

A RANDOMIZED DOUBLE-BLIND COMPARATIVE STUDY OF TWO DIFFERENT DOSES OF INTRAVENOUS DEXMEDETOMIDINE ON POST-SPINAL ANAESTHESIA SHIVERING

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ABSTRACT

Background: Shivering is a common post-anaesthesia adverse event with multiple etiologies. The aim of this study was to compare the efficacy of two different dosages of dexmedetomidine in the treatment of post-spinal anaesthesia (SA) shivering as well as to compare their side-effect profile.

Materials and Methods: This prospective, double-blind, randomized controlled trial was conducted in the department of anaesthesia, Vinayaka Mission Medical College and Hospital, Karaikal. A total of 100 patients having shivering after SA were enrolled, out of which 50 received dexmedetomidine 0.5 mcg/kg (Group A) and 50 received dexmedetomidine 1 mcg/kg (Group B). The response rate, time to cessation of shivering and side effects (if any) were noted. All the results were analyzed using Student's t-test and Chi-square test.

Results: All patients who received both the dosages of dexmedetomidine had cessation of shivering. The time to cessation of shivering was significantly less with dexmedetomidine 1 mcg/kg (168 ± 23.3 s) than with dexmedetomidine 0.5 mcg/kg (174 ± 14.5 s) ($P=0.024$). The recurrence rate of shivering with dexmedetomidine 1 mcg/kg was less as compared to dexmedetomidine 0.5mcg/kg. Nausea and vomiting were found to be higher in the group of dexmedetomidine 1 mcg/kg. On the other hand, dexmedetomidine 0.5 mcg/kg caused moderate sedation (modified Ramsay sedation score = 3 – 4) from which the patient could be easily waken up.

Conclusion: Dexmedetomidine 0.5 mcg/kg offers better results than dexmedetomidine 1 mcg/kg with fewer side effects.

Keywords: Dexmedetomidine, post-spinal anaesthesia, shivering

1. INTRODUCTION

Regional anaesthesia (spinal anaesthesia) is widely used as a safe anaesthetic technique for both elective and emergency operations. Shivering is known to be a frequent complication, reported in 40 to 70% of patients undergoing surgery under regional anaesthesia^(1,2). Shivering is a potentially serious complication, resulting in increased metabolic rate; increased oxygen consumption (up to 100-600%) along with raised carbon dioxide (CO₂) production; ventilation and cardiac output; adverse postoperative outcomes, such as wound infection; increased surgical bleeding; and morbid cardiac events. It causes arterial hypoxemia, lactic acidosis, increased intraocular pressure (IOP), increased intracranial pressure (ICP); and interferes with pulse rate, blood pressure (BP) And electrocardiographic (ECG) monitoring^(3,5). Shivering is a physiological response to core hypothermia in an attempt to raise the metabolic heat production. The main causes of intra/post-operative shivering are temperature loss, increased sympathetic tone, pain, and systemic release of pyrogens. Spinal anaesthesia significantly impairs the thermoregulation system by inhibiting tonic vasoconstriction, which plays a significant role in temperature regulation. It also causes a redistribution of core heat from the trunk (below the block level) to the peripheral tissues. These factors predispose patients to hypothermia and shivering^(4,6).

The treatment of shivering includes both pharmacological and non-pharmacological methods. The non-pharmacological management is by external heating like the use of forced air warming, warming blankets, warmed fluids etc., According to the results of a meta-analysis, the most frequently reported pharmacological interventions include clonidine, pethidine, tramadol, nefopam and ketamine⁽⁶⁾. Unfortunately, no gold standard treatment is known for shivering as the administration of all the available drugs is associated with various adverse effects.

During the last decade, Tramadol has become a favoured and commonly used drug for post-spinal anaesthesia shivering. However, it has many adverse effects like nausea, vomiting, dizziness etc., which cause further discomfort to the patient^(7,8). Clonidine is another agent which has gained popularity during the last few years. Various studies, which have been conducted to compare them have concluded that clonidine has better efficacy and less adverse effects as compared to tramadol^(7,8). But there was 5-10% incidence of hypotension and bradycardia with clonidine.⁽⁷⁾ Dexmedetomidine, a congener of clonidine, is a highly selective α_2 -adrenoceptor agonist. It has been used as a sedative agent and is known to reduce the shivering threshold.⁽⁹⁾ Few studies which have explored its anti-shivering potential have inferred that dexmedetomidine is an effective drug without any major adverse effect and provides good haemodynamic stability.^(9,10,11)

The aim of the study is to compare the efficacy, potency, haemodynamic effects, complications and side effects of two doses of dexmedetomidine for control of shivering intra operatively.

