ORIGINAL ARTICLE

Comparison of Tramadol and Dexmeditomidine for the Control of Intraoperative Shivering under Spinal Anaesthesia: A Prospective, Randomized Clinical Trial

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ABSTRACT

Objective: **To compare the efficacy of two drugs, dexmedetomidine (0.5 Â mcg/kg) and tramadol (0.5 Â mg/kg), with respect to time from drug administration to control shivering and adverse effects of each drug.**

Methods: **All patients in our study received spinal anesthesia in the left lateral position using a 25G Quincke needle via the midline approach in the L3-L4 intervertebral space under strict aseptic precautions and local anesthesia of the skin. Following free flow of CSF, 0.5% bupivacaine (hyperbaric) was injected depending on the requirement for surgery (3-4 ml). Patients who developed shivering after administering spinal anesthesia were included in the study. When patients developed shivering of above mentioned grades, they were randomly allotted to one of the two study groups (50 each), group D- Dexmedetomidine group receiving single intravenous bolus dose of 0.5mcg/kg over 5 min and group T –Tramadol group patients receiving 0.5 mg/kg IV over 5 min. The time from drug administration to the control of shivering was recorded in seconds. Patients were closely monitored for side effects.**

Results: **The incidence rate of shivering was 58 %. There was no statistically significant difference with respect to baseline heart rate (HR) or HR at the onset of shivering. However, the HR decreased significantly in Group D compared to that in Group T immediately after the cessation of shivering. The time to onset of shivering and severity of shivering were not statistically different between the two groups. The mean interval between the injection of the drugs (dexmedetomidine and tramadol) and complete cessation of shivering was significantly lower in the dexmedetomidine group. Mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) during shivering were statistically insignificant. The side effects of tramadol were more severe than those of dexmedetomidine.**

Conclusion: **The time taken for cessation of postspinal shivering was lower with dexmedetomidine than with tramadol. Dexmedetomidine has negligible adverse effects, whereas tramadol is associated with significant nausea and vomiting.**

KEY WORDS

aneathesia, shivering, tramadol, dexmedetomidine

INTRODUCTION

Spinal anesthesia is a safe method that is widely used in both elective and emergency surgeries. Shivering is a relatively common problem faced after central neuraxial (spinal and epidural) anaesthesia. Shivering following administration of spinal anesthesia is a common event, with reported incidences of up to 76%[1)]. Shivering may be defined as an involuntary, oscillatory muscular activity that augments metabolic heat production up to 600% above the basal metabolic level 2 and clinically is associated with clonic or tonic skeletal muscle hyperactivity at different frequencies[3)]. Shivering typically occurs as a thermoregulatory response to cold conditions. Post-spinal shivering is an unpleasant, thorough discomfort and frequent complication after surgery with many grades, that is, from a mild form of skin eruptions to a severe form with generalized continuous com skeletal muscle contractions with a prevalence of up to 50-80%[4)]. Shivering following neuraxial blockade may result from various mechanisms. However, perioperative heat loss, skin

Received on January 27, 2023 and accepted on February 12, 2023

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exposure in a cool operating theatre, surgical exposure leading to evaporation, provision of unwarmed intravenous fluids, systematic release of pyrogens, pain, and inhibition of the thermoregulation system by inhibiting tonic vasoconstriction are the main factors that predispose patients to shiver[5].

Shivering, in addition to being physiologically stressful to the patient, also causes discomfort to anesthesiologists and surgeons. Shivering may negate orthopedic procedures such as fractures and dislocations. Increase in minute ventilation, increase in oxygen consumption, and hypercarbia are several undesirable physiological consequences of shivering. It induces arterial hypoxemia, lactic acidosis, increased intraocular pressure and intracranial pressure, and interferes with patient monitoring[1].

Drugs, such as pethidine, morphine, tramadol, clonidine, ketamine, neostigmine, magnesium sulfate, have been used for post-spinal shivering. tramadol hydrochloride, an opioid receptor agonist, inhibits the reuptake of serotonin (5-hydroxytryptamine) and norepinephrine in the spinal cord. It facilitates serotonin release, which influences thermoregulatory control. Currently, it is widely used for the control of shivering[6]. dexmedetomidine, a centrally acting alpha 2-adrenergic agonist, has been used as a sedative agent and is known to reduce the shivering threshold[6]. In the quest for safer and more efficacious drugs, we compared two easily available and safe drugs, dexmedetomidine and tramadol, intravenously administered to treat shivering in patients who received spinal anesthesia for various surgical procedures.

AIMS AND OBJECTIVES

To compare the efficacy of two drugs 0.5mcg/kg of dexmedetomidine and 0.5mg/kg of tramadol with respect to

- Time from drug administration to shivering control
- Adverse effects of each drug.

