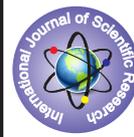


## Comparison of Tramadol and Dexmedetomidine for the control of intraoperative shivering under spinal anesthesia, a double blind randomized control study.



## Anesthesiology

**KEYWORDS:** Dexmedetomidine, Tramadol, Shivering.

**Dr. Kapurkar Vilas S**

MD (MD Anaesthesiology), Associate Professor Department of Anaesthesiology  
Krishna Institute of Medical Sciences, Karad, Maharashtra, India

### ABSTRACT

**Aims and Objectives:** To compare the efficacy of 2 drugs 1mcg/Kg Dexmedetomidine and 50 mg Tramadol with respect to

- Time from drug administration to control of shivering.
- Recurrence of shivering after administration of drug.
- Adverse effects.
- Hemodynamic changes.

**Materials and Methods:** A prospective randomized, double blind study involving 20 patients in each group was conducted. One group (Group D) received Dexmedetomidine 1mcg/Kg over 5 min and the other received 50mg Tramadol IV over 5 min. The efficacy of the drug in terms of disappearance of shivering, time of disappearance was noted and also side effects. The grading of shivering was assessed by using Crossley and Mahajan Scale.

**Results:** The Results were analyzed statistically

- Dexmedetomidine and Tramadol are effective in treating patients with post spinal shivering but the time taken for control of shivering was shorter with Dexmedetomidine as compared to the Tramadol.
- Dexmedetomidine causes fewer side effects as compared to Tramadol.
- Arousable sedation caused by Dexmedetomidine provides additional comfort to the patient.

**Conclusion:** Dexmedetomidine controls the post spinal shivering faster than Tramadol and it has fewer side effects as compared to Tramadol.

### Introduction:

The Spinal cord is the lower part of the central nervous system responsible for establishing contact between the brain in the cranial cavity and the peripheral end organs. It occupies the upper two thirds of the spinal canal which is composed of the vertebral bones and fibro-cartilaginous intervertebral discs. The spinal column usually forms a double C, being convex anteriorly in the cervical and lumbar regions. The spinal canal contains the spinal cord with its coverings the meninges, fatty tissue and a venous plexus. Spinal cord is bathed in the cerebrospinal fluid (CSF), the volume of which is about 150ml, and correlates well with the changes in body habitus and weight of the patient.<sup>2</sup>

The principal site of action of spinal anesthesia is the nerve root. Local anesthetic solution injected into the subarachnoid space blocks conduction of impulses along the all nerves with which it comes in contact, although some nerves are more easily blocked than the others. Blockade of the neural transmission in the posterior nerve root fibers interrupts somatic and visceral sensation, while blockade of anterior nerve root fibers prevents efferent motor and automatic out flow. Generally, autonomic and pain fibers are blocked first and motor fibers the last, although the dorsal roots are generally larger than the anterior roots. It is estimated that CSF volume accounts for 80% variability in peak block height and regression of the sensory and motor block.<sup>2</sup>

The processing of thermoregulatory response has 3 components: afferent thermal sensing, central regulation and efferent responses. Together they work to maintain core body temperature.<sup>3,4,5</sup>

Shivering is an involuntary, oscillatory muscular activity that augments metabolic heat production. Vigorous shivering increases metabolic heat production upto 600% above basal level. Shivering is elicited when preoptic region of the hypothalamus is cooled. Efferent signals mediating shivering descend in the medial fore brain bundle. Thermally induced changes in neuronal activity in mesencephalic reticular formation and dorsolateral pontine and medullary reticular formation exert descending influences on the spinal cord that increase muscle tone. Spinal motor neurons and their axons is the final common path for both co-ordinated movement and shivering.