2. MATERIALS AND METHODS

After obtaining approval of the ethics committee and informed written consent, hundred American Society of Anaesthesiologists class-I & II(ASA 1&2) patients of either sex aged 18 to 60 years scheduled for elective lower abdominal, orthopaedic and gynaecological surgeries under spinal anaesthesia with no prior pre-medication, were included in this prospective randomized double blind clinical controlled study. Patients with known hypersensitivity to dexmedetomidine, known history of alcohol or substance abuse, hyperthyroidism, cardiovascular diseases, psychological disorder, severe diabetes or autonomic neuropathies and urinary tract infection (UTI) were excluded. The study was conducted in the department of anaesthesia, Vinayaka Mission Medical College & Hospital, Karaikal.

Randomization method was done according to computer generated random table. Patients who fulfilled the inclusion criteria and developed post spinal anaesthesia shivering will be randomly allocated into two groups: Group A (Dexmedetomidine 0.5 mcg/kg IV) and Group B (Dexmedetomidine 1 mcg/kg IV). Closed envelopes were used to reveal randomization. Dexmedetomidine is available as 100 micrograms in one ml ampoule(100 mcg/ml).

The individual collecting data of patients and the anaesthesiologist performing spinal anaesthesia were all blinded from knowing the drug used in the study. Dexmedetomidine(100 mcg/ml) is diluted to 10 mcg/ml in 10 ml disposable syringe to achieve blinding for both dosages and given by slow intravenous (one minute duration) at the start of shivering. In order to facilitate blinding, the test solution was prepared by the first anaesthesiologist who was not involved in the study. Neither the recording (second) anaesthesiologist nor the patients were aware of the drug. Patients were observed for shivering intraoperatively. Presence of shivering was observed by an anaesthesiologist who was blinded to the study drug. The second anaesthesiologist performed spinal anaesthesia procedure and data collection in the patients was blinded from the study drug given to the patient.

Upon arrival in the operation theatre, an 18 G venous cannula was inserted and preloading done with Ringer's Lactate solution 10 ml/kg before giving spinal anaesthesia and maintained at 6 ml/kg/h after spinal anaesthesia. Before starting the procedure, standard monitors were attached and all the baseline parameters such as heart rate (HR), non-invasive blood pressure (NIBP), oxygen saturation (SPO₂), electrocardiography (ECG), and body temperature (axillary) were recorded. Neuraxial blockade was administered with 0.5% heavy bupivacaine (15 mg) at L₂₋₃ or L₃₋₄ interspace using 25G Quincke's spinal needle under aseptic conditions. All operation theatres were maintained at an ambient temperature of around 24°C-25°C. Supplemental oxygen was administered to all the patients at the rate of 5 l/min with face mask and patients were covered with drapes but not actively warmed. IV fluids and anaesthetics were administered at room temperature. Vital parameters such as HR, NIBP, and SPO₂ were recorded at intervals of every 5 min for first 30 min and every 15 min for the rest of the observation period. Continuous ECG monitoring was done.

Shivering was graded using a four point scale as per Wrench⁽¹²⁾

Grade 0: No shivering

Grade 1: One or more of the following: Piloerection, peripheral vasoconstriction, peripheral cyanosis, but without visible muscle activity

Grade 2: Visible muscle activity confined to one muscle group

Grade 3: Visible muscle activity in more than 1 muscle group

Grade 4: Gross muscle activity involving the whole body

Patients who developed either Grades 3 or 4 shivering were included in the study. Either of the two drugs was given as slow IV bolus injection. The attending anaesthesiologist recorded the time in minutes at which shivering started after spinal anaesthesia (onset of shivering), severity of the shivering, time to the disappearance of shivering and response rate (shivering ceasing within 15 min after treatment). Duration of surgery was recorded and duration of spinal anaesthesia was noted by assessing spontaneous recovery of sensory block using the pin-prick method and observing spontaneous movements of limbs in the post-operative period. Recurrence of shivering was also noted. In case there was recurrence of shivering, patients were treated with an additional dose of dexmedetomidine (0.5 µg/kg IV) or tramadol (0.5 mg/kg IV) in the respective groups.

