               | 9                |       |        |        |        |
| had uretroscopy (27)     |                  |                  |                  |       |        |        |        |
| No of patients           | 7                | 6                | 7                |       |        |        |        |
| had urethroscopy (20)    |                  |                  |                  |       |        |        |        |
| No of patients           | 5                | 6                | 6                |       |        |        |        |
| had TURP (17)            |                  |                  |                  |       |        |        |        |
**Table (2): Shivering incidence and grades**

| Grading | C Group (n=35) | M Group (n=35) | D Group (n=35) | P    | p1   | p2   | p3  |
|---------|----------------|----------------|----------------|------|------|------|------|
| Grades  | No. | % | No. | % | No. | % |      |      |      |
| No shivering | 14  | 40.0 | 24  | 68.6 | 30  | 85.7 | <0.001* | 0.016* | <0.001* | 0.088 |
| I       | 0   | 0.0 | 0   | 0.0 | 0   | 0.0 | -     | -     | -     | -     |
| II      | 0   | 0.0 | 2   | 5.7 | 0   | 0.0 | 0.331 | 0.493 | -     | 0.493 |
| III     | 1   | 2.9 | 1   | 2.9 | 2   | 5.7 | 1.000 | 1.000 | 1.000 | 1.000 |
| IV      | 20  | 57.1 | 5   | 14.3 | 3   | 8.6 | <0.001* | <0.001* | <0.001* | 0.716 |

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**Table (3): Need of meperdine**

| Grading | C Group (n=35) | M Group (n=35) | D Group (n=35) | P    | p1   | p2   | p3  |
|---------|----------------|----------------|----------------|------|------|------|------|
| No.     | % | No. | % | No. | % |      |      |      |
| No. of patients needed meperdine | 21 | 60.0 | 6 | 17.4 | 5 | 14.3 | <0.001* | <0.001* | <0.001* | 0.743 |
| Timing after block/min.  | 39.52±8.05 | 44.50±11.17 | 52.0±14.40 | 0.175 | 0.586 | 0.058 | 0.268 |
| Recurrence of shivering | 6 | 17.1 | 2 | 5.7 | 1 | 2.8 | 0.136 | <0.001* | <0.001* | 0.002* |

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p1: p value for comparing between Control and MgSO4

p2: p value for comparing between Control and Dex

p3: p value for comparing between MgSO4 and Dex

*: Statistically significant at p ≤ 0.05.
p1: p value for comparing between Control and MgSO4

p2: p value for comparing between Control and Dex

p3: p value for comparing between MgSO4 and Dex

*: Statistically significant at p ≤ 0.05.

Table (4): Complications

| Complication     | C Group (n=35) | M Group (n=35) | D Group (n=35) | P     | p1   | p2   | p3   |
|------------------|----------------|----------------|----------------|-------|------|------|------|
|                  | No. | %  | No. | %  | No. | %   |      |      |
| Nausea           | 3   | 8.6| 2   | 5.7| 2   | 5.7 | 1.000| 1.000|
| Vomiting         | 0   | 0.0| 0   | 0.0| 0   | 0.0 | -    | -    |
| Bradycardia      | 4   | 11.4| 4   | 11.4| 3   | 8.6 | 1.000| 1.000|
| Hypotension      | 7   | 20.0| 6   | 17.1| 7   | 20.0| 0.940| 0.759|
| Sedation (maxim    | 1   | 0.0| 0   | 0.0| 0   | 0.0 | 0.364| 0.239|
| hun score)       | 2   | 35 | 32  | 91.4| 33  | 94.3| 0.493| 1.000|
| 3                | 0   | 0.0| 3   | 8.6| 2   | 5.7 |      |      |
| 4                | 0   | 0.0| 0   | 0.0| 0   | 0.0 |      |      |
| 5                | 0   | 0.0| 0   | 0.0| 0   | 0.0 |      |      |
| 6                | 0   | 0.0| 0   | 0.0| 0   | 0.0 |      |      |

p1: p value for comparing between Control and MgSO4

p2: p value for comparing between Control and Dex

p3: p value for comparing between MgSO4 and Dex

*: Statistically significant at p ≤ 0.05.

Figures
Figure 1
Consort flow chart
Figure 2

Comparison between the three studied groups according to Systolic blood pressure and diastolic blood pressure (mmHg)
Figure 3
Comparison between the three studied groups according to Heart Rate (Beat/min.) and SPO2 (%).

Figure 4
Comparison between the three studied groups according to temperature (° C).
Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

CONSORT-2010-Checklist shivering.pdf