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Effect of Intrathecal Dexmedetomidine in Preventing Intra-operative Shivering after Spinal Anesthesia

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Dexmedetomidine (DEX) has sedative, analgesic, sympatholytic, anesthetic-sparing and hemodynamic-stabilizing properties. This study aims to evaluate the effects of intrathecal DEX as an adjuvant to hyperbaric bupivacaine in the prevention of shivering in patients who underwent surgeries under Intrathecal anesthesia.
Methods: A prospective double-blind, controlled, randomized study was conducted on 100 patients aged above 21 years old, ASA I & II undergoing lower limb orthopedic surgeries under intrathecal anesthesia. Patients were subdivided randomly into 2 equal group; Group Bupivacaine-Dexmedetomidine (BD): 5 µg dexmedetomidine diluted in 0.5 ml 0.9% normal saline was added to 12.5 mg heavy bupivacaine 0.5% and Group Bupivacaine (B): 0.5 ml 0.9% normal saline was added to 12.5mg heavy bupivacaine 0.5% (3ml volume).
Results: Shivering occurred in 9 patients (18%) in group BD and 23 patients (46%) in group B with a significant decrease in group BD compared to group B (P = 0.003). The relative risk of developing shivering was decreased 53% (95% Confidence Interval: 74 – 16%) with group BD compared to group B. Tsai and Chu score was significantly better in group BD (P = 0.013).
Conclusion: The use of intrathecal DEX (5µg) in conjugation with heavy bupivacaine help decrease the incidence and intensity of shivering when compared with heavy bupivacaine alone in surgeries under spinal anesthesia.

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Keywords: Intrathecal; dexmedetomidine; prevention; shivering; spinal anesthesia.

1. INTRODUCTION

Intrathecal anesthesia has been widely used to provide anesthesia and analgesia which allows a patient to remain awake while avoiding the risks of general anesthesia. Even though the risk of spinal anesthesia is lower than that of general anesthesia [1].

The adverse events caused by intrathecal anesthesia, such as shivering, are still present during surgical procedures. Shivering is defined as an involuntary, repetitive activity of skeletal muscles, which is one of the common complications involving regional anesthesia, causing discomfort for the patients. The incidence of shivering is up to 55% according to a previously published study. Shivering may lead to increased oxygen consumption and thereby causing hypoxemia, lactic acidosis and negative effects on pulse, oxygen saturation, and blood pressure. Severe adverse effects may occur if the patient has cardiopulmonary insufficiency. Therefore, the prevention of shivering is rational and could result in better perioperative outcomes [2].

Shivering may occur as a response to hypothermia, however, it may also occur in normothermic patients [3]. Intrathecal anesthesia impairs the thermoregulation system by inhibiting tonic vasoconstriction below the level of anesthesia through sympathetic and somatic neural blockade [4].

Different pharmacological and nonpharmacological techniques have been attempted to prevent shivering, but a gold-standard method has not yet been determined [5].

Non-pharmacological techniques: the combined application of warmed intravenous fluids and forced-air warming has the potential to minimize core temperature loss. Forced-air warming warms the patient from outside in, whereas the warmed intravenous fluid may prevent a decrease in body temperature in the setting of redistribution hypothermia [6].

Pharmacological techniques (anti-shivering medication) includes centrally acting analgesics (tramadol), opioid receptor agonists (meperidine, fentanyl), meperidine (the most commonly intravenous drug used for treating and preventing shivering; skin warming and meperidine use were the most commonly cited strategies), N-methyl-D-aspartate receptor antagonists (ketamine, magnesium sulfate), alpha 2 -central agonists (dexmedetomidine, clonidine), anti-serotonergic (ondansetron), and anti-inflammatory drugs (dexamethasone) [7].

Dexmedetomidine has highly specific alpha 2-adrenergic receptor-agonist properties, with strong impacts on the central nervous system without respiratory depression. Dexmedetomidine has sedative, analgesic, sympatholytic, anesthetic-sparing and hemodynamic-stabilizing properties [8].

