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Comparative effect of intrathecal meperidine, tramadol, magnesium sulfate, and dexmedetomidine on preventing post-spinal anesthesia shivering and adverse events in hip fracture repair patients: A randomized clinical trial

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ABSTRACT

Objective: To compare effect of intrathecal meperidine, tramadol, magnesium sulfate, and dexmedetomidine on the prevention of post-spinal anesthesia shivering and adverse events in hip fracture repair patients.

Methods: In a randomized, double-blind trial, 132 patients with American Society of Anesthesiology (ASA) I and II spinal anesthesia who needed hip fracture surgery were enrolled. Patients were stratified into 4 intervention groups based on a randomized block pattern: meperidine, tramadol, magnesium sulfate, and dexmedetomidine. Hemodynamic parameters including blood pressure, heart rate, and oxygen saturation, as well as the severity of shivering, core body temperature, Ramsay sedation score, adverse events, meperidine consumption were recorded and compared.

Results: There was no statistically significant difference in the normal hemodynamic parameters, temperature, duration of surgery, meperidine consumption, and adverse events such as dizziness, hypotension, nausea, and bradycardia among groups (P>0.05). Compared to other groups, severity of shivering was the lower in the dexmedetomidine group 6 and 8 h after surgery. The Ramsay sedation scores were higher in the dexmedetomidine and meperidine groups 4 h after surgery (P=0.020).

Conclusion: Dexmedetomidine acts better than the other three adjuvants in reducing complications such as shivering. Overall, these four adjuvants are helpful to prevent postoperative shivering and could be put forward as promising local anesthetics in spinal anesthesia, based on anesthesiologists' discretion and patients' general conditions.

Clinical registration: The study was approved by the Research and Ethics Committee at the Valiasr Hospital (Arak, Iran) with the clinical trial code of IRCT20141209020258N153.

KEYWORDS: Dexmedetomidine; Hip fracture; Intrathecal injection; Magnesium sulfate; Meperidine; Shivering; Spinal; Tramadol

Significance

Dexmedetomidine is the most effective in reducing shivering with fewer complications. Ramsay sedation score was higher in the dexmedetomidine and meperidine groups. Overall, all the adjuvants may help to prevent postoperative shivering.

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1. Introduction

Spinal anesthesia was arguably recognized as a successful regional analgesic technique[1]. Spinal anesthesia with nerve block in the subarachnoid space is reported to have several benefits, such as the fast onset of action, comfort, less adjuvant needed, and good sensory and motor block[1,2]. Even though spinal anesthesia is widely regarded as a reasonable anesthetic option for patients undergoing orthopedic lower limb surgery[3], shivering is still a prevalent adverse event in patients with spinal anesthesia, with an incidence of up to 56.7% during spinal anesthesia[4]. Common physiologic mechanisms of shivering include raised oxygen consumption, lactic acidosis, carbon dioxide production, and metabolic rate by up to 400%, leading to serious complications in patients with cardiovascular disease[5]. Post-spinal anesthesia shivering may interfere with intraoperative measurement and monitoring of the electrocardiogram, blood pressure, and oxygen saturation[5,6].

Thermoregulation can be implemented by triggering the core temperature, and then by alternating vascular tone of the autonomic nervous system (vasoconstriction and vasodilation); and thusly raising the skin surface temperature. This is the fastest way to increase the shivering threshold[7]. Because it increases oxygen demands, shivering may lead to multiple complications such as myocardial ischemia and tremors that increase intraocular and intracranial pressure, as well as postoperative problems and higher costs[6]. The consequences of postoperative shivering may include an increase in oxygen consumption per minute (VO_2), carbon dioxide production per minute (VCO_2), metabolic rate, and sympathetic tone, which results in increased cardiac output and minute ventilation. The incidence of myocardial ischemia augments myocardial infarction[8].

