Original Article

Comparative study of dexmedetomidine and tramadol for control of post-spinal anesthesia shivering

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ABSTRACT

Background and Aim: Dexmedetomidine, a congener of clonidine is an α_2 adrenoceptor agonist, commonly used for sedation, also known to have antishivering potential. Its use as an agent to treat and control post-spinal anesthesia shivering has been inadequately studied. This study is thus aimed to evaluate the efficacy, hemodynamic changes and side effects of dexmedetomidine in comparison to tramadol when used to control post-spinal anesthesia shivering. **Materials and Methods:** A prospective randomized, and double-blind study was conducted in 60 ASA Grade I and II patients of either gender, aged between 18 and 60 years, undergoing various surgical procedure under spinal-anesthesia and developing shivering. The patients were randomized into two groups of n = 30 each to receive either dexmedetomidine - 0.5 µg/kg (Group D) or tramadol - 0.5 mg/kg (Group T) as an intravenous infusion on appearance of shivering. The time of onset, grade of shivering, time taken for cessation of shivering, response rate, and adverse effect were observed at scheduled intervals. SPSS-20 was used for statistical analysis, unpaired t-test for numerical data and chi-square test for categorical data. **Results:** Both the drugs effectively controlled shivering, taking almost the same time for its cessation. It was observed that patients in Group D were found to have a greater sedation score, whereas the side effects such as nausea and vomiting requiring treatment was more in Group T. The incidence of recurrence of shivering was higher in Group T. **Conclusions:** Dexmedetomidine effectively controls shivering taking almost the same time for cessation as that of tramadol. It provides an additional benefit of intraoperative sedation.

Key words: *Bupivacaine, Dexmedetomidine, Post-spinal anesthesia shivering, Tramadol*

Regional anesthesia is a popular and safe anesthetic technique for various surgeries when executed properly. It produces certain side effects such as hypotension, bradycardia, and shivering. Around 40-60% of patients under regional anesthesia develop shivering [1]. Shivering is defined as an involuntary, repetitive activity of skeletal muscles occurring as an attempt to generate heat in response to core hypothermia. Spinal anesthesia inhibits tonic vasoconstriction, causes a redistribution of core heat from trunk to the peripheral tissues. These factors predispose patients to hypothermia and shivering [2]. It increases the metabolic rate, oxygen consumption, and carbon dioxide production [3]. It may induce arterial hypoxemia and acidosis. Shivering leads to increases in intraocular and intracranial pressure, and may contribute to increased wound pain, stretch on suture lines, delayed wound healing and delay in discharge from post-anesthesia care unit [4,5]. It can be detrimental to patients with low cardiorespiratory reserve [6]. Shivering can be very unpleasant and stressful to the patients and it, therefore, deserves primary prevention and rapid control on occurrence.

There are various measures available to prevent and control shivering intraoperatively. The intervention can be pharmacological or nonpharmacological. The nonpharmacological management involves use of forced air warming, warming blankets, warm fluids, etc.

Pharmacological interventions include the use of drugs such as clonidine, pethidine, buprenorphine, ketanserine, tramadol, nefopam, doxapram, and ketamine. [7]. Methylphenidate was one of the first pharmacological agents found to be effective against post anesthesia shivering following halothane anesthesia [8]. However, no gold standard treatment has been established, as the administration of all the available drugs is associated with various adverse effects.

For the past few years tramadol has become a favored and commonly used drug for post-spinal anesthesia shivering. However, it is not free from adverse effects such as nausea, vomiting, and dizziness, which causes further discomfort to the patient [9,10].

Clonidine is another agent which has gained attention for its antishivering property. Various studies conducted to compare them, have concluded that clonidine has better efficacy and less adverse effects as compared to tramadol [9,10]. However, there is a high incidence of hypotension and bradycardia associated

with the use of clonidine [9]. 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 increase the shivering threshold [11]. Few studies which have explored its antishivering potential have inferred that dexmedetomidine is an effective drug without any major adverse effect and provides good hemodynamic stability [11-13]. Its use as an agent to treat and control post-spinal anesthesia shivering has been inadequately studied. Hence, we planned to do a comparative study to evaluate and compare the efficacy, hemodynamic and adverse effects of intravenous (IV) dexmedetomidine and tramadol when used to control post-spinal anesthesia shivering.