Epidural and spinal anesthesia decrease the vasoconstriction and shivering thresholds to a comparable degree (by 0.6°C), but to a lesser amount than when measured at the level above the upper level of the block.<sup>5</sup> The gain of shivering response is reduced by 63% and maximum intensity by 33% in regional anesthesia. This occurs because shivering above the block compensates for the inability of muscles below the block to engage in shivering. Shivering during regional anesthesia is like that after general anesthesia is preceded by core hypothermia and vasoconstriction above the level of block. With reduced gain and maximum intensity, the shivering which is induced by core hypothermia after regional anesthesia is usually ineffective in preventing core hypothermia.<sup>5</sup> The main effect of post-anesthetic shivering is the increase in oxygen consumption (VO<sub>2</sub>). By affecting several muscular groups for periods of 45 minutes or more, postanesthetic shivering triggers an increase in metabolic demand, which generally translates into higher VO<sub>2</sub> combined with increased minute ventilation. Sometimes metabolic demand can exceed the capacity to deliver oxygen peripherally and result in anaerobic Metabolism.<sup>5,6,7</sup>

### Measures to combat shivering:

- **Passive insulators-:** Cotton blankets, cloth or paper surgical drapes, disposable plastic drapes, plastic bags. Passive insulators reduce heat loss to environment.
- **Active warming:** Convection warming systems where warmed air is forced through the quilt like porous blanket, which passes over the skin warming it directly and also replaces the normal body air envelope with warm air envelope.
- **Pharmacotherapy:** Potent antishivering properties have been attributed to numerous drugs belonging to several classes.

### • Tramadol

It is a synthetic, centrally acting analgesic agent that is structurally related to codeine and morphine. Tramadol acts as opioid agonist with selectivity to mu-opioid receptors and also binds weakly to kappa and delta receptors.<sup>8</sup> It also inhibits the neuronal reuptake of Norepinephrine and serotonin. Opioid and non opioid actions of Tramadol are thought to act synergistically on descending inhibitory pathways in the central nervous system, resulting in modulation of second order neurons in the spinal cord.

Opioid analgesics are generally associated with respiratory

depression. This is mediated through a decrease in the sensitivity of the respiratory centre to CO<sub>2</sub> which results in decrease in respiratory rate and tidal volume.<sup>8</sup> Some of the other side effects noted are nausea, vomiting and alteration in appetite. Tramadol also produces some CNS effects like dizziness, sedation, and headache.

Advantage of Tramadol is low gastrointestinal inhibition.<sup>9</sup> It is therefore expected to improve gastrointestinal recovery from abdominal surgery and reduce the risk of postoperative paralysis and ileus compared with other opioids. Antishivering effect of Tramadol is mediated via serotonergic or noradrenergic activity.<sup>9</sup>

**• Dexmedetomidine**

Dexmedetomidine is a new alpha2-agonist used as sedative analgesic. Dexmedetomidine is suitable for sedation and analgesia during the whole perioperative period. The mechanism of action of Dexmedetomidine is unique. Activation of alpha2-adrenergic receptors in the CNS results in augmentation of cardiac-vagal activity. Combined these effects can produce analgesia, sedation and anxiolysis. The spinal action is the principal mechanism for the analgesic action of Dexmedetomidine even though there is a clear evidence for both a supraspinal and peripheral sites of action.<sup>10</sup> Dexmedetomidine induced sedation quality resembles normal sleep. Alpha2-adrenoreceptors do not have an active role in the respiratory center; therefore Dexmedetomidine has minimal effects on the respiratory system. Co administration of Dexmedetomidine with other sedatives or opioids is likely to cause additive effects.<sup>11</sup> Dexmedetomidine causes a dose dependent increase in coronary vascular resistance and oxygen extraction, but the supply /demand ratio is unaltered.<sup>12</sup> Hypotension and bradycardia induced by Dexmedetomidine are reversed by ephedrine and atropine respectively, but large doses are required.<sup>12</sup>

Dexmedetomidine possesses anxiolytic, sedative, analgesic, antisialogogue and sympatholytic properties which render it suitable as a premedication agent. Dexmedetomidine potentiates the anesthetic effects of all intraoperative anesthetics.<sup>14,15,16</sup> The use of intraoperative Dexmedetomidine may increase hemodynamic stability because of attenuation of the stress induced sympathoadrenal response to intubation, during surgery and during emergence from anesthesia.

**Materials and Methods:**

The study was conducted at Krishna Hospital, Karad and those patients who developed intraoperative shivering following spinal anesthesia for various surgical procedures were included in the study.

**Inclusion Criteria:**

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

**Exclusion Criteria:**

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

A prospective randomized comparative study was conducted after a written informed consent from the patients. 20 patients were selected in each group. All patients included in the study were pre-medicated with Tablet Diazepam 10 mg on the night before the surgery. Patient who developed shivering after administering spinal anesthesia were included in the study. Shivering of grades 2 and 3 as proposed by Crossley and Mahajan Scale of Shivering was considered to require treatment. When patients developed shivering they were

randomly allotted to one of the 2 study groups.