Various underlying causes of postoperative shivering have been reported, including uninhibited spinal reflexes, decreased sympathetic activity, adrenal suppression, respiratory alkalosis, and response to hypothermia[9]. Clinical efficacies of some medicines have been adequately proven in controlling shivering following neuraxial blockade, including intravenous or epidural meperidine (25 mg), intravenous clonidine (75 μg), dexmedetomidine, magnesium sulfate, and tramadol, among which the first is commonly used[10,11].

Dexmedetomidine is an α2-adrenergic agonist and can relieve postoperative pain[12]. Numerous studies have supported the efficacy of intravenous dexmedetomidine in the treatment and prevention of post-spinal anesthesia shivering[12,13]. To date, few studies addressed the efficacy of intrathecal dexmedetomidine in the prevention of post-spinal anesthesia shivering[14,15]. Magnesium is the fourth most important cation in the body and magnesium sulfate has analgesic properties[16] primarily by regulating intracellular calcium levels. It acts as an antagonist of *N*-methyl-*D*-aspartate receptors[17]. Varying studies established the sedative efficacy of intrathecal magnesium sulfate as a spinal adjuvant to bupivacaine[17,18], while Faiz *et al*. suggested that intrathecal magnesium sulfate can help to lessen shivering in women undergoing Cesarean section[19]. Tramadol, a low-cost oral atypical synthetic analgesic, exerts its analgesic effects centrally and appears to be intrathecally effective in reducing postoperative pain and shivering (both in incidence and in intensity)[20,21].

Our study aimed to compare the efficacy of meperidine, tramadol, magnesium sulfate, and dexmedetomidine in preventing post-spinal anesthesia shivering and adverse events following hip fracture repair.

2. Patients and methods

2.1. Study setting

A total of 132 patients were recruited in this phase III double-blind, randomized study in Valiasr Hospital, Arak, Iran from April 2021 to December 2021.

2.2. Ethical approval

The study was approved by the Research and Ethics Committee at the Valiasr Hospital (Arak, Iran) with the ethics code of IR.ARAKMU.REC.1399.297 and clinical trial code of IRCT20141209020258N153. The trial registry can be found at: https://en.irct.ir/trial/54731.

2.3. Inclusion criteria

Inclusion criteria included patients aged 18 to 75; of both genders; American Society of Anesthesiologists class I and II; those scheduled for hip fracture repair surgery under spinal anesthesia; no history of drug abuse, seasonal allergies, or any of the drugs used in this study; absent of neuromuscular diseases, Raynaud's phenomenon, cardiomyopathy, and coagulation disease. In addition, patients were excluded from the study if they experienced failure in the anesthesia methods used in the study or expressed unwillingness to continue the participation.

2.4. Study design

The study was double-blind. Patients were not aware of the type of drug given. Adjuvants were prepared by a nurse anesthetist and spinal anesthesia was performed by an anesthesiologist, whereas an intern, who was unaware of the patient grouping, recorded the patient's clinical symptoms. Moreover, the gathered data were submitted to the statistician, after being coded. The subjects were randomly divided into 4 groups using a balanced block randomization scheme with a block size of 8, whose order was determined individually.

All our subjects were hospitalized for at least 1 day and had no food or drink 8 h before surgery. All subjects were treated with 10 mL/kg of crystalloid (Ringer) after being transferred to the operating room.

Each participant was administered with the following adjuvants along with 12.5 mg of hyperbaric (0.5%) in 2.5 mL of bupivacaine (AstraZeneca Pharmaceutical Industry Company, United Kingdom, imported by Cobel Darou, Tehran, Iran). Consequently, the total intrathecal injection volume was adjusted to 3 mL. The dexmedetomidine group received 5 μg of dexmedetomidine (Iran Eksir, Tehran, Iran)[16]; the magnesium sulfate group received 25 mg of 10% magnesium sulfate (Pasteur Institute of Iran, Tehran, Iran) [21]; the meperidine group received 0.2 mg/kg of meperidine (Gerot Pharmazeutika, Vienna, Austria, ordered by Darupakhsh)[22], and the tramadol group received 10 mg of tramadol (Caspian Tamin Pharmaceutical Company, Rasht, Iran)[21].

