



## Dexmedetomidine for post – spinal anaesthesiashivering : (comparison with Tramadol).

### KEYWORDS

Dexmedetomidine, post-spinal anaesthesia shivering, tramadol

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**ABSTRACT** *Aims: The aim of this study was to evaluate and compare the efficacy, haemodynamic and adverse effects of dexmedetomidine with those of tramadol, when used for control of post-spinal anaesthesia shivering.*

*Methods: A prospective, randomized and double blind study was conducted in 50 American Society of Anaesthesiologists Grade I and II patients of either gender, aged between 20 and 50 years, scheduled for various surgical procedures under spinal anaesthesia. The patients were randomised in two groups of 25 patients each to receive either dexmedetomidine 0.5 µg/kg or tramadol 0.5 mg/kg as a slow intravenous bolus. Grade of shivering, onset of shivering, time for cessation of shivering, recurrence, response rate, and adverse effects were observed at scheduled intervals. Unpaired t-test was used for analysing the data. Results: Time taken for cessation of shivering was significantly less with dexmedetomidine when compared to tramadol. Nausea and vomiting was observed only in tramadol group (30% and; 25% respectively). There was not much difference in the sedation profile of both the drugs. Conclusion: We conclude that although both drugs are effective, the time taken for cessation of shivering is less with dexmedetomidine when compared to tramadol. Moreover, dexmedetomidine has negligible adverse effects, whereas tramadol is associated with significant nausea and vomiting.*

### INTRODUCTION

Shivering, is defined as an involuntary, repetitive activity of skeletal muscles. It can double or even treble oxygen consumption and carbon dioxide production. Shivering also increases intraocular and intracranial pressure, and may contribute to increased wound pain, delayed wound healing, and delayed discharge from post-anaesthetic care. 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. These factors predispose patients to hypothermia and shivering.

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, blankets, warmed fluids. Pharmacological interventions include clonidine, pethidine, tramadol, nefopam and ketamine. There is no gold standard treatment as the administration of all the available drugs is associated with various adverse effects.

Since last ten years, Tramadol has been commonly used drug for post-spinal anaesthesia shivering. But it has many adverse effects like nausea, vomiting, dizziness etc., which is uncomfortable to the patient. Clonidine has been used during last few years as it has better efficacy and less adverse effects compared to tramadol. But there is 5-10% incidence of hypotension and bradycardia with clonidine.

Dexmedetomidine, is an  $\alpha_2$ -adrenoceptor agonist that decreases vasoconstrictor and shivering threshold and when administered with Meperidine additively reduces the shivering threshold in healthy volunteers. Few studies which showed its anti-shivering potential have inferred that dexmedetomidine is an effective drug without any major adverse effect and provides good haemodynamic stability. Hence, we planned to do a comparative study of the ef-

ficacy, haemodynamic, and adverse effects of tramadol and dexmedetomidine when used for the control of post-spinal anaesthesia shivering.

### METHODS

A prospective double blind randomized study was conducted at Kurnool medical college & Government general hospital Kurnool after taking approval from Institutional Ethics Committee. All subjects gave written informed consent to participate in the study. 50 American Society of Anaesthesiologists (ASA) Grade I and II consenting patients of either gender aged 20-50 years scheduled for elective lower abdominal, lower limb and urological surgeries under spinal anaesthesia were included in the study. Patients with known hypersensitivity to dexmedetomidine or tramadol, cardio-pulmonary, renal or hepatic disease, hyperthyroidism, psychiatric disorder, urinary tract infection, severe diabetes or autonomic neuropathies, known history of substance or alcohol abuse, patients receiving any pre-medication were not included in the study.

All patients who fulfilled the inclusion criteria and developed post-spinal anaesthesia shivering were enrolled into either of the two groups. Group Dm (n = 25) were administered dexmedetomidine 0.5 µg/kg intravenous (IV) and Group Tm (n = 25) received tramadol 0.5 mg/kg IV.