The aim of this study is to evaluate the effects of intrathecal dexmedetomidine as an adjuvant to hyperbaric bupivacaine in the prevention of shivering in patients who are undergoing surgeries under Intrathecal anesthesia.

2. PATIENTS AND METHODS

A prospective double-blind, controlled, randomized study was conducted after approval of the ethical committee of faculty of medicine, Tanta University from October 2019 to March 2020. Informed consent was taken from the nearest relatives of the patients. All data of the patients were confidential with secret codes and private files for each patient.

Inclusion criteria

- Age above 21 years old.
- Patients with ASA I & II.
- Patients undergoing lower limb orthopedic surgeries under intrathecal anesthesia.

Exclusion criteria

- Patients refusing intrathecal anesthesia or with contraindication to spinal anesthesia.
- Patients with primary core body temperature of more than 37.5°C or lower than 36.5°C.
- Patients taking alpha-receptor antagonist drugs.
- Patients with coagulopathies or bleeding tendencies.
- Patients with allergy to dexmedetomidine or local anesthetics.

- Patients with Body Mass Index (BMI) of ≥35.

Group allocation

One hundred patients were subdivided randomly into 2 equal groups:

Group Bupivacaine-Dexmedetomidine (BD): (n = 50)

5 micrograms of preservative-free dexmedetomidine diluted in 0.5 ml 0.9% normal saline was added to 12.5 mg heavy bupivacaine 0.5% (3ml volume)

Group Bupivacaine (B): (n = 50)

0.5 ml 0.9% normal saline was added to 12.5mg heavy bupivacaine 0.5% (3ml volume).

Randomization was done by computer generated random numbers and closed opaque envelopes technique.

2.1 Study Design

2.1.1 Pre-anesthetic interventions

Upon patient arrival at the anesthesia room, a 18G venous cannula were inserted and fixed in the dorsum of the hand. Patients were then preloaded with lactated Ringer's solution (10 mL/kg) and maintained with 8 mL/kg/h. Fluids were stored at room temperature.

Before Intrathecal anesthesia, standard monitoring, including noninvasive blood pressure, electrocardiography, and pulse oximetry were applied for all patients and values recorded.

2.1.2 Study interventions

Using a complete aseptic technique, Intrathecal anesthesia was performed by the first investigator (who was not involved in data gathering) with the patient in sitting position at the L3–L4 or L4–L5 interspaces with a 25 G spinal Quincke-tip needle. In the bupivacaine–dexmedetomidine (BD) group, 5 micrograms of preservative free-dexmedetomidine (100 *μ*g/mL) diluted in 0.5 ml 0.9% normal saline was added to 12.5 mg (2.5ml) 0.5% heavy-bupivacaine. In the bupivacaine (B) group, 0.5 ml 0.9% normal saline was added to 12.5 mg 0.5% heavy bupivacaine . After completion of the intrathecal anesthesia, all patients were turned to the supine position immediately, while supplemental oxygen was administered at the rate of 4-6L/min via a face mask.

The study drugs were prepared by an anesthesiologist, who had no prior knowledge of the study design for both groups. The temperature of the operating room and post-anesthesia care unit was kept at 22°C–26°C throughout the study. During the operation, the whole bodies of the patient, except the head, neck, and operation site, were covered with one layer of surgical drapes. In the post-anesthesia-care unit the patient's body was covered with one cotton blanket.

2.2 Measurements

All measurements were recorded by an investigator who is not aware about the study design or intervention.

1. The incidence and intensity of shivering which was classified by the method of Tsai and Chu [9].
2. Core body and peripheral temperatures were measured from the tympanic membrane and forehead-skin surface once before intrathecal anesthesia and then at 15 minutes intervals.
3. Vital parameters, such as heart rate, mean blood pressure, and SpO2, were monitored continuously and recorded at intervals of 5 minutes for the first 30 minutes then at 15 minutes for the first hour and then at 30 minutes of the observation period.
4. Anesthesia complications such as hypotension, bradycardia, and shivering were recorded and treated as following:

- Any episode of hypotension (mean blood pressure <60) was treated with incremental intravenous ephedrine (5_10 mg) and then further infusion of crystalloid (250 mL) fluid as required.
- The decrease in the heart rate <50 beats per min was treated with incremental doses of intravenous atropine (0.3–0.5 mg).
- Moderate to severe shivering was treated with intravenous meperidine (15-20 mg).