The degree of sedation was graded on a four point scale as per Filos *et al*⁽¹³⁾

Grade 1: Awake and alert

Grade 2: Drowsy, responsive to verbal stimuli

Grade 3: Drowsy, arousable to physical stimuli

Grade 4: Unarousable

Side effects like nausea, vomiting, bradycardia (<50/min), hypotension (>20% of baseline), dizziness; and sedation score were recorded. Bradycardia, hypotension and vomiting were treated with atropine, mephentermine and metoclopramide, respectively, in titrated doses when required.

Statistical Analysis

The Statistical analysis was performed by Statistical package SPSS (version 16.0) and STATA 11.2 (College Station TX USA). Shapiro wilk test was used to check normality. Students Independent sample size t-test was used to find the significance difference between the age, duration of surgery, Heart rate, Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Pressure, SpO₂, respiratory rate, time of onset of shivering, severity of shivering, time to disappearance of shivering and time of recurrence with treatment of shivering groups and these were expressed as mean and standard deviation. Chi square test was used to measure the association between the gender distribution with the treatment groups and these were expressed as frequency and percentage. P<0.05 was considered as statistically significant.

3. RESULTS

In the present study, a total of 100 patients out of 120 consecutive patients met the inclusion criteria and consented for study. These 100 patients were randomized into two groups of 50 each. As it was an intra-operative study, no patient was lost to follow-up [Figure 1].