2.5. Measurement

Age, sex, body mass index, and duration of surgery were obtained based on patients' records. Levels of mean arterial blood pressure, heart rate, and arterial oxygen saturation were measured every 5 min for the first 15 min, then every 15 min until the end of the operation and recovery, 1 and 2 h postoperatively. Systolic blood pressure below 100 mmHg or a >20% reduction from the baseline was corrected by increasing the rate of normal saline infusion and treated with 5 to 10 mg of intravenous ephedrine. Furthermore, bradycardia was defined as a decrease in heart rate below 45 bpm, and a fall in oxygen saturation of arterial blood (SaO_2) to below 92%, and, if occurred, appropriate treatment was performed and recorded.

The severity of shivering was assessed and recorded intraoperatively and every 15 min in recovery and 2, 4, 6, 8, and 12 h postoperatively, and graded on a 4-point scale (0-3) where 0: no shivering; 1: mild fasciculation of the face and neck; 2: visible tremor involving more than one muscle group; and 3: gross muscular activity involving the entire body[22]. Moreover, the core body temperature measured by a digital infrared thermometer (LEYU DT-8806H) was recorded at the beginning of the recovery period, every 15 min until the end of the recovery, and then at 2, 4, 6, 8, 10, and 12 h postoperatively.

If the patients experienced shivering of grade 3, 0.5 mg/kg *i.v.*, meperidine was administered each time after spinal anesthesia. The level of sedation intraoperatively and up to 12 h after the operation was monitored using Ramsay sedation score in all groups.

Other adverse events, like nausea and vomiting, bradycardia, hypotension, and dizziness were also recorded.

2.6. Primary and secondary outcomes

The primary and secondary outcomes in this study were shivering severity and sedation score, respectively.

2.7. Statistical analysis

Sample size was calculated based on the results of our recent study[23]. Considering the study power being equal to 80%, as well as the confidence interval of 95%, each group requires at least 32 patients.

The data were entered into SPSS software release 20. Categorical variables were presented as absolute numbers and percentages, while continuous variables were presented as mean±SD. Non-normally distributed data are expressed as median and first and third quartiles (Q1, Q3). ANOVA and chi-square tests were used to analyze. Difference was considered significant if $P<0.05$.

3. Results

3.1. Demographic characteristics

A total of 132 patients were included (Figure 1). The mean age was (46.11±8.70) years, ranging from 23 to 62 years. The mean body mass index was (24.59±2.55) kg/m and 66 (50.0%) were female.

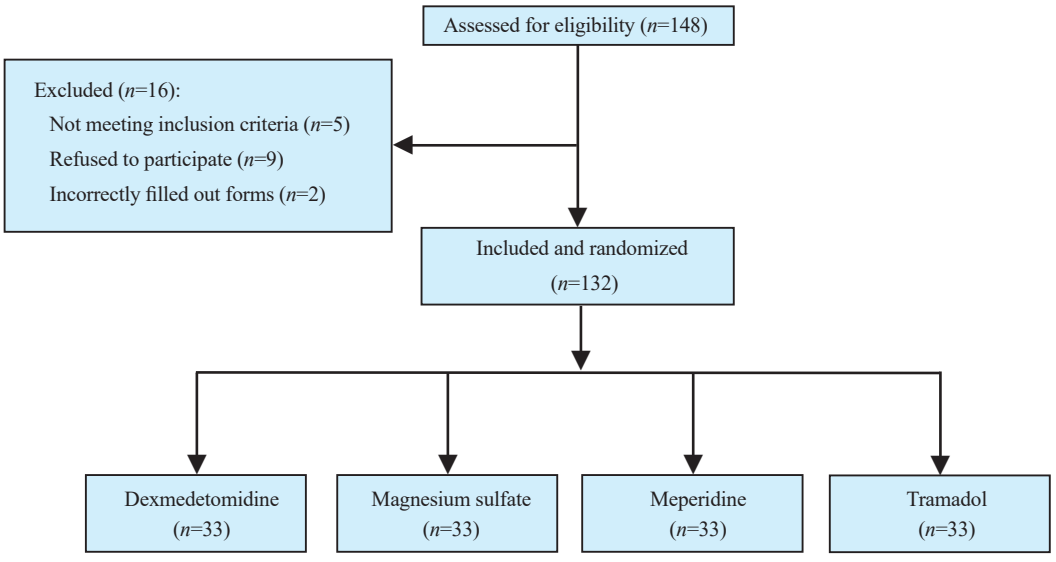

Figure 1. The study flowchart.