MATERIALS AND METHODS

After approval from Institutional Ethical Committee, a prospective randomized, and double-blind study was conducted in 60 ASA Grade I and II patients of either gender, aged between 18 and 60 years, undergoing various surgical procedure under spinal-anesthesia and developing shivering. The anticipated duration of surgery within 2 h was included. The patients were randomized into two groups of n=30 each using a computer generated sequence. Allocation concealment was done using sealed envelope technique. Depending on the group allocation either dexmedetomidine - 0.5 µg/kg (Group D) or tramadol - 0.5 mg/kg (Group T) was given on appearance of shivering. Drugs were diluted using normal saline to 10 ml and given IV slowly, over 10 min through an infusion pump, by another anesthesiologist. Patients with known hypersensitivity to dexmedetomidine or tramadol, cardiopulmonary, renal or hepatic disease, hyperthyroidism, psychiatric disorder, known history of substance or alcohol abuse, patients receiving any premedication were not included in the study. The time of onset, grade of shivering, time taken for cessation of shivering, response rate, adverse effect, and recurrence if any were noted at scheduled intervals.

Power based sample size calculation was done. Based on the previous study, the time taken for cessation of shivering [14] by the reference drug, tramadol, was found to be 5.92±0.81 min. Considering the difference of 10% to be significant and taking α=0.05 with power of 80% (two-tailed test), the sample size was calculated to be 29.2, therefore, 30 patients were taken in each group.

On entering the operating room, a brief preanesthetic evaluation was performed and on ensuring the fitness for surgery, the monitor was attached and the baseline reading of the pre-operative vitals such as heart rate (HR), noninvasive blood pressure (NIBP), respiratory rate (RR), electrocardiogram, oxygen saturation (SpO_2), and core body temperature (by nasal probe) were recorded. IV line was established using an 18 G IV cannula and preloading was done with ringer lactate at a dose of 10 ml/kg infused over a period of 15 min. Ambient temperature was maintained at 24-26°C. Drugs and fluids were administered at room temperature.

Spinal anesthesia (subarachnoid block) was administered in L3-L4 interspace by inserting a 25 G Quincke's needle through midline approach in lateral decubitus position. On ensuring the free flow of CSF, the drug, 15 mg of bupivacaine heavy (i.e., 3 ml) was administered at a rate of 0.2 ml/s. On completing the procedure, a dressing was applied at the injection site and the patient was turned to lie on back in supine position with a pillow under the head. After confirmation of the block, patients were covered with drapes. Supplemental oxygen was given at the rate of 4 L/min by face mask and the surgery was started. Continuous monitoring of the intraoperative vitals was done. Intraoperative fluid management was done according to the type of surgery and patient's body weight. Patients who developed shivering of grade ≥2 (Crossley and Mahajan scale: Grade 0 - no shivering, Grade 1 - piloerection, peripheral vasoconstriction, no visible muscle activity, Grade 2 - muscular activity in one muscle group, Grade 3 - muscular activity in more than one muscle group not involving the entire body, and Grade 4 - generalized muscle activity involving the entire body) were included in the study.

Time of onset of shivering was noted and recorded as 0 h. The grade of shivering along with vital parameters, i.e., HR, NIBP, RR, SpO_2, and core body temperature was also recorded. The specified drug as per the random allocation for this patient was prepared and given. Assessment and recording of the above said parameters was done at 2 min interval for 10 min, then at 10 min interval for 1 h, and at 90 min. Time taken for cessation of shivering was noted. The level of sedation was also assessed, graded, and recorded simultaneously. Grading was done using the Ramsay sedation scale (Ramsay sedation scale: Score 1 - anxious, agitated or restless; Score 2 - cooperative, oriented, and tranquil; Score 3 - responds to verbal command; Score 4 - asleep with brisk response; Score 5 - asleep with sluggish response; Score 6 - asleep with no response).

Hypotension among the patients was defined as a decrease in systolic blood pressure (SBP) <90 mm of Hg or a decrease of SBP by 30% or more from the baseline value. It was treated with injection mephentermine 5 mg IV stat. Bradycardia among patients was defined as a decrease in HR <50 beats/min and was treated with injection atropine 0.6 mg IV stat. Intraoperative nausea and vomiting if any was treated with injection ondansetron 4 mg IV stat. Recurrence of shivering was treated with tramadol at a dose of 0.5 mg/kg given slow IV. It was an intraoperative study so no patient was lost. Out of 193 consecutive patients, 60 met the inclusion criteria and were included in the study.

SPSS 20 was used for statistical analysis; Student's *t*-test for continuous variables and Chi-square test for categorical variables. The continuous data were reported as mean±standard deviation (SD) and the categorical data were reported as number (%). $p<0.05$ was considered significant. Microsoft word and Microsoft excel were used for text, graphs, and tables.

RESULTS

Various demographic parameters such as age, weight, height, sex, ASA grade, and duration of surgery were found to be comparable (Table 1).