The primary outcome was the incidence of intraoperative shivering. The secondary outcomes were changes in hemodynamic

parameters and changes in the core and peripheral temperature.

2.3 Sample Size Calculation

The sample size calculation based upon the previous study reveals that at least 50 patients were required in each group to detect a significant decrease in the incidence of intraoperative shivering from 55% without the use of dexmedetomidine to 27.5% with the use of intrathecal dexmedetomidine (50% reduction) [10] at 0.05 alpha value, 80% power of the study and ratio of cases to control 1:1.

2.4 Statistical Analysis

Once data was collected, a code sheet was developed. Organization, tabulation, presentation and analysis of data were performed by using SPSS V25 (IBM©, USA). Quantitative data (e.g. age) was presented as mean and standard deviation (SD) and the Student's t test was used for statistical analysis. Categorical data (e.g. sex) was presented as number and percentage and the chi-square or Fisher's Exact test was used for statistical analysis. The level of significance was adopted at $p<0.05$.

3. RESULTS

In this study, 118 patients were assessed for eligibility, 11 patients did not meet the criteria and 7 patients refused to participate in the study. The remaining 100 patients were randomly allocated into two groups (50 patients in each one); Group Bupivacaine-Dexmedetomidine (BD): 5 micrograms of preservative free-dexmedetomidine (100 μg/mL) diluted in 0.5 ml 0.9% normal saline was added to 12.5 mg (2.5ml) 0.5% heavy-bupivacaine and Group bupivacaine (B): 0.5 ml 0.9% normal saline was added to 12.5 mg 0.5% heavy bupivacaine. All patients were followed-up and analyzed statistically (Fig. 1).

Table 1 shows an insignificant difference between both groups as regard to patients' characteristics (age, BMI, Sex, ASA physical status and duration of surgery).

Heart rate decreased significantly in group BD than group B at 20, 25, 30, 45, 60, 75 and 90 minute (P <0.001, <0.001, <0.001, <0.001, <0.001, <0.001, 0.030) but there was insignificant differences between both groups at baseline, 5, 10, 15, 120 minute and at the end (Fig. 2).

Mean arterial blood pressure decreased significantly in group BD than group B at 10, 15, 20 and 25 minute (P <0.001, 0.04 and <0.001) but there were insignificant differences between both groups at baseline, 5, 30, 45, 60, 75, 90, 120 minute and at the end (Fig. 3).

3.1 Peripheral Temperature

There were insignificant differences at all time measurements between-group BD and group B regarding peripheral temperature (Table 2).

3.2 Core Temperature

There were insignificant differences at all time measurements between both groups regarding core temperature (Table 3).

There were insignificant differences at all time measurements between both groups regarding SpO_2 (Table 4).

There was a significant difference between both groups as regard to Tsai and Chu score (P = 0.013) (Table 5).

Shivering occurred in 9 patients (18%) in group BD and 23 patients (46%) in group B with a significant decrease in group BD compared to group B (P = 0.003). The relative risk of developing shivering was decreased 53% (95% Confidence Interval: 74 – 16%) with group BD compared to group B (Table 6).

There were insignificant differences between both groups as regard to PONV but there were significant differences as regard to hypotension, bradycardia and sedation (P = 0.037, 0.041 and 0.002) (Table 7).

4. DISCUSSION

Dexmedetomidine, a selective and potent α_2-receptor agonist, has been used intrathecally for its antinociceptive benefits. Intra and postoperative shivering is a distressing event. Various pharmacological methods have been examined for treatment or prevention of postoperative shivering; however, there is no gold-standard drug or method to prevent its occurrence [5].

Several studies reported that intravenous dexmedetomidine decreases vasoconstriction

and shivering thresholds. However, when administered by the intravenous route, dexmedetomidine can induce some negative side effects, such as bradycardia and hypotension. Unlike intravenous dexmedetomidine, information about the effects of intrathecal dexmedetomidine on shivering remains limited.