METHODOLOGY

Source of Data (Sample)

This study was carried out in the Department of Anaesthesiology, Al Ameen medical college and research centre, Vijayapura, India, on those patients who developed intra-operative shivering following spinal anaesthesia for various surgical procedures were included in the study.

Design of the study and sample size

Prospective randomized clinical trial

The present study was a randomized controlled trial conducted on 100 American Society of Anesthesiologists (ASA) Grade I/II adult patients (> 18 years) with shivering during surgery under spinal anesthesia (SA), of which 50 received dexmedetomidine (Group D) and 50 received tramadol (Group T). The sample size was determined by keeping the value of alpha (α) = 0.05 and beta (β) = 0.2. We hypothesized that the test drug will be significantly better if it decreased the time taken to abolish shivering by 1 min as compared to control group drug (tramadol).[6] We took the maximum standard deviation (SD) which was 1.69 as per previous study[7].

Applying the formula for a two-sided study:

n (size per group) $=2c/\delta 2 + 1$

where, $\delta = (\mu 2 - \mu 1)/\Phi$ is the standardised effect size

μ 1 and μ 2 are the means of the two treatment groups

Φ is the common SD

c = 7.9 for 80% power

Hence, $n = 2 \times 7.9/(1/1.69)\ 2 + 1 = 46.1$

Rounding off, we took the sample size as 50 per group.

INCLUSION CRITERIA

- Patients of either gender aged between 20-60 years
- ASA grade of I -II
- Patients who develop shivering following spinal anaesthesia
- Shivering of grade 2-3 (Crossley and Mahajan scale)[8]

EXCLUSION CRITERIA

- Patients not belonging to the above-mentioned age, weight, or ASA grade.
- Patients with fever, drug allergy, thyroid disease, and neuromuscular diseases.
- Surgeries lasting more than 4hours.
- Patients who developed shivering even before administering spinal anesthesia.
- Patients requiring general anesthesia supplementation

All patients included in the study were pre-medicated with tablet diazepam 10 mg on the night before the surgery and tablet diazepam 5 mg on the morning of the surgery, administered orally with sips of water two hours prior to the planned surgery. They were preloaded with 500 ml of Ringer's lactate solution.

Patients were shifted to the operation theatre, and baseline parameters were recorded using monitors. The baseline temperature was recorded using a mercury thermometer in the axilla, which was placed in the vicinity of the axillary artery. The operating temperature was maintained at 22-25°C.

All patients in our study received spinal anesthesia in the left lateral position using a 25G Quincke needle via the midline approach in the L3-L4 intervertebral space under strict aseptic precautions and local anesthesia of the skin. Following free flow of CSF, 0.5% Bupivacaine (hyperbaric) was injected depending on the requirement of surgery (3-4 ml). Patients were administered 5 litres of oxygen using a Hudson transparent face mask and were adequately covered with surgical drapes. Patients who developed shivering after administering spinal anaesthesia were included in the study. Shivering of grades 2 and 3 as proposed by Crossley and Mahajan Scale[8] of Shivering was considered to require treatment.

Grade 0: No shivering

Garde 1: No visible muscle activity, but one or more piloerections, peripheral vasoconstriction, or peripheral cyanosis (other causes excluded).

Grade 2: Muscular activity in only one muscle group.

Grade 3: Moderate muscular activity in more than one muscle group, but not generalized shaking.

Grade 4: Violent muscular activity that involves the entire body.[8]

When patients developed shivering of above mentioned grades, they were randomly allotted to one of the two study groups (50 each)

1) Group D- Dexmedetomidine group receiving single intravenous bolus dose of 0.5mcg/kg over 5 min.

2) Group T –Tramadol group patients receiving 0.5 mg/kg IV over 5 min.

The study drug was then administered intravenously in the allotted group. The time from drug administration till the control of shivering was accurately noted in seconds. Patients were monitored at intervals of 1, 3, and 5 min, and thereafter 10, 20, and 30 min until the end of surgery. Patients were closely monitored for side effects such as nausea, vomiting, bradycardia (< 50/min), hypotension (> 20% of baseline), dizziness and sedation

Statistical Analysis

Data obtained were analyzed using IBM SPSS version 22. Chi-square test, T test, and ANOVA tests were applied. Statistical P value at $P < 0.05$.

RESULTS

In the present study, the incidence of shivering was 58%. A total of 170 patients undergoing various surgeries under SA were enrolled, and written informed consent was obtained from all participants until time100 patients developed shivering and were enrolled in the study.

Both the groups were comparable with respect to sex (Figure 1), age, weight, (Figure 2) ASA grade, grades of shivering (Figure 3) temperature prior to spinal anaesthesia (Table 1).

There was no statistically significant difference with respect to baseline HR and HR at the onset of shivering. However, the HR decreased significantly in Group D as compared to Group T immediately after cessation of shivering. (Table 3).