Both the drugs effectively controlled shivering and the time taken for cessation of shivering was almost same (Table 2). The incidence of recurrence was higher in Group T which was 13% (4 patients) as compared to 3% (1 patient) in Group D (Table 2).

Hemodynamic parameters remained well within the normal range in both the study groups, except for the greater incidence of bradycardia and atropine requirement in Group D (3 patients) as compared to Group T (1 patient) (Table 3). There was no incidence of hypotension or respiratory depression. Shivering was preceded by a fall in core body temperature in both the groups by about 1°C (Fig. 1). The incidence of nausea and vomiting was observed only in Group T amounting to 7 patients. There was no incidence of nausea and vomiting in Group D (Table 3).

It was also observed that patients in Group D were found to have a greater sedation score during the surgery after the administration of drug (Table 4).

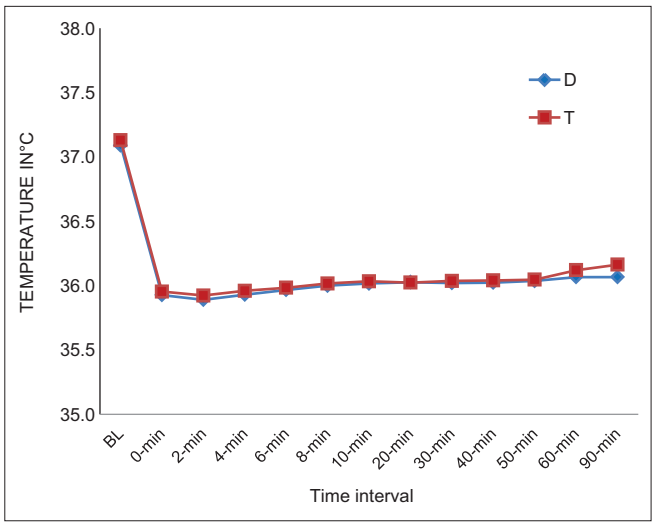

Figure 1: Temperature recordings of the two groups

Table 1: Demographic profile of the patients of both groups

Parameters	(n=30)		p value	Significance
	Group-D	Group-T		
Age (in years)	37.90±10.57	40.73±10.42	0.300[a]	NS
Sex (F:M)	13:17	15:15	0.605[b]	NS
Height (in cm)	155.13±6.73	155.73±7.79	0.751[a]	NS
Weight (in kg)	51.37±7.17	51.60±5.09	0.885[a]	NS
Duration of surgery (min)	65.10±14.43	61.53±18.40	0.407[a]	NS
ASA (Grade I/II)	22:8	24:6	0.542[b]	NS

[a]Student's t-test applied, [b]Chi-square test applied

Table 2: Cessation and recurrence of shivering

Parameters	Group D	Group T	p value
Average time taken for cessation of shivering (in minutes)	6.20±1.21	5.87±1.47	0.344
Incidence of recurrence of shivering (%)	1 (3)	4 (13)	0.161

DISCUSSION

Injection dexmedetomidine, a new drug in the armamentarium has the property of decreasing the central thermosensitivity by suppressing the neuronal conductance [15], thereby increasing the threshold of shivering [16]. Hence, we assessed and compared the efficacy, hemodynamic derangement and side effect profile of dexmedetomidine with tramadol, the drug being commonly used as treatment to control shivering following spinal anesthesia. It was found that both the drugs effectively controlled the shivering at their specified doses, dexmedetomidine at 0.5 mcg/kg and tramadol at 0.5 mg/kg being given as IV infusion. This result matches the findings of previous studies done by Mittal et al. [14], Elvan et al. [17], Usta et al. [12], and Talakoub and Meshkathi [18] showing that both the study drugs effectively controls shivering at the specified dose. The response rate in our study by 10 min was 100% which closely resembles the findings of Reddy and Chiruvella [10], which was 95.56% and Shukla et al. [9], which was 92.5%. The average time taken for cessation of shivering was also comparable, being expressed in minute as mean±SD. It was 6.20±1.21 min for dexmedetomidine and 5.87±1.47 min for tramadol. This result about dexmedetomidine closely corroborates with the study done by Blaine Easley et al. [19] in which there was complete cessation of shivering by 5 min, in children being treated with dexmedetomidine infusion at a dose of 0.5 mcg/kg given over a period of 3-5 min for post anesthesia shivering, whereas the finding on tramadol matches the finding of Mittal et al. [14] in which the mean time taken for cessation of shivering by tramadol was 5.9 min. The time taken for cessation of shivering by dexmedetomidine does vary from the study of