There were no significant differences in age, sex, or body mass index for all participants (Table 1).

3.2. Clinical baseline characteristics

The study analysis revealed no statistically significant difference in oxygen saturation, mean blood pressure, heart rate, temperature, duration of surgery, meperidine consumption, and postoperative adverse events including dizziness, hypotension, nausea, and bradycardia (P>0.05).

3.3. Severity of shivering

There was statistically significant difference in severity of shivering among 4 groups at 8 and 10 postoperatively (P<0.05), and it was lower in the dexmedetomidine group (Table 2).

3.4. Ramsay sedation score

There was statistically significant difference in Ramsay sedation score (Table 3) at 4 h postoperatively (P=0.020). The score was higher in the dexmedetomidine and meperidine groups.

Table 1. Demographic and clinical baseline characteristics.

Variable	Dexmedetomidine, n=33	Magnesium sulfate, n=33	Meperidine, n=33	Tramadol, n=33	F/χ^2	P
Age, years, mean±SD	46.48±8.86	46.42±8.89	46.42±8.12	45.12±9.21	0.188	0.905
Male, n, %	16 (48.48)	16 (48.48)	17 (51.51)	17 (51.51)	0.121	0.982
Body mass index, kg/m^2, mean±SD	24.78±2.61	24.75±2.57	24.84±2.61	24.00±2.44	0.806	0.493
Mean arterial pressure, mmHg, mean±SD	92.66±6.06	92.63±5.52	92.51±4.77	92.57±4.82	0.001	0.998
Heart rate, bpm, mean±SD	90.24±7.77	90.35±7.38	90.28±7.23	90.18±7.35	0.001	0.998
Oxygen saturation, %, mean±SD	98.10±0.61	97.50±0.63	97.56±0.55	97.62±0.89	0.000	0.999
Temperature, ℃, mean±SD	37.10±2.12	37.25±2.35	37.21±2.26	37.02±1.98	0.001	0.999
Duration of surgery, min, mean±SD	102.37±6.02	101.91±5.56	102.25±4.12	101.99±5.19	0.073	0.974
Postoperative adverse events, n, %	2 (6.06)	4 (12.12)	1 (3.03)	4 (12.12)	2.670	0.440

Table 2. Score of shivering severity (medium, Q1, Q3).

Time	Dexmedetomidine, n=33	Magnesium sulfate, n=33	Meperidine, n=33	Tramadol, n=33	U	P
During surgery	0 (0.0, 0.0)	0 (0.0, 0.0)	0 (0.0, 0.0)	0 (0.0, 0.0)	3.100	0.377
Recovery						
0 min	0 (0.0, 0.0)	0 (0.0, 0.0)	0 (0.0, 0.0)	0 (0.0, 0.0)	6.240	0.101
15 min	0 (0.0, 0.0)	0 (0.0, 0.0)	0 (0.0, 0.0)	0 (0.0, 0.0)	3.660	0.301
30 min	0 (0.0, 0.0)	0 (0.0, 0.0)	0 (0.0, 0.0)	0 (0.0, 0.0)	4.320	0.229
45 min	0 (0.0, 0.0)	0 (0.0, 0.0)	0 (0.0, 0.0)	0 (0.0, 0.0)	3.450	0.290
After surgery						
2 h	0 (0.0, 1.0)	0 (0.0, 0.5)	0 (0.0, 1.0)	0 (0.0, 0.0)	1.790	0.616
4 h	0 (0.0, 0.0)	0 (0.0, 0.0)	0 (0.0, 0.0)	0 (0.0, 0.0)	0.517	0.915
6 h	0 (0.0, 0.0)	0 (0.0, 0.0)	0 (0.0, 0.5)	0 (0.0, 0.0)	0.106	0.991
8 h	0 (0.0, 0.0)	0 (0.0, 0.0)	0 (0.0, 0.0)	0 (0.0, 0.5)	14.200	0.003*
10 h	0 (0.0, 0.0)	0 (0.0, 0.0)	0 (0.0, 0.0)	0 (0.0, 0.0)	11.700	0.008*
12 h	0 (0.0, 0.0)	0 (0.0, 0.0)	0 (0.0, 0.0)	0 (0.0, 0.0)	0.000	1.000

