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Original Research Article

A Prospective, Randomized, Double-Blinded Control Study on Comparison of Tramadol, Clonidine and Dexmedetomidine for Post Spinal Anesthesia Shivering

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Abstract

Background: Shivering, a typical intraoperative issue with spinal anaesthetic, causes discomfort and anguish for the patient, the anesthesiologist, and the surgeon. It also significantly increases oxygen use. The goal of the current study was to determine whether tramadol, clonidine, and dexmedetomidine are useful in treating post-spinal anaesthetic shivering as well as to identify any potential negative effects.

Methods: Ninety patients who experienced shivering while under spinal anaesthetic participated in this prospective, randomised, double-blind control research. They were divided into three groups at random and given different medications: Group T received tramadol 1 mg/kg, Group C received clonidine 1 mcg/kg, and Group D received dexmedetomidine 0.5 mcg/kg. The duration of shivering control, recurrence rate, hemodynamic factors, sedation score, and negative effects were tracked.

Results: Tramadol took 6.76±0.93 minutes and clonidine took 9.43± 0.93 minutes to reduce shivering, respectively. Dexmedetomidine was faster, taking 5.7± 0.79 minutes. Dexmedetomidine had a substantially lower recurrence rate (3.3% vs. 10% and 23.3%, respectively) than clonidine and tramadol. Dexmedetomidine provided a more comfortable level of sedation than clonidine or tramadol. Four extra occurrences of vomiting occurred in the tramadol group, while six episodes of hypotension and two cases of bradycardia occurred in the dexmedetomidine group. The bradycardia and hypotension were experienced by two of the clonidine patients.

Conclusion: Due to its quicker start and lower recurrence rate, dexmedetomidine performs better in the control of shivering than tramadol and clonidine. The dexmedetomidine group experiences complications, but they are manageable.

Keywords: Clonidine; Dexmedetomidine; Hypothermia; Shivering; Spinal anesthesia; Tramadol

Introduction

Shivering is an oscillatory, involuntary mechanical muscular action that serves as the body's natural defence mechanism against overheating. Shivering is an attempt by the body to increase metabolic heat production and return to homeostasis [1]. Humans typically keep their core temperatures in a narrow range, known as the interthreshold range or thermoneutral zone, between 36.5 to 37.50C. When core temperature drops below the usual range, thermoregulatory reactions such vasoconstriction and shivering are triggered [2].

The preoptic nucleus of the anterior hypothalamus serves as the central location for the spinal motor neurons and their axons, which mediate the neurological mechanism of shivering [3]. There is some uncertainty regarding the prevalence of shivering after spinal anaesthesia, with some sources citing as high as 30–60% [4]. Shivering causes a 600% increase in heat output and a threefold increase in oxygen use. Numerous metabolic problems, including hypoxemia, hypercarbia, lactic acidosis, and raised intraocular and intracranial pressure, may result from this [5,6].

Shivering can worsen myocardial function in people with coronary artery disease [7]. There is no agreed-upon gold standard therapy for the treatment of shivering, however a number of pharmaceutical and nonpharmacological techniques are available [8]. The non-pharmacological options include the use of external warmers, warm intravenous fluids, and blankets. Several medications have been investigated for the prevention and treatment of shivering. This contains dexmedetomidine, granisetron, tramadol, nefopam, ketamine, pethidine, tramadol, magnesium sulphate, dexamethasone, and urapidil [9]. But regrettably, no single medication has been proven to be efficient and free of side effects. Pethidine was once thought to be the best medication to reduce shivering, but due to its negative effects, many institutions now steer clear of it [8,10]. This prospective, randomised, double-blinded control trial compares tramadol, clonidine, and dexmedetomidine for treating shivering after spinal anaesthesia in terms of effectiveness, recurrence rate, hemodynamics, and consequences.

Materials and Methods

Patients at the Nalanda Medical College and Hospital in Patna, Bihar, a tertiary medical college hospital, provided their informed consent before the study was carried out between January 2022 and June 2022. The study comprised patients who were between the ages of 18 and 70, ASA 1 and 2 members, set to have elective procedures under spinal anaesthesia, and who began to shiver.

Patients who had an ASA of 3 or higher, heart, liver, or renal illnesses, were allergic to any of the research treatments, refused the trial's medications, pregnant women, were also not allowed to participate. Thirty patients from each group of patients who had shivering during spinal anaesthesia were randomly assigned to each group.