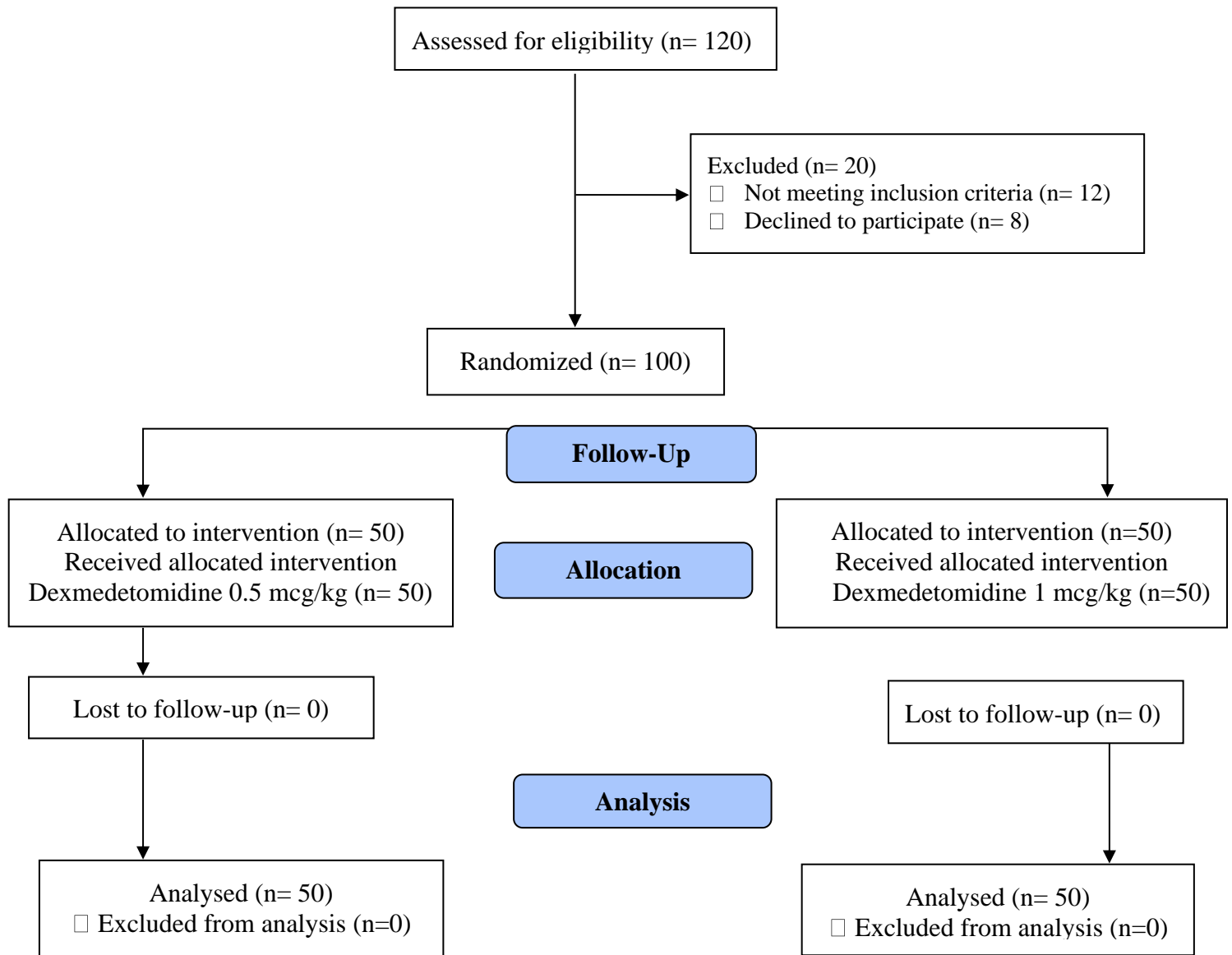


Figure 1: The study flow diagram

Both the groups were comparable with respect to age, duration of surgery, Heart rate, Systolic Blood pressure, Diastolic Blood Pressure, Mean Arterial Pressure, SpO₂, respiratory rate, time of onset of shivering, severity of shivering, time to disappearance of shivering and time of recurrence (Table No:1)

TABLE 1: DEMOGRAPHIC PROFILE OF PATIENTS OF BOTH GROUPS

Parameter	Group A (n=50)	Group B (n=50)	P value
Age(years)	36.54 ± 10.92	39.74 ± 9.72	0.125
Gender(M/F)	39/11	32/18	0.123

Weight(kg)	71.6 ± 8.5	73.3 ± 9.3	0.424
Height(cm)	173.6 ± 7.3	171.7 ± 6.5	0.329
ASAI/ASAII	15/35	13/37	0.482
Duration of surgery(hours)	1.28 ± 0.65	1.12 ± 0.55	0.185
Duration of spinal anaesthesia(mins)	136.2 ± 14.1	132.7 ± 11.6	0.295
Crystalloids infused	1553 ± 527.2	1483 ± 392.7	0.372

Data are presented as mean ± SD, number. *n* = number of patients.

M/F = males/females, ASA = American Society of Anesthesiologists physical status.

There were no statistically significant differences between the two groups with respect to demographic data, patient's characteristics related to spinal anaesthesia, duration of surgery and sensory block level.

TABLE 2: COMPARISON OF HEART RATE VARIABLES BETWEEN TWO GROUPS

	Group A	Group B	P-Value
	Mean ± SD	Mean ± SD	
Baseline	80.40 ± 13.74	77.76 ± 11.17	0.294
0 Minute	79.72 ± 11.14	76.84 ± 10.81	0.193
2 Minutes	79.72 ± 9.88	72.82 ± 9.12	0.001
5 Minutes	80.12 ± 10.83	71.40 ± 9.74	<0.001
10 Minutes	79.84 ± 10.63	68.44 ± 8.48	<0.001
20 Minutes	79.71 ± 10.58	67.22 ± 9.14	<0.001
30 Minutes	79.05 ± 9.92	67.58 ± 8.43	<0.001
45 Minutes	78.83 ± 9.75	68.19 ± 8.94	<0.001
60 Minutes	78.59 ± 10.12	71.71 ± 8.78	0.014
120 Minutes	70.0 ± 10.36	73.0 ± 7.07	0.441

In our study the heart rate variability was compared in both the groups and at 2 minutes, the mean value of group A was (79.72) and standard deviation was (9.88) and in the group B the mean value was (72.82) and standard deviation was (9.12) ; p value is 0.01 which is statistically significant.

At 5 mins the mean value of group A was (80.12) and standard deviation was (10.83) and in the group B the mean value was (71.40) standard deviation was (9.74) ; the p value is < 0.001 which is statistically highly significant.