*Significant at α=0.05.

Table 3. Ramsay sedation score (mean±SD).

Time	Dexmedetomidine, n=33	Magnesium sulfate, n=33	Meperidine, n=33	Tramadol, n=33	F	P
During surgery	2.00±0.00	2.00±0.00	2.00±0.00	2.00±0.00	<0.001	0.999
Recovery	2.00±0.00	1.90±0.29	2.00±0.00	1.90±0.29	2.133	0.099
After surgery						
2 h	2.00±0.00	2.00±0.00	2.00±0.00	1.96±0.17	1.000	0.395
4 h	2.00±0.00	1.90±0.29	2.00±0.00	1.90±0.29	3.340	0.020*
6 h	2.00±0.00	1.93±0.24	2.00±0.00	1.90±0.29	1.890	0.134
8 h	2.00±0.00	2.00±0.00	2.00±0.00	2.00±0.00	<0.001	0.999
10 h	2.00±0.00	2.00±0.00	2.00±0.00	2.00±0.00	<0.001	0.999
12 h	2.00±0.00	2.00±0.00	2.00±0.00	2.00±0.00	<0.001	0.999

*Significant at α=0.05.

Table 4. Meperidine consumption for patients experienced shivering of grade 3 (n, %).

Meperidine consumption	Dexmedetomidine, n=33	Magnesium sulfate, n=33	Meperidine, n=33	Tramadol, n=33	χ^2	P
Not consumed	32 (96.96)	29 (87.87)	32 (96.96)	30 (90.90)	12.300	0.359
Consumed	1 (3.03)	4 (12.12)	1 (3.03)	3 (9.09)		

3.5. Meperidine consumption for patients experienced shivering of grade 3

No statistically significant difference (Table 4) was observed in meperidine consumption for patients experienced shivering of grade 3 (P=0.359).

4. Discussion

A total of 132 patients who were candidates for hip fracture surgery were included in the study and randomly allocated into 4 interventional groups. Our results showed no statistically significant differences in oxygen saturation, mean blood pressure, heart rate, temperature, duration of surgery, meperidine consumption, and adverse events like dizziness, hypotension, nausea, and bradycardia.

Severity of shivering was lower in the dexmedetomidine group at 8 and 10 h postoperatively. Significant differences in Ramsay sedation score were found at 4 h postoperatively and Ramsay sedation score was higher in the dexmedetomidine and meperidine groups. Overall, all the adjuvants may help to prevent postoperative shivering.

A study by Omar *et al*. compared intrathecal dexmedetomidine and intrathecal magnesium sulfate in preventing post-spinal anesthesia shivering and magnesium sulfate is recommended owing to more availability and cheaper price[16]. Gupta *et al*. explored the effect of intrathecal 10 and 20 mg of tramadol on post-spinal anesthesia shivering and found that tramadol reduces the incidence of shivering, while 20 mg of tramadol prolongs the duration of postoperative analgesia compared to 10 mg of tramadol, but both are not different in terms of postoperative shivering[21], whose results for tramadol were consistent with our study.