Tramadol 1 mg/kg was given to Group T patients, clonidine 1 mcg/kg was given to Group C patients, and dexmedetomidine 0.5 mcg/kg was given to Group D patients. The computer-generated random envelope method was used to determine the group allocation. The research drug is added to a 100 mL of normal saline by the first anesthesiologist before giving it to the

second anesthesiologist, who is blind to the study drug. The patient is watched while the head administers the medication during a 10-minute period. All patients underwent routine monitoring of their electrocardiogram, noninvasive blood pressure, oxygen saturation, and axillary temperature. For every procedure, the operating room's temperature was kept at 22^0C. All patients received fluids at room temperature without the use of any external warming devices.

Depending on the type of surgery, the patients had spinal anaesthesia with a 25 gauge Quincke spinal needle to reach a level of at least T10. The study included patients who experienced shivering. According to Wrench, the level of shivering was rated on a scale of 1-4. Patients with grade 1 had one or more of the following symptoms, but no obvious muscular activity: piloerection, peripheral vasoconstriction, or cyanosis.

Visible muscle activity that is restricted to one muscle group is included in grade 2. Grade 3 involved multiple muscle groups showing apparent muscle activation. Gross muscular activity involving the entire body was considered to be grade 4. Patients who have shivering with at least a Grade 2 were included in the trial. After the study medication was administered, the hemodynamic monitoring was kept up. The amount of time it took to stop shaking, how often it happened, and how much sedation it caused was all noted. The suggested sedation score by Filos *et al*. was used. Grade 1 was considered to be an awake and alert patient. Patient in grade 2 reacting to verbal cues when asleep. Grades 3 and 4 were classified as unarousable patients who were drowsy yet responsive to physical stimuli. Following the delivery of spinal anaesthetic, the monitoring was kept up for another two hours. The Statistical Package for Social Sciences version 17.0 software was used to conduct the statistical analysis (IBM Corporation, Armonk, NY, USA).

Utilizing the One-way Analysis of Variance (ANOVA) test, demographic data were examined. The length of time needed to control shivering, heart rate, and blood pressure were all expressed as means with standard deviations, and one-way ANOVA with a post-test was used for statistical analysis. P-values less than 0.05 were deemed statistically significant, while p-values less than 0.01 were deemed extremely significant. The level for all analyses was set at $p = 0.05$. The Students' t-test was conducted between the two groups to ascertain statistical significance whether the p-value was significant. The two-way ANOVA test for block design was used to examine the sedation score, recurrence rate, and side effects.

Results

This prospective, randomised, double-blind control research included 90 individuals who shivered while receiving spinal anaesthesia. According to the demographic profiles of the 3 groups, there was no statistically significant difference, as indicated in Table 1.

Table 1: Demographic characteristics

Patients characteristics	Group T	Group C	Group D	p-value
Age (years)	37.42±6.27	36.84±5.87	35.78±6.76	0.596[a]
Body weight (kg)	66.65±7.46	68.73±8.34	67.34±7.62	0.578 [a]
Height (cm)	166.34±10.45	164.42±11.23	162.72±10.72	0.433 [a]
ASA physical status 1/2	14/16	15/15	12/18	1.001 [a]
Gender (M/F)	12/18	13/17	12/18	0.667 [a]

Mean duration of anaesthesia(min)	62.43±3.78	64.54±4.42	63.32±4.43	0.157 [a]
Mean axillary temperature (^{0}C)	36.88±0.55	36.77±0.14	36.83±0.24	0.097 [a]

[a]Not significant

Additionally, there were no notable baseline differences in either the mean axillary temperature or hemodynamic parameters. Tramadol (6.72±1.27 min), and clonidine (9.48±0.95 min) groups took substantially longer to suppress shivering than the dexmedetomidine (5.76±1.14 min) group. According to the One Way Analysis of Variance (ANOVA) test, the p-value was 0.0001, which was considered very significant. After the study medicine was administered, there were substantial differences in the heart rates across the three groups, as shown in Table 2.