GRAPH 1: MEAN HEART RATE DISTRIBUTION OF TWO GROUPS

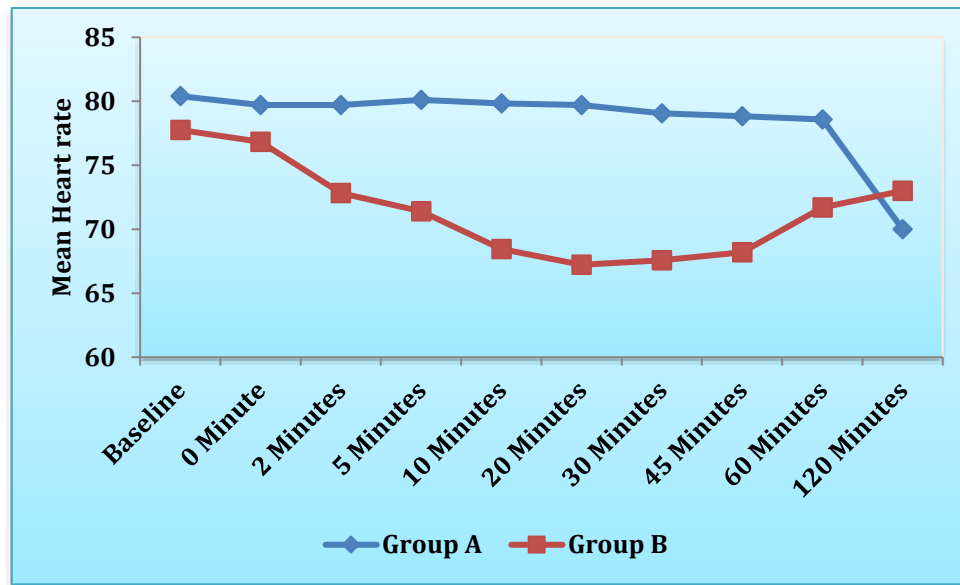


TABLE 3 COMPARISON OF MEAN ARTERIAL PRESSURE VARIABLES BETWEEN TWO GROUPS

	Group A	Group B	P-Value
	Mean \pm SD	Mean \pm SD	
Baseline	93.98 \pm 1.79	92.29 \pm 4.14	0.009
0 Minute	93.20 \pm 2.32	89.42 \pm 3.74	<0.001
2 Minutes	91.48 \pm 2.89	87.62 \pm 5.18	<0.001
5 Minutes	84.50 \pm 2.65	84.20 \pm 5.83	0.741
10 Minutes	81.84 \pm 3.59	84.18 \pm 7.17	0.042
20 Minutes	75.48 \pm 3.14	76.90 \pm 4.61	0.075
30 Minutes	78.88 \pm 4.52	74.16 \pm 1.86	<0.001
45 Minutes	78.78 \pm 6.53	72.94 \pm 2.18	<0.001
60 Minutes	83.66 \pm 4.91	71.85 \pm 2.19	<0.001
120 Minutes	84.36 \pm 5.42	72.86 \pm 4.13	<0.001

In our study the Mean Arterial Pressure variability is compared in both the groups and at the baseline minute, the mean value of group A was (93.98) and standard deviation was (1.79) and in the group B mean value was (92.29) and standard deviation was (4.14); p value is 0.009 which is statistically significant.

At initial (0) minute, the mean value of group A was (93.20) and standard deviation was (2.32) and in the group B the mean value was (89.42) and standard deviation was (3.74) ; the p value is < 0.001 which is statistically highly significant.

At 2 minutes, the mean value of group A was (91.48) and standard deviation was (2.89) and in the group B the mean value was (87.62) and standard deviation was (5.18); the p value is < 0.001 which is statistically highly significant.

At 10 minutes, the mean value of group A was (81.84) and standard deviation was (3.59) and in the group B the mean value was (84.18) and standard deviation was (7.17); the p value is 0.042 which is statistically significant.

At 30,45,60,120 minutes, both the groups A & B were compared and the p value is 0.001 which is statistically highly significant.