Consistent with our results for meperidine, another study showed that adding 20 μg of fentanyl or 0.2 mg/kg of meperidine to 0.5% bupivacaine intrathecal significantly decreased the incidence of shivering in lower limb orthopedic surgeries. They concluded that the adjuvants could reduce the severity of shivering and the overall need for intravenous meperidine to control intraoperative shivering compared to the control group, while no significant difference was found in hemodynamic parameters[23]. Other findings similar to ours on the efficacy of intrathecal dexmedetomidine confirmed that dexmedetomidine reduced the incidence of shivering following prostatectomy[24].

Ellakany *et al*. studied the efficacy of intrathecal dexmedetomidine and meperidine on post-spinal anesthesia shivering and reported that dexmedetomidine lessens shivering while reducing nausea, vomiting, and pruritus[25]. The results were consistent with our study. Furthermore, Faiz *et al*. suggested that intrathecal magnesium sulfate can prevent post-spinal anesthesia shivering following Cesarean delivery[19].

Our study demonstrates that dexmedetomidine acts better than the other three adjuvants in reducing complications such as shivering. But overall, all the adjuvants can prevent postoperative shivering without complications. Based upon the anesthesiologists' discretion and the patient's medical conditions, these adjuvants could be used as an anesthetic in spinal anesthesia to prevent postoperative shivering.

Conflict of interest statement

The authors report no conflict of interest.

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Authors' contributions

MK, HM, and EM contributed to the conception and design of the interpretation of data, and final approval of the article. MA contributed to the acquisition and analysis of data and drafting the article.

References

[1] Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL. *Miller's anesthesia*. 7th ed. Philadelphia: Elsevier Churchill Livingstone; 2010, p. 1624-1630.

[2] Dalens BJ, Monnet JP, Harmand Y. Epidural anesthesia. In: Dalens BJ, Monnet JP, Harmand Y, editors. *Pediatric regional anesthesia*. New York: Routledge; 1990, p. 375-415.

[3] Mauermann WJ, Shilling AM, Zuo Z. A comparison of neuraxial block versus general anesthesia for elective total hip replacement: A meta-analysis. *Anesth Analg* 2006; **103**(4): 1018-1025.

[4] Lin YC, Chen CY, Liao YM, Liao AH, Lin PC, Chang CC. Preventing shivering with adjuvant low dose intrathecal meperidine: A meta-analysis of randomized controlled trials with trial sequential analysis. *Sci Rep* 2017; **7**(1): 15323.

[5] Zhou Y, Mannan A, Han Y, Liu H, Guan HL, Gao X, et al. Efficacy and

safety of prophylactic use of ketamine for prevention of postanesthetic shivering: A systematic review and meta analysis. *BMC Anesthesiol* 2019; **19**(1): 245.

[6] Liu J, Wang Y, Ma W. Shivering prevention and treatment during cesarean delivery under neuraxial anesthesia: A systematic review. *Minerva Anestesiol* 2018; **84**(12): 1393-1405.

[7] Sessler DI. Thermoregulatory defense mechanisms. *Crit Care Med* 2009; **37**(7 Suppl): S203-S210.

[8] Hara K, Kuroda H, Matsuura E, Ishimatsu Y, Honda S, Takeshita H, et al. Underbody blankets have a higher heating effect than overbody blankets in lithotomy position endoscopic surgery under general anesthesia: A randomized trial. *Surg Endosc* 2021; **36**(1): 670-678.

[9] Akhavan Sepahi M, Eftekhari SS, Rashidinia S, Shahmoradi S, Shokrollahi SM, Pormehr S. The relationship between urinary reflux and nephrolithiasis in children: A cross-sectional study. *Int J Pediatr* 2017; **5**(5): 4965-4973.

[10]Ibrahim IT, Megalla SA, Khalifa OS, salah El Deen HM. Prophylactic vs. therapeutic magnesium sulfate for shivering during spinal anesthesia. *Egypt J Anaesth* 2014; **30**(1): 31-37.

[11]Mahmood MA, Zweifler RM. Progress in shivering control. *J Neurol Sci* 2007; **261**(1-2): 47-54.

[12]Modir H, Yazdi B, Moshiri E, Mohammadbeigi A, Afshari S. Efficacy of dexmedetomidine versus remifentanil to blunt the hemodynamic response to laryngoscopy and orotracheal intubation: A randomized clinical trial. *Med Gas Res* 2018; **8**(3): 85-90.