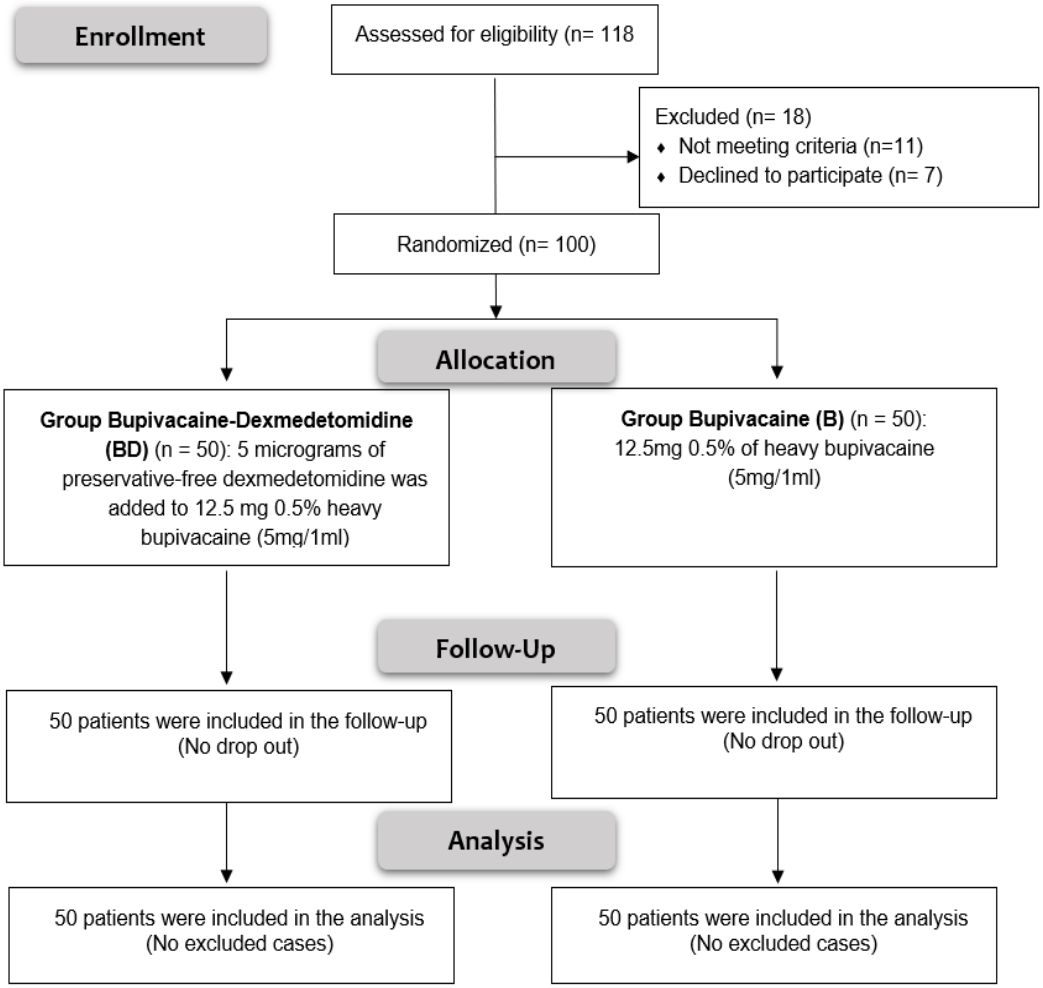

Fig. 1. Patient flowchart

Table 1. Patients' characteristics of both studied groups

		Group BD (n = 50)	Group B (n = 50)	P value
Age (y)	Mean	42.1	39.2	0.270
	± SD	11.49	14.83	
BMI	Mean	29.1	30.7	0.140
(kg/m^2)	± SD	5.45	4.85	
Sex	Male	28 (56%)	31 (62%)	0.542
	Female	22 (44%)	19 (38%)	
ASA physical status	ASA I	37 (74%)	39 (78%)	0.64
	ASA II	13 (26%)	11 (22%)	
Duration of surgery	Mean	103.2	99.0	0.485
(min)	± SD	29.45	30.46	