GRAPH 2: MEAN ARTERIAL PRESSURE(MAP) DISTRIBUTION OF TWO GROUPS

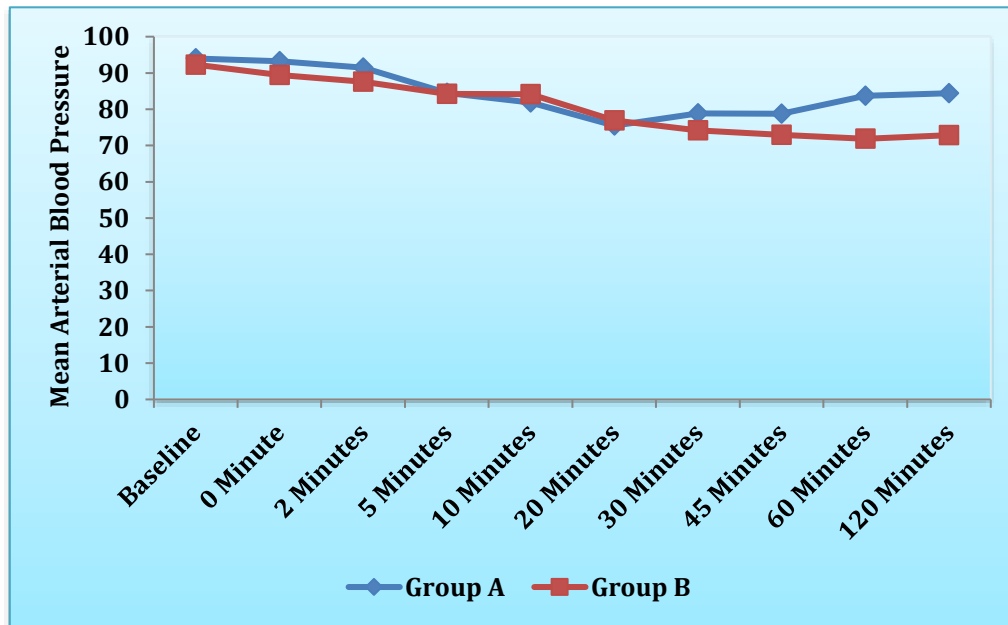


TABLE 4: COMPARISON OF THE TIME OF ONSET OF SHIVERING, SEVERITY OF SHIVERING, TIME TO DISAPPEARANCE OF SHIVERING AND TIME OF RECURRENCE IN THE TWO STUDY GROUPS

	GroupA (n=50)	GroupB(n=50)	P
Time of onset of shivering(min)	72.30 ± 41.35	72.66 ± 41.64	0.965
Severity of shivering	3.8 ± 0.27	3.96± 0.12	0.405
Time to disappearance of shivering(Sec)	174 ± 14.5	168 ± 23.3	0.0024
Time of recurrence	70 ± 17.3	75 ± 21.17	0.42

In our study the time of onset of shivering variability is compared in both the groups and the mean value of group A was (72.30) and standard deviation was (41.35) and in the group B mean value was (72.66) standard deviation was (41.64); p value is 0.965 which is statistically insignificant.

In severity of shivering p, the mean value of group A was (3.8) and standard deviation was (0.27) and in the group B the mean value was (3.96) and standard deviation was (0.12); the p value is 0.405 which is statistically insignificant.

In time to disappearance of shivering(sec), the mean value of group A was (174) and standard deviation was (14.5) and in the group B the mean value was (168) and standard deviation was (23.3); the p value is 0.0024 which is statistically significant.

TABLE 5: COMPARISON OF COMPLICATIONS IN BOTH GROUPS

Complication	Group A (n=50)	Group B (n=50)
Hypotension	15(30%)	30(60%)
Bradycardia	12(24%)	35(70%)
Nausea	2(4%)	6(12%)
Vomiting	0(0)	3(6%)
Sedation Grade1	30(60%)	40(80%)
Grade2	15(30%)	10(20%)
Dry mouth	2(4%)	6(12%)

In our study, complications like hypotension, bradycardia, nausea, vomiting, Sedation Grade 1, Sedation Grade 2, dry mouth were compared in both Groups. Percentage of complications were more in Group B than in Group A. There was no incidence of hypotension in either group, which is similar to previous studies. Similarly, none of the patients in either group had itching.