Time for onset of shivering and severity of shivering were not statistically between the two groups. The mean interval between the injec-

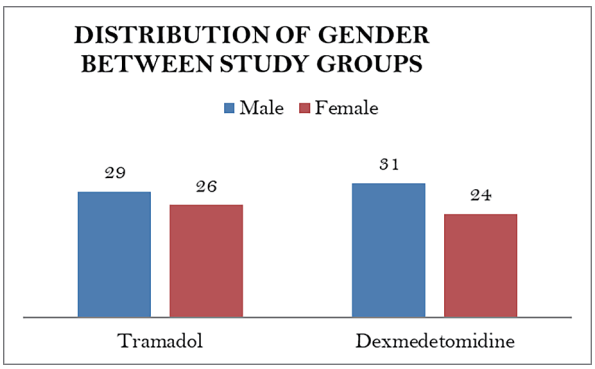

Figure 1: The gender distribution was comparable with no statistical difference between two groups.

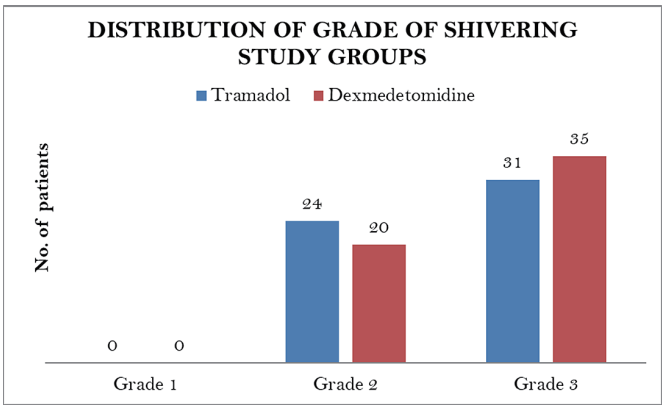

Figure 3: The grades of shivering was comparable with no statistical difference between two groups.

Table 1: The temperature prior to spinal anaesthesia, temperature during shivering was comparable with no statistical difference between two groups.

TEMPERATURE	Tramadol	Dexmedetomidine	p value
	Mean ± SD	Mean ± SD	
PRE-OPERATIVELY	37.1 ± 0.23	36.9 ± 0.62	0.844
DURING SHIVERING	37.3 ± 0.15	37.4 ± 0.33	0.712

Table 3: The mean heart rate after the control of shivering was statistically significant between the two groups
MEAN HEART RATE BETWEEN STUDY GROUPS

Heart rate	Tramadol	Dexmedetomidine	p value
	Mean ± SD	Mean ± SD	
DURING SHIVERING	86.4 ± 8.1	80.3 ± 6.4	p = 0.1
AFTER CONTROL OF SHIVERING	84.2 ± 5.7	73.2 ± 2.6	p = 0.021 (Sig)

Table 5: Comparison of Mean SBP during shivering and after control of shivering
MEAN DBP BETWEEN STUDY GROUPS

TABLE	Tramadol	Dexmedetomidine	p value
DBP	Mean ± SD	Mean ± SD	
DURING SHIVERING	71.8 ± 2.6	65.1 ± 6.6	p = 0.32 (Sig)
AFTER CONTROL OF SHIVERING	66.9 ± 1.5	63.3 ± 4.8	p = 0.008 (Sig)

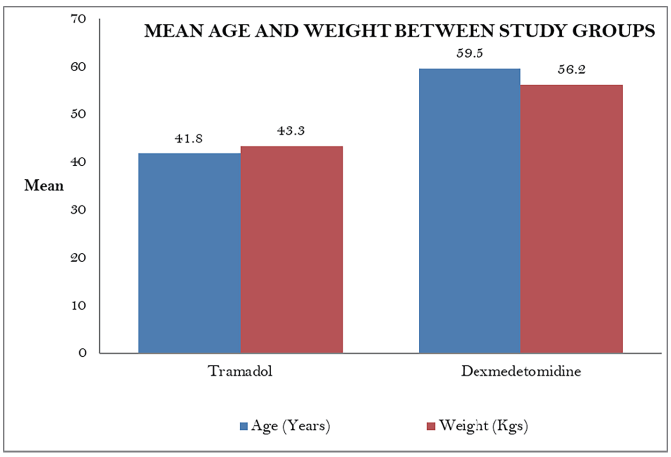

Figure 2: The age and weight distribution was comparable with no statistical difference between two groups.