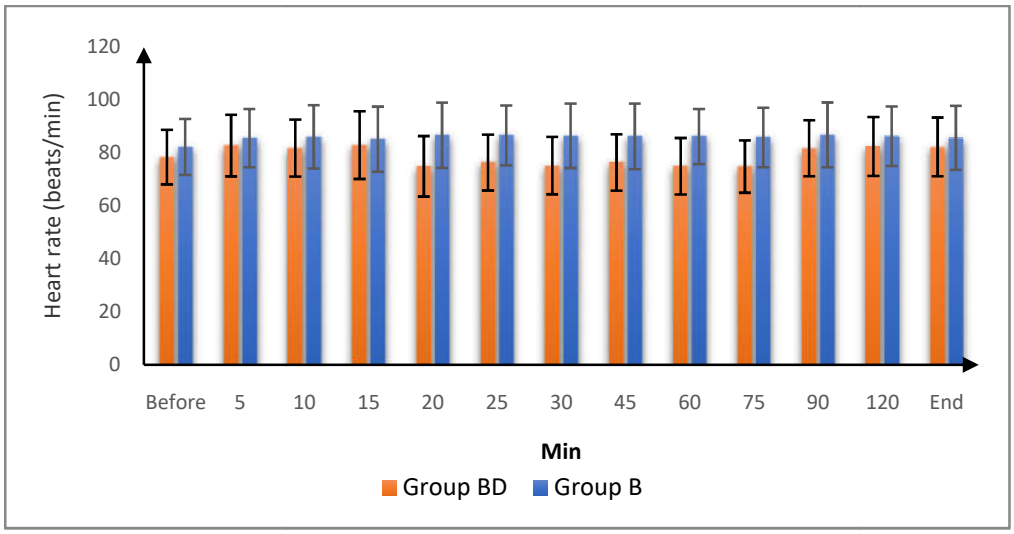

Fig. 2. Heart rate in both groups

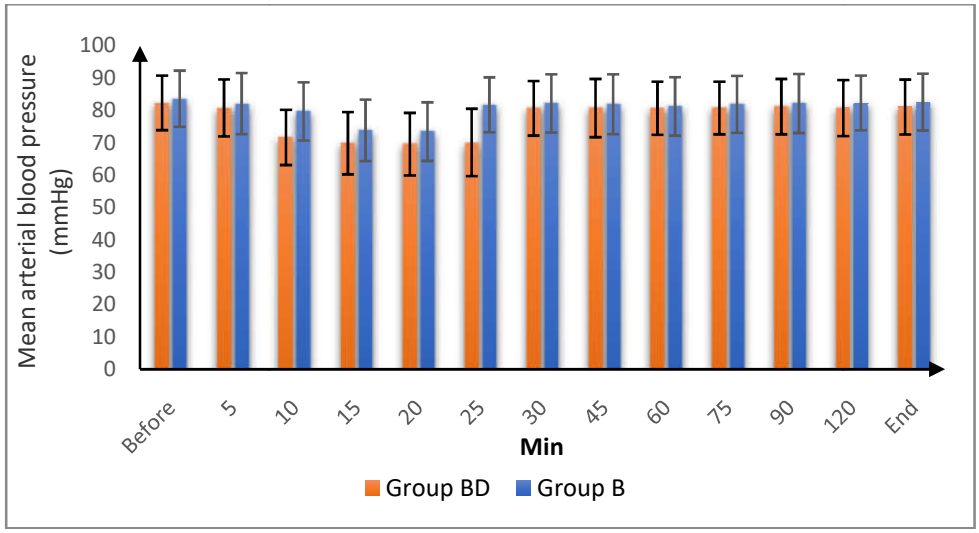

Fig. 3. Mean arterial blood pressure in both groups

Table 2. Peripheral temperature in both groups

	Group BD		Group B		P value
	Mean	± SD	Mean	± SD	
Before	36.56	0.30	36.54	0.34	0.755
5	36.55	0.31	36.56	0.35	0.904
10	36.56	0.30	36.53	0.34	0.690
15	36.49	0.32	36.46	0.36	0.681
20	36.46	0.33	36.44	0.37	0.775
25	36.50	0.30	36.45	0.37	0.391
30	36.56	0.32	36.54	0.34	0.832
45	36.56	0.30	36.56	0.36	0.976
60	36.56	0.31	36.53	0.36	0.723
75	36.56	0.32	36.54	0.33	0.716
90	36.59	0.33	36.56	0.34	0.721
120	36.55	0.31	36.54	0.37	0.862
End	36.56	0.30	36.56	0.36	0.928

Table 3. Core temperature in both groups

	Group BD		Group B		P value
	Mean	± SD	Mean	± SD	
Before	36.02	0.37	36.01	0.40	0.938
5	36.03	0.38	36.03	0.41	0.980
10	36.04	0.37	36.00	0.38	0.561
15	35.96	0.38	35.90	0.41	0.465
20	35.90	0.38	35.93	0.43	0.695
25	35.93	0.43	35.91	0.40	0.773
30	36.00	0.39	36.00	0.43	0.981
45	36.00	0.39	36.01	0.42	0.941
60	36.01	0.38	36.00	0.43	0.922
75	36.01	0.36	36.02	0.43	0.940
90	36.04	0.37	36.01	0.43	0.712
120	36.01	0.38	35.99	0.43	0.805
End	36.02	0.38	36.01	0.40	0.879

Table 4. SpO2 in both groups

	Group I		Group II		P value
	Mean	± SD	Mean	± SD	
Before	97.94	1.39	97.60	1.34	0.216
5	98.02	1.52	97.96	1.41	0.838
10	97.96	1.51	97.90	1.31	0.833
15	97.74	1.43	98.00	1.53	0.381
20	97.68	1.27	97.96	1.43	0.303
25	97.80	1.36	98.00	1.53	0.490
30	97.96	1.47	97.84	1.46	0.683
45	97.86	1.46	98.04	1.54	0.549
60	97.88	1.41	98.08	1.51	0.495
75	97.88	1.36	97.82	1.42	0.830