Table 3: Various side effects among two groups

Side effects	Group D	Group T	p value
Bradycardia	3	1	0.301
Hypotension	0	0	-
Respiratory depression	0	0	-
Nausea and vomiting	0	7	0.005*

*p<0.05, thus showing significance

Table 4: Mean sedation score at different time interval

Time	Group D	Group T	p value
0-min	2±0.0	2±0.0	-
2-min	2±0.0	2±0.0	-
4-min	2±0.0	2±0.0	-
6-min	2.03±0.183	2±0.0	0.321
8-min	2.17±0.379	2±0.0	0.019*
10-min	2.27±0.450	2±0.0	0.002*
20-min	2.27±0.450	2.07±0.254	0.038*
30-min	2.23±0.430	2.07±0.254	0.073
40-min	2.13±0.346	2.10±0.305	0.694
50-min	2.07±0.254	2.03±0.183	0.321
60-min	2±0.0	2±0.0	-
90-min	2±0.0	2±0.0	-

*p<0.05, thus showing significance

Mittal et al. [14] who reported it to be 2.52 min where as in our study we found it to be 6.2 min which can be easily correlated to the method and duration of drug administration. They gave the drug as slow IV bolus where as we gave it in IV infusion over 10 min.

The recurrence of shivering in our study was found to be 13% for tramadol and 3% for dexmedetomidine. Our finding regarding recurrence of shivering in tramadol group was slightly more compared to the findings of Maheshwari et al. [20] which was 8%, while for dexmedetomidine it was similar to the findings of Bajwa et al. [11] who reported a 5% recurrence of shivering in patients receiving dexmedetomidine at 1 mcg/kg intraoperatively. Intraoperative sedation is an added advantage, both for the patient as well as the surgeon. In our study, there was a difference in the level of sedation among the patients receiving dexmedetomidine. The assessment of sedation using Ramsay sedation score showed significant difference among the two groups at 8, 10, 20 and 30 min time since administration of drug. This finding corroborates with the findings of previous studies done by Bajwa et al. [11] and Mittal et al. [14] who reported significant sedation among the group receiving dexmedetomidine. There is one contradictory result reported by Karaman et al. [13] of negligible sedation with the use of dexmedetomidine. The group receiving tramadol did not show significant sedation which is similar to the results of the above said studies. Maintenance of hemodynamic parameters within the normal range perioperatively is the foremost aim of anesthesiologist and an important factor for the well-being of patients. In our study, we found that these parameters remained well within the specified range. The values of SBP, DBP, MAP, SpO_2, and RR remained within the 20% of the baseline value and were comparable among the two groups. These finding corroborates with the findings reported by Talakoub and Meshkathi [18] and Chan et al. [21] that there is no major changes in the above said parameters among the patients receiving either of the drug. The HR showed a little variation which can be easily inferred by the incidence of bradycardia and atropine requirement among the two groups. The incidence was 10% among group receiving dexmedetomidine and 3% in group receiving tramadol, therefore, 3 patients in group receiving dexmedetomidine and 1 patient in in group receiving tramadol needed atropine respectively. Other studies that reported higher incidence of bradycardia and atropine treatment among group receiving dexmedetomidine compared to placebo were Al-Mustafa et al. [22] and Whizar et al. [23], however, the incidence reported by them was higher, being 16% and 30%, respectively. This higher incidence can be easily attributed to known side effect at higher dose and continuous infusion of dexmedetomidine in their study. There was a fall in temperature by about 1°C from the baseline at the onset of shivering in both the groups. This result is similar to the findings of Harrison et al. [24] who reported a fall in core body temperature by 2.1°F and found a positive correlation with shivering. Drawkins [25] and Johnstone [26] also reported similar findings. This theory was further supported by Lyons et al. [27] who reported that heat loss and fall in core body temperature were the main cause of post anesthesia shivering. Contrary to this Tewari et al. [28] found no correlation between temperature fall and shivering.

Nausea and vomiting were the major adverse effects that occurred among the patients receiving tramadol. The occurrence of nausea and vomiting to a level where rescue antiemetic needed to be given was around 23% in group receiving tramadol compared to 0% in dexmedetomidine group. These findings corroborate with the study of Mittal et al. [14] where the incidence of vomiting among patients receiving tramadol was 20%. Talakoub and Meshkathi [18] reported the use of antiemetic among 30% of the patients receiving tramadol. Regarding dexmedetomidine Elvan et al. [17] found similar result that none of the patient complained of nausea and vomiting.

CONCLUSION

Dexmedetomidine effectively controls shivering and takes almost the same time for cessation of shivering as that of tramadol. It provides additional benefit of intraoperative sedation without any incidence of nausea and vomiting. The recurrence of shivering was more with tramadol.

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