In the operation theatre, an 18G 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 (SPO<sub>2</sub>), electrocardiography (ECG), and body temperature (axillary) were recorded. Spinal anaesthesia was administered with 0.5% heavy bupivacaine (15 mg) at L3-4 or L4-5 interspace using 26G 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. 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 and 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 drugs were diluted to a volume of 5 ml in a 5 ml syringe. 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. Adverse effects such as nausea, vomiting, bradycardia (<50/min), hypotension (>20% of baseline), dizziness; and sedation score were noted. 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.

Nausea and vomiting were treated with injection metoclopramide 10 mg IV as and when required.

## RESULTS

A total of 50 patients consented for study. These 50 patients were randomized into two groups of 25 each. Out of the total patients, 25 were male, and 25 were female. Both groups were comparable with respect to age, gender, ASA grade, duration of surgery and the duration of spinal anaesthesia. Duration of spinal anaesthesia ranged from 90 min to 150 min (Table 1).

All the patients had Grade 3 shivering. There was no statistically significant difference in time for the onset of shivering between the two groups. However, the difference in the time interval between administration of drug after the onset of shivering and cessation of shivering was significantly shorter in the dexmedetomidine group when compared to tramadol group. There was recurrence of shivering in 2 patient in dexmedetomidine group and 4 patients in tramadol group. The patients were given rescue doses of dexmedetomidine or tramadol, respectively (Table 2).

Nausea and vomiting was observed only in tramadol group. Almost similar number of patients were sedated in both groups and the sedation score in all the patients was 2. There was no evidence of respiratory depression, hypotension or bradycardia in any of the patients. HR, mean blood pressure, body temperature, and SPO2 remained within normal limits throughout the procedure in both

groups [Table 3].

**Table 1: Demographic profile of patients of both groups**

Parameter	(n=25)		P value
	Dexmedetomidine	Tramadol	
Age (years)	39.04±12.02	36.16±9.69	0.78
Gender (male/female)	15/10	12/13	0.23
Duration of surgery (min)	60.00±12.58	64.40±15.02	0.27
Duration of spinal anaesthesia (min)	143.60±16.30	117.60±20.26	0.25

Age, duration of surgery, duration of anaesthesia are presented as mean±SD.

Test done was unpaired t-test. n – Number of patients SD – Standard deviation

**Table 2: Parameters for post-spinal anaesthesia shivering**

Parameter	Dexmedetomidine group (%)	Tramadol group (%)	P value
Onset of shivering (min)	21.40±12.95	20.00±13.23	0.71
Time for cessation of shivering after medication (min)	2.32±0.44	6.52±0.81	0.0024
Response rate (%)	100	100	
Recurrence	2/25 (8)	4/25 (16)	

Data was analysed using unpaired t-test. Statistically significant at P<0.05

## DISCUSSION

The possible mechanisms of post operative shivering include impairment of central thermoregulation, internal redistribution of body heat, and heat loss to the environment. Potential risk factors for hypothermia in spinal anaesthesia include ageing, level of sensory block, temperature of the operation theatre and IV solutions. In this study, all operation theatres (OTs) maintained an ambient temperature of 23-25°C, and all fluids and drugs were at room temperature during the surgery. Demographic factors such as age, gender, duration of anaesthesia and surgery have also been matched to reduce any confounding bias.

The neurotransmitter pathways involved in shivering are multiple and involve opioids, α2 adrenergic, serotonergic, and anticholinergic receptors. Hence, drugs acting on these systems which include opioids (pethidine, nalbuphine, or tramadol), ketanserin, propofol, doxapram, clonidine, ketamine and nefopam are utilized in the treatment of shivering. However, adverse effects such as hypotension, hypertension, sedation, respiratory depression, nausea and vomiting limit their use.

Tramadol is an opioid analgesic with opioid effect mainly mediated via mu receptor with minimal effect on kappa and delta receptors. It also activates the monoaminergic

receptors of the descending spinal inhibitory pain pathway. The anti-shivering action of tramadol is probably mediated via its opioid or serotonergic and noradrenergic activity or both. It is a well-established agent in the treatment of post-anaesthetic shivering.