Table 2: Variations in heart rate after study drug administration

Time (min)	Group T (beat/min)	Group C (beat/min)	Group D (beat/min)	p-value	Intergroup comparison when p<0.05
0	73.72±4.68	74.9±5.21	74.41±4.25	0.625[c]	-
10	76.83±3.78	70.42±3.17	68.53±2.49	<0.0001[b]	<0.001[d] <0.001[e] 0.013[f]
20	74.74±5.21	71.28±5.39	65.42±4.95	<0.0001[b]	0.0259[d] <0.001[e] <0.001[f]
30	70.5±3.94	72.39±4.27	68.42±4.83	0.002[a]	0.065[d] 0.060[e] 0.001[f]
40	71.31±3.19	71.43±3.55	69.39±2.73	0.023[a]	0.890[d] 0.065[e] 0.023[f]
50	71.19±4.82	72.37±4.57	70.33±5.03	0.258[c]	-
60	72.1±4.04	72.32±4.44	71.49±3.89	0.734[c]	-

[a]Significant, [b]Highly significant. [c]Not significant. [d]Group T vs. Group C. [e]Group T vs. Group D. [f]Group C vs. Group D.

The heart rate was decreased in the groups receiving dexmedetomidine and clonidine, but not much in the tramadol group. Tables 3 and 4 detail the changes in systolic and diastolic pressure following medication administration.

Table 3: Variations in systolic blood pressure after study drug administration

Time (min)	Group T (beat/min)	Group C (beat/min)	Group D (beat/min)	p-value	Intergroup comparison when p<0.05
0	108.32±9.56	107.54±8.72	108.47±9.52	0.916[c]	-
10	104.65±7.41	102.53±9.58	98.68±10.72	0.047[a]	0.3417[d] 0.0149[e] 0.1479[f]
20	106.53±8.63	98.8±7.91	94.88±8.48	<0.0001[b]	0.0006[d]

					0.0001[e] 0.0692[f]
30	104.59±8.29	103.5±9.48	99.39±9.48	0.069[c]	-
40	104.89±10.42	103.6±6.92	103.77±9.38	0.834[c]	-
50	102.66±6.83	104.7±8.99	102.79±10.29	0.582[c]	-
60	103.58±9.82	102.69±10.69	102.29±8.73	0.872[c]	-

[a]Significant, [b]Highly significant. [c]Not significant. [d]Group T vs. Group C. [e]Group T vs. Group D. [f]Group C vs. Group D.

Table 4: Variations in diastolic blood pressure after study drug administration

Time (min)	Group T (beat/min)	Group C (beat/min)	Group D (beat/min)	p-value	Intergroup comparison when p<0.05
0	75.63±4.82	74.75±5.86	76.33±4.47	0.486a	-
10	72.43±6.18	70.83±7.84	68.43±6.38	0.081a	-
20	71.88±3.91	68.6±5.28	66.18±6.35	0.0003b	0.0083[c] 0.0001[d] 0.1139[e]
30	70.96±5.37	69.27±6.39	67.88±4.72	0.103a	-
40	72.82±6.49	71.15±4.92	70.19±6.48	0.235a	-
50	74.7±3.73	73.47±6.20	72.55±5.62	0.292a	-
60	76.85±4.72	77.28±3.72	75.66±7.36	0.498a	-

[a]Significant, [b]Highly significant. [c]Not significant. [d]Group T vs. Group C. [e]Group T vs. Group D. [f]Group C vs. Group D.

More so than the clonidine and tramadol groups, the dexmedetomidine group experienced a decrease in systolic and diastolic blood pressure. In the dexmedetomidine group, the sedation score was much higher, with 70% of patients receiving a score of 2% and 23.3% receiving a score of 3. But no patient in any group of patients achieved a score of 4. For these patients receiving spinal anaesthetic, the sedation obtained during the treatment of shivering proved advantageous. The tramadol group had the highest recurrence rate (23.3%), while the dexmedetomidine group had a substantially lower rate (3.3%). The recurrence rate in the clonidine group was 10%. Two patients receiving clonidine and one receiving tramadol had shivering that could not be managed, thus rescue medication pethidine was given to them. Vomiting occurred more frequently in the tramadol group (13.3%) than in the clonidine (3.3%) or dexmedetomidine groups (0 patients). However, two individuals in the dexmedetomidine and clonidine groups experienced bradycardia each, which was successfully treated with atropine. In comparison to the clonidine (13.3%) and tramadol (6.6%) groups, the incidence of hypotension was substantially higher in the dexmedetomidine (20%) group.