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

Group T- Tramadol group patients receiving 50mg Tramadol IV over 5 min.

The study drug was then administered i.v as per the allotted group. The time from drug administration till disappearance of shivering was accurately noted in seconds. Patient were monitored at intervals of 1 minute, 3 min, 5 min and thereafter 10,20 and 30 minutes till end of surgery.

Sedation score was assessed with a four point scale as per Filos.

1. Awake and alert
2. Drowsy response to verbal stimuli
3. Drowsy Arousable to physical stimuli
4. Unarousable.

**Parameters studied**

- Time for onset of shivering (min).
- Grade of shivering: Crossley and Mahajan Scale
- Grade 0- No shivering
- Grade 1- Piloerection, peripheral vasoconstriction, peripheral cyanosis without other cause but without visible muscular activity.
- Grade 2- Visible muscular activity confined to one muscle group.
- Grade 3- Visible muscular activity more than one muscle group.
- Grade 4- Gross muscular activity involving the entire body.
- Temperature at the onset of shivering.
- Time from drug administration to control of shivering
- Time from drug administration to disappearance of shivering
- Recurrence of shivering after drug administration
- Hemodynamic changes
- Adverse effects of drugs.

Data analysed using independent 't' test for parametric data, Chi-square test and Fischer's test for non parametric data.

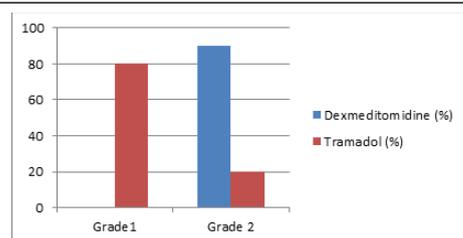
**Observations and Results:**

Grades of shivering

The grades of shivering was comparable with no statistical difference between the 2 groups

**Table No-1 Grades of shivering**

	Group D	Group T
Grade 2	7	11
Grade 3	13	9
P value- 0.34		



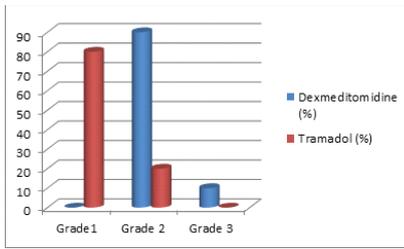
**Graph No-1 Grades of shivering**

Temperature monitoring and time of onset of shivering

The temperature prior to spinal anesthesia, temperature during shivering and time of onset of shivering was comparable with no statistical difference between the 2 groups with p value of 1, 0.1 and 0.6 respectively.

**Table No- 2 Temperature monitoring and time of onset of shivering**

	Group D	Group T	P value
Temperature prior to spinal anesthesia	37.7+ <sub>-</sub> 0.34	37.7+ <sub>-</sub> 0.34	1
Temperature during shivering (°C)	36.17+ <sub>-</sub> 0.32	36.35+ <sub>-</sub> 0.37	0.102
Time of onset of shivering (Min)	39.95+ <sub>-</sub> 9.60	41.05+ <sub>-</sub> 7.02	0.68



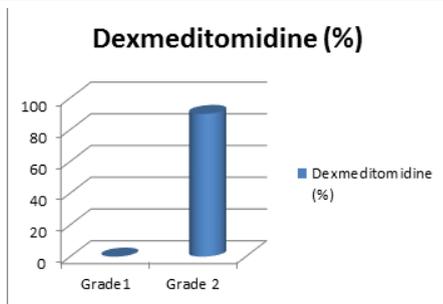
**Graph No-2 Temperature monitoring and time of onset of shivering**

Time for control and disappearance of shivering

The time for control of shivering and disappearance of shivering was statistically significant between the 2 groups with P value of 0.00 and 0.00 respectively.