[13]Modir A, Yazdi B, Moshiri E, Azami M, Almasi-Hashiani A. Effect of various analgesics combined with ropivacaine on pain, sensory-motor block and hemodynamic changes in intravenous regional anesthesia. *Formos J Surg* 2020; **53**(2): 41-47.

[14]Abdel-Ghaffar HS, Mohamed SA, Fares KM, Osman MA. Safety and efficacy of dexmedetomidine in treating post spinal anesthesia shivering: A randomized clinically controlled dose-finding trial. *Pain Physician* 2016; **19**(4): 243-253.

[15]Lamontagne C, Lesage S, Villeneuve E, Lidzborski E, Derstenfeld A, Crochetièle C. Intravenous dexmedetomidine for the treatment of shivering during Cesarean delivery under neuraxial anesthesia: A randomized-controlled trial. *Can J Anaesth* 2019; **66**(7): 762-771.

[16]Omar H, Aboella WA, Hassan MM, Hassan A, Hassan P, Elshall A, et al. Comparative study between intrathecal dexmedetomidine and intrathecal magnesium sulfate for the prevention of post-spinal anaesthesia shivering in uroscopic surgery; (RCT). *BMC Anesthesiol* 2019; **19**(1): 190.

[17]Alebouyeh M, Imani F, Entazary S, Yusefvand-Mansuri T, Rahimzaheh P. Effect of adding magnesium to bupivacaine and fentanyl for spinal anesthesia in lower limb orthopaedic surgeries. *J Anesthesiol Pain* 2011; **1**(2): 43-51. [In Persian].

[18]Nath MP, Garg R, Talukdar T, Choudhary D, Chakrabarty A. To evaluate the efficacy of intrathecal magnesium sulphate for hysterectomy under subarachnoid block with bupivacaine and fentanyl: A prospective randomized double blind clinical trial. *Saudi J Anaesth* 2012; **6**(3): 254-258.

[19]Faiz SH, Rahimzadeh P, Imani F, Bakhtiari A. Intrathecal injection of magnesium sulfate: Shivering prevention during cesarean section: A randomized, double-blinded, controlled study. *Korean J Anesthesiol* 2013; **65**(4): 293-298.

[20]Subedi A, Biswas BK, Tripathi M, Bhattarai BK, Pokharel K. Analgesic effects of intrathecal tramadol in patients undergoing caesarean section: A randomised, double-blind study. *Int J Obstet Anesth* 2013; **22**(4): 316-321.

[21]Gupta P, Gupta M. Intrathecal tramadol for prevention of postanesthesia shivering after subarachnoid block: A prospective randomized placebo-controlled comparison of two different doses (10 and 20 mg). *Anesth Essays Res* 2018; **12**(2): 495-500.

[22]Safavi M, Honarmand A, Rahmanikhah E, Badiei S, Attari M. Intrathecal Meperidine versus intrathecal Fentanyl for prevention of shivering in lower limb orthopedic surgeries under spinal anesthesia: A randomized double-blind placebo-controlled trial. *J Res Pharm Pract* 2014; **3**(4): 137-141.

[23]Modir H, Yazdi B, Piri M, Almasi-Hashiani A. An investigation of the effects of dexmedetomidine and fentanyl as an adjuvant to ropivacaine on pain scores and hemodynamic changes following laparoscopic cholecystectomy. *Med Gas Res* 2021; **11**(3): 88-93.

[24]Moawad HE, Elawdy MM. Efficacy of intrathecal dexmedetomidine in prevention of shivering in patients undergoing transurethral prostatectomy: A randomized controlled trial. *Egypt J Anaesth* 2015; **31**(2): 181-187.

[25]Ellakany MH, Abdelhamid SA, MessehaGirgis MM. Intrathecal dexmedetomidine or meperidine for post spinal shivering. *Int J Anesthetic Anesthesiol* 2014; **1**(2): 004.

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