4. DISCUSSION

Shivering is known to be a frequent complication in patients undergoing surgery under neuraxial anaesthesia. Shukla et al. have reported the incidence of shivering in patients undergoing surgery under regional anaesthesia at 40–70% based on previous studies. The incidence of shivering in our study was 41%.⁽⁸⁾

Regional anaesthesia, either central neuraxial block or peripheral nerve block, is a safe and very popular technique used for various surgeries. However, 40% to 70% of patients undergoing regional anaesthesia develop shivering, though it is also found to occur after general anaesthesia^(1,2)

In this study, we studied the efficacy of dexmedetomidine in the treatment of post-spinal anaesthesia shivering in patients undergoing various elective surgeries. Although tramadol is an established drug in the treatment of shivering, in this study, we found that dexmedetomidine (0.5 mcg/kg) is equally effective as dexmedetomidine (1 mcg/kg) in treating of post-spinal anaesthesia shivering.

Prevention of post-anaesthetic shivering (PAS) mainly entails preventing perioperative heat loss by increasing ambient temperature of operative room, using conventional warm air blankets and using warmed intravenous (I.V.) fluids. Although the neurotransmitter pathways involved in the mechanism of PAS are complex and still anonymous, there are various pharmacological drugs available for the management of PAS such as meperidine, clonidine, tramadol and ketamine. However, every drug has its own adverse effect and the ideal anti-shivering drug is still not found. The efficacy of dexmedetomidine is similar to that of a

previous study by Blaine Easley et al who studied the role of dexmedetomidine in the treatment of postoperative shivering in adults.⁽¹⁵⁾

Dexmedetomidine displays specific and selective α_2 -adrenoceptor agonism in the brain and spinal cord. The responses to activation of these receptors include decreased sympathetic tone with attenuation of the neuroendocrine and hemodynamic responses to anaesthesia and surgery. Thus, dexmedetomidine can mediate both the beneficial and unwanted effects of shivering provoked by hypothermia, such as increased catecholamine concentrations, oxygen consumption, blood pressure and heart rates^(16,17,18)

Alpha-2 adrenergic agonists are widely used nowadays in anaesthesia and intensive care settings. Dexmedetomidine is an α_2 adrenoceptor agonist, with antihypertensive, sedative, analgesic, and anti-shivering properties⁽¹⁹⁾. The anti-shivering effects of alpha adrenoceptor agonists are mediated by binding to α_2 receptors that mediate vasoconstriction and the anti-shivering effect. In addition, it has hypothalamic thermoregulatory effects. Dexmedetomidine comparably reduces the vasoconstriction and shivering thresholds, thus suggesting that it acts on the central thermoregulatory system rather than preventing shivering peripherally⁽²⁰⁾. It has been successfully used as an adjunct to local anaesthetics in spinal anaesthesia and peripheral nerve blockade, for the sedation of mechanically ventilated patients in the Intensive Care Unit, as well as supplementation of post-operative analgesia^(19,21). The role of dexmedetomidine in the treatment of shivering has been evaluated in a few studies.^(9,10,11) It may be a good choice because of its dual effects, 'anti-shivering' and sedation.

In our study complications like hypotension, bradycardia, nausea, vomiting, Sedation Grade1, Sedation Grade2, Dry mouth were compared in both the groups. Percentage of complications were more in Group B than Group A. There was no incidence of hypotension in either group, which is similar to previous studies. Similarly, none of the patients in either group had itching.

The major limitation of our study is the small sample size. A bigger sample size would have increased the robustness of our results. Another limitation was that the present study included short duration surgeries as the mean duration of surgical period was calculated to be approximately 1 hour in both the groups. The anti-shivering effect of dexmedetomidine needs to be seen in surgeries of longer duration where chances of developing hypothermia are more. Axillary temperature was recorded at regular intervals perioperatively until the end of the study.

5. CONCLUSION

Both Dexmedetomidine (0.5 mcg/kg) and Demedetomidine (1 mcg/kg) are useful for cessation of post-spinal anaesthesia shivering, but Dexmedetomidine (0.5 mcg/kg) has less complications and side effects compared to Dexmedetomidine(1 mcg/kg). So we conclude that Dexmedetomidine(0.5mcg/kg) is a good choice for post-spinal anaesthesia shivering.

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