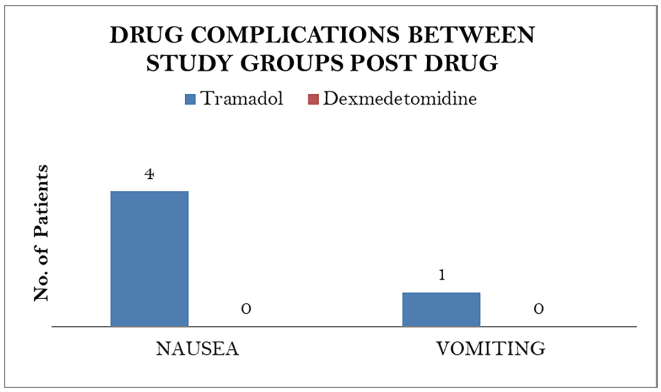

Figure 4: Comparing complications between study groups post drug.

Table 2: The time for control of shivering was comparable with (p value of 0.0006) which was statistically significant
MEAN DURATION BETWEEN STUDY GROUPS

DURATION	Tramadol	Dexmedetomidine	p value
	Mean ± SD	Mean ± SD	
TIME REQUIRED TO CONTROL SHIVERING AFTER DRUG (sec)	281.06 ± 12.42	206.1 ± 15.2	p = 0.0006 (Sig)

Table 4: Comparison of Mean SBP during shivering and after control of shivering
MEAN SBP BETWEEN STUDY GROUPS

SBP	Tramadol	Dexmedetomidine	p value
	Mean ± SD	Mean ± SD	
DURING SHIVERING	112.2 ± 1.8	105.6 ± 1.8	p= 0.44
AFTER CONTROL OF SHIVERING (Sig)	112.6 ± 3.6	105.3 ± 2.9	P = 0.023

tion of the drugs (dexmedetomidine and tramadol) and complete cessation of shivering was significantly lower in the dexmedetomidine group (Table 2).

Mean SBP and DBP during shivering were statistically insignificant but after control of shivering Mean SBP and DBP were found to have statistically significant difference between both the groups (Table 4 and 5).

The side effects were found to be higher in the case of tramadol as compared to dexmedetomidine. In this study,

The incidence of nausea was significantly higher in the tramadol group than that in the dexmedetomidine group. Similarly, the incidence of vomiting was significantly higher in the tramadol group compared to dexmedetomidine group.

DISCUSSION

Shivering is a complication frequently found in patients undergoing surgery under neuraxial anesthesia. Shukla *et al*.[9] have reported the incidence of shivering in patients undergoing surgery under regional anesthesia at 40-70% based on previous studies. The physiologic role of shivering is to provide heat. The probable mechanism under regional anaesthesia could either be a abnormal heat loss brought on by vasodilatation, impaired shivering in the area of the block, and rapid intravenous infusion of cold fluids.

In the above study, we studied the efficacy of dexmedetomidine in the treatment of post-spinal anaesthesia shivering in adults and compared its efficacy with tramadol for the treatment of shivering after Spinal anaesthesia in patients undergoing various elective surgeries. Even though tramadol is a well proved drug in the treatment of shivering, in this study, we found that dexmedetomidine is equally effective as tramadol in treatment of post-spinal anaesthesia shivering. It reduces the vasoconstriction threshold and the shivering threshold and is associated with a lower incidence of shivering[10]. dexmedetomidine is an α2 adrenoceptor agonist, with analgesic, antihypertensive, sedative, and antishivering properties. It reduces the vasoconstriction and shivering thresholds, thus suggesting that it acts on the central thermoregulatory system rather than preventing shivering peripherally[10,11]. The role of dexmedetomidine in the treatment of shivering has been evaluated in a few studies. It can be a good choice due to its dual effects related to antishivering and sedation[12].

The demographic parameters between the two groups were comparable, with respect to age, sex height and weight. In our study shivering was controlled in 281.06 ± 12.42 seconds after drug administration in patients in the tramadol group while it was 206.1 ± 15.2 seconds with patients in dexmedetomidine group. The results between the two groups were statistically significant with P value (0.0006).

In a study by Blaine Easley R *et al*, all children had a cessation of shivering behaviour within 5 min following the completion of dexmedetomidine administration. The onset of effect was 3.5 +/- 0.9 min, which was comparable with our study.[13] In a study by Mittal *et al*, control of shivering took 2.52 ± 0.44 minutes in dexmedetomidine group and 5.92 ± 0.81 minutes in tramadol group which was comparable with our group. The side effects were found to be higher in the case of tramadol as compared to dexmedetomidine. the incidence of nausea and vomiting with dexmedetomidine in our study was 0%, and was highly significant in tramadol group compared to the dexmedetomidine group ($p < 0.001$)[14].

CONCLUSION

We conclude that although both drugs are effective, the time taken for cessation of post-spinal shivering is less with dexmedetomidine when compared to tramadol. Moreover, dexmedetomidine has negligible adverse effects, whereas tramadol is associated with significant nausea and vomiting.

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