90	98.00	1.46	97.90	1.34	0.722
120	97.80	1.34	98.10	1.33	0.264
End	97.70	1.37	98.20	1.32	0.067

Table 5. Tsai and Chu score of shivering in both groups

Score	Group BD (n = 50)	Group B (n = 50)	P value
0	41 (82%)	27 (54%)	0.013*
1	7 (14%)	12 (24%)	
2	2 (4%)	8 (16%)	
3	0 (0%)	3 (6%)	
4	0 (0%)	0 (0%)	

**significant as P value <0.05*

Table 6. Shivering in both groups

	Group BD (n = 50)	Group B (n = 50)	P value
Yes	9 (18%)	23 (46%)	0.003*
No	41 (82%)	27 (54%)	

**significant as P value <0.05*

Table 7. Adverse effects in both groups

	Group BD (n = 50)	Group B (n = 50)	P value
Hypotension	13 (26%)	5 (10%)	0.037*
Bradycardia	11 (22%)	3 (6%)	0.041*
PONV	18 (36%)	21 (42%)	0.538
Sedation	12 (24%)	0 (0%)	<0.001*

**significant as P value <0.05*

- Our results regarding score of shivering showed a significant decrease in shivering in group BD in comparison to group B.

In agreement with our results, Sushruth and Rao, [11] concluded that adding dexmedetomidine 5 μg as an adjuvant to intrathecal hyperbaric 0.5% bupivacaine 9 mg in cesarean sections is associated with a decrease the incidence of shivering [11].

Also, Gautam et al. [12] concluded that the effects of adding intrathecal dexmedetomidine to hyperbaric bupivacaine for saddle spinal block in adults undergoing peri-anal surgeries is associated with decreasing the incidence of shivering [12].

In agreement with our results, Bi et al. [13] concluded that adding low dose of dexmedetomidine as an adjuvant to bupivacaine in cesarean surgery was associated with a decrease the incidence of shivering [13].