Alpha-2 adrenergic agonists are widely used nowadays in anaesthesia and intensive care settings. Dexmedetomidine is an  $\alpha_2$  adrenoceptor agonist with antihypertensive, sedative, analgesic, and anti-shivering properties. The anti-shivering effects of alpha adrenoceptor agonists are mediated by binding to  $\alpha_2$  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. 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.

With same dose, that is, 0.5 mg/kg of tramadol, the response rate reported by Shukla et al. was 92.5%, by Reddy and Chiruvella as 95.56% and by Tsai and Chu, 87%. We found 100% response rate in our study. Maheshwari et al. reported similar recurrence rate with tramadol. The recurrence rate in the study by Shukla et al. was 5%. The incidence of nausea and vomiting with tramadol in our study was 28% and 20%, respectively. The results correspond with that of other studies by Reddy and Chiruvella, Tsai and Chu; Bansal and Jain. However, in the study by Shukla et al., the incidence of nausea was quite high (77.5%), whereas Wason et al. have reported the incidence of nausea as only 4%. These variations could be explained by the peculiar patient characteristics in different studies. Maheshwari et al. have reported a very high incidence of sedation to the extent of 84%, which as mentioned earlier could be due to the higher dose as opposed to 28% sedation in our study.

In a study by Easley, all children who had post-anaesthesia shivering were treated with a single IV bolus dose of dexmedetomidine 0.5  $\mu$ g/kg over 3-5 min. All children had cessation of shivering behaviour within 5 min following the completion of dexmedetomidine administration. There was no recurrence of shivering and no adverse effects occurred. We found a response rate of 100% and apart from sedation, there was no other adverse effect observed. But there was recurrence in 2 patient who had to be given a rescue dose. All other studies have used higher dose of dexmedetomidine (1  $\mu$ g/kg), so comparison of results would not be appropriate.

The other  $\alpha$  agonist clonidine is associated with a high incidence of hypotension and bradycardia. In this respect, dexmedetomidine has an edge as it causes less variations in haemodynamics.

**Table 3 : Pattern of adverse reactions in both groups**

Adverse effects	n = 25(%)	
	Dexmedetomidine	Tramadol
Nausea	0	7(28)
Vomiting	0	5(20)
Sedation	6(21.4)	7(28)
Hypotension	0	0
Bradycardia	0	0
Respiratory depression	0	0

Data expressed as percentage.n – Number of patients

The results of this study indicate that dexmedetomidine takes lesser time to control shivering. The incidence of adverse effects like nausea and vomiting was found to be higher in case of tramadol compared to dexmedetomidine

There was not much difference in the number of patients who were sedated in either group. The sedation seen with dexmedetomidine, in the absence of nausea and vomiting, is beneficial for the surgeon, anaesthetist as well as the patient. It provided more comfort to the patient, maintained more cardio-respiratory stability, improved surgical conditions and also provided amnesia during surgery.

The anti-shivering effect of dexmedetomidine needs to be seen in surgeries of longer duration where chances of developing hypothermia are more. Also, we did not assess different doses of dexmedetomidine; further studies are needed to evaluate the anti-shivering and haemodynamic effects of dexmedetomidine with various doses.

The search continues for drugs that sufficiently improve the tolerance of thermoregulation without simultaneously producing respiratory depression, or haemodynamic instability.

## CONCLUSION

Both dexmedetomidine (0.5  $\mu$ g/kg) and tramadol (0.5 mg/kg) are effective in treating patients with post-spinal anaesthesia shivering, but time taken for complete cessation of shivering was shorter with dexmedetomidine as compared to tramadol, the difference being statistically significant. Furthermore, dexmedetomidine causes fewer adverse effects like nausea and vomiting. Sedation caused by dexmedetomidine provides additional comfort to the patient.

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