**Table NO-3 Time for control and disappearance of shivering**

	Group D	Group T	P Value
Control (Sec)	205+ <sub>-</sub> 18.3 (3.4+ <sub>-</sub> 0.3min)	413+ <sub>-</sub> 16.9 (6.9+ <sub>-</sub> 0.28 min)	0.00
Disappearance (Sec)	295+ <sub>-</sub> 8.7 (4.9+ <sub>-</sub> 0.1 min)	514+ <sub>-</sub> 9.5 (8.5+ <sub>-</sub> 0.1 min)	0.00
95% C.I= 3.31 to 3.69			



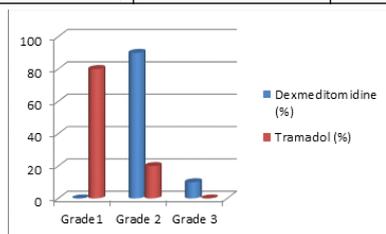
**Graph NO-3 Time for control and disappearance of shivering**

**Adverse effects:**

The incidence of nausea and vomiting with Tramadol in our study was 20% and 25% respectively and was seen only in Tramadol group.

**Table NO-4 Adverse effects**

Adverse effects	Dexmedetomidine (%)	Tramadol (%)
Nausea	0	4 (20%)
Vomiting	0	5 (25%)
Recurrence of shivering	0	2 (10%)



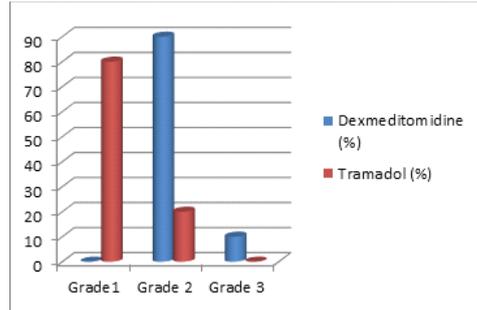
**Graph No- 4 Adverse effects**

**Grades of sedation:**

The Grades of sedation is statistically significant between the 2 groups (P value: <0.0001)

**Table No-5 Grades of sedation**

Grades of sedation	Dexmedetomidine (%)	Tramadol (%)
Grade 1	0	16 (80%)
Grade 2	18 (90%)	4 (20%)
Grade 3	2 (10%)	0



**Graph NO-5 Grades of Sedation**

**Discussion:**

Spinal anesthesia is a safe and popular anesthetic technique used world over for various surgeries. Variety of factors contributes to decrease the core body temperature in patients receiving spinal anesthesia. These include sympathetic block causing peripheral vasodilatation, increased cutaneous blood flow resulting in increased heat loss through the skin, cold operating room, rapid i.v infusion of cold i.v fluids, and direct effect of cold anaesthetic solution upon the thermo sensitive structures of the spinal cord. Opioid and non opioid mechanisms of action of Tramadol are thought to act synergistically. Antishivering effect of Tramadol is mediated via its serotonergic or noradrenergic activity.

Dexmedetomidine reduces the vasoconstriction threshold and the shivering threshold and is associated with a lower incidence of shivering. Dexmedetomidine comparably reduces the vasoconstriction and shivering thresholds thus suggesting that it acts on the central thermoregulatory system rather than preventing shivering peripherally. It may be a good choice because of its dual effects related anti-shivering and sedation.

Following spinal anaesthesia the mean temperature at which shivering occurred in patients in our study was 36.17°C+<sub>-</sub>0.3 for group Dexmedetomidine and 36.35°C+<sub>-</sub>0.3 for group Tramadol. This result was in accordance to the study by Aditi Dhimar et al.<sup>13</sup> In a study by Mittal G et al<sup>14</sup> control of shivering was 2.52+<sub>-</sub>0.44 in Dexmedetomidine group and 5.92+<sub>-</sub>0.81 in Tramadol group which was comparable with our group. The incidence of nausea and vomiting with Tramadol in our study was 20% and 25% respectively which corresponds to other study by Reddy V S and et al.<sup>15</sup>

In our study the recurrence rate was 10% seen only in Tramadol group which is comparable with Maheshwari et al<sup>1</sup> reported similar recurrence rate in their study (8%) and also with study by Mittal G et al<sup>15</sup> where the recurrence rate was 8%.

**Conclusion:**

- Both Dexmedetomidine (1 mg/Kg) and Tramadol (50 mg) are effective in treating patients with post- spinal anesthesia shivering, but time taken for control of shivering was shorter with Dexmedetomidine as compared to Tramadol.
- Dexmedetomidine causes lesser side effects as compared to Tramadol; Arousable sedation caused by Dexmedetomidine provides additional comfort to the patient.

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