Nasseri et al. [5] concluded that the incidence of shivering was significantly higher in group bupivacaine (B) (52%) than group Bupivacaine-Dexmedetomidine (BD) (24%) which is also in agreement with this study results [5].

Also, He et al. [1] observed that the addition of 5*μ*g dexmedetomidine to hyperbaric bupivacaine for spinal anesthesia in parturient reduced the incidence of intraoperative shivering and in the absence of any noticeable side-effects, however supplementation of bupivacaine with only 2.5*μ*g dexmedetomidine did not decrease the incidence nor the intensity of shivering at all. Therefore, he showed that the anti-shivering effect of dexmedetomidine behaves in a dose-dependent manner when given intrathecally [1].

Qi et al. [14] compared the effects of 5 μg intrathecal dexmedetomidine with 100 μg morphine as supplements to 10 mg bupivacaine in 120 parturients undergoing elective CS under SA. Only 7.7% of patients in the dexmedetomidine group had shivering, while 30% and 35.9% of patients in the morphine and bupivacaine groups experienced shivering, respectively. Although these results regarding lowering shivering are in agreement with our study, the incidence of shivering in that study was significantly lower than the present study, which may be attributed to different communities, sample size or methodology [14].

Moawad and Elawdy et al. [15] investigated the effect of subarachnoid dexmedetomidine in the reduction and prevention of shivering in 80 patients who received SA for transurethral resection of the prostate. Subarachnoid block was achieved by either 12.5 mg of hyper- baric bupivacaine plus 0.5 mL of isotonic saline or 12.5 mg of hyperbaric bupivacaine plus 10 μg dexmedetomidine in 0.5 mL of isotonic saline. The incidence of shivering was significantly lower (15%) in the dexmedetomidine group than the saline group (57%). They concluded that adding 10 μg dexmedetomidine to hyperbaric bupivacaine in the transurethral resection of the prostate procedure could further reduce the incidence of shivering [15].

This comes in agreement with the current results. However, the lower incidence of shivering in Moawad and Elawdy et al, [15] results compared with our study may relate to the higher dose of dexmedetomidine used in their study (10 μg versus 5 μg) [15].

Abdelhamid and El-Lakany [16] also reported a low incidence (6.5%) of shivering following SA by heavy bupivacaine 0.5% plus 5 μg intrathecal dexmedetomidine for lower abdominal surgeries compared with 38.7% in the control group. The key factors that may contribute to these differences are those that could increase shivering during SA. These factors are aging, sensory-block levels, temperatures of the intrathecal local anesthetics, intravenous fluids, and operation room. In the current study, the age of patients in the two groups, the ambient temperature of the operating and recovery rooms (22C–26C), temperatures of the intrathecal drugs, and intravenous solutions (room

temperature) were comparable. It seems that none of these factors differed from the other studies; therefore, these variations in the results could be explained by different patient characteristics in the different studies [16].

Elvan et al. [17] reported a similar result, 7/45 (15%) in dexmedetomidine group and 21/45 (46%) in saline group developed shivering (P = 0.001) [17].

On the other hand, Liu et al [1] stated that although dexmedetomidine shows superiority over placebo, but not over other anti-shivering agents such as meperidine and tramadol. Therefore, considering its high price and potential adverse events, dexmedetomidine may not be appropriate solely for the purpose of the prevention of postoperative shivering [1].

One of the limitations of our study, limited age range as we excluded geriatrics whom the loss of thermoregulatory mechanisms associated with aging and suffering from diseases that may influence disease is known.

5. CONCLUSION

The use of intrathecal DEX (5μg) in conjugation with heavy bupivacaine help decrease the incidence and intensity of shivering when compared with heavy bupivacaine alone in surgeries under spinal anesthesia.

CONSENT AND ETHICAL APPROVAL

A prospective double-blind, controlled, randomized study was conducted after approval of the ethical committee of faculty of medicine, Tanta University from October 2019 to March 2020. An informed consent was taken from the nearest relatives of the patients.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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