Discussion

Shivering is a defence mechanism against hypothermia that is a result of a centrally regulated thermoregulatory response [11]. Shivering is a common side effect of regional anaesthetic that can be brought on by either a drop in core body temperature or inaccurate information from receptors [12]. Shivering while under anaesthesia not only

increases oxygen use but also results in tachycardia, hypertension, and disrupts the ECG, blood pressure, and pulse oximeter monitoring. Despite the fact that there are several medications available to treat shivering, no single medication has been found to reliably stop shivering without causing any negative side effects. The □2 agonists that are frequently used to treat shivering work by reducing the nervous system's ability to regulate body temperature [13]. They lessen the release of nor-adrenaline from the hypothalamic axonal terminals [14].

The hypothalamus contains a high density of □2 receptors, and activation of these receptors causes hypothermia by decreasing the production of heat via metabolic activity. Dexmedetomidine has the advantage of producing dose-dependent drowsiness and can be used as an adjuvant for anaesthesia [15-17]. Tramadol works by preventing serotonin and noradrenaline from entering neurons and increasing the release of hydroxytryptamine [18]. When compared to the tramadol group, the dexmedetomidine group was able to suppress the shivering more quickly. Dexmedetomidine and tramadol were compared in a research by Mittal *et al*. for post-spinal anaesthesia shivering. They came to the conclusion that dexmedetomidine had a quicker onset to reduce shivering in 2.52± 0.44 min at a dose of 0.5 mcg.kg [19]. Under spinal anaesthesia, Bansal conducted a comparison research on the shivering control effects of tramadol, butorphanol, and clonidine. They claimed that when it came to controlling shivering, tramadol outperformed clonidine [20].

Dexmedetomidine infusion was studied by Usta *et al*. to see if it could stop shivering during spinal anaesthesia. They discovered that a 0.4 mcg.kg. dexmedetomidine infusion worked well to stop shivering and provide sedation for simple surgical procedures [21]. The dexmedetomidine group attained a greater level of sedation than the clonidine and tramadol groups. The drowsiness that was produced was advantageous for these individuals because the surgery was performed under spinal anaesthesia. However, none of the patients in any of the three groups lost their ability to arouse. In a research on the impact of pre-emptive tramadol and dexmedetomidine on shivering during arthroscopy, Bozgeyik *et al*. They found that dexmedetomidine was superior in raising the level of sedation to prevent anxiety without having any negative side effects, in addition to its usefulness in preventing shivering [22]. Only one patient in the dexmedetomidine group experienced a recurrence of shivering, but pethidine was used to treat the recurrence in the tramadol group, seven patients, and three patients in the clonidine group.

The shivering recurrence was twice in the tramadol group compared to the dexmedetomidine group, according to Mittal *et al*.[19]. Recurrence rates of 26% with clonidine and 30% with tramadol were reported by Bansal *et al*. [20]. These investigations also support the finding that the dexmedetomidine group saw fewer recurrences of shivering than the tramadol and clonidine groups. Four patients in the tramadol group and one in the clonidine group experienced vomiting, with the tramadol group experiencing it more frequently. Each of the two patients receiving clonidine and dexmedetomidine had bradycardia. The dexmedetomidine group, however, had hypotension more frequently than the other groups. However, treatment for bradycardia and hypotension was effective. When given dexmedetomidine at a dose of 1 mcg/kg [22], Kim *et al*. found that 6.6% of patients had hypotension and 16.6% had bradycardia. Dexmedetomidine 0.5 mcg/kg did not cause hypotension in Mittal *et al*.,

although the tramadol group experienced 20% more vomiting [23].

The sample size of our study was rather limited, which is one of its weaknesses. Dexmedetomidine was successful in treating shivering, although it was also associated with manageable side effects. A larger investigation is required to identify the best medication for shivering. Second, we only recorded the axillary temperature for each patient rather than the core temperature. Thirdly, if we had employed external warming devices on all of our patients, the rate of shivering would have been lower.

Conclusion

For the treatment of shivering, dexmedetomidine is superior to tramadol and clonidine due to its quicker onset, lower recurrence rate, and improved sedation. The documented side effects of dexmedetomidine were manageable and did not significantly affect clinical outcomes. Although tramadol causes more painful vomiting, it is more effective than clonidine at treating shivering.

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