

# **Efficacy of Intravenous Clonidine & Tramadol on Post Spinal Anaesthesia Shivering in Elective Lower Segment Caesarean Section: A Randomized Comparative Study**

**S. Kulshrestha, R.K. Mehta**

Department of Anaesthesia, Rama Medical College, Hospital & Research Centre, Mandhana, Kanpur-209217

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## **Abstract:**

The aim of this study was to evaluate the efficacy, potency and side effects of clonidine as compared to tramadol in post spinal anaesthesia shivering. In this double blind comparative study, 90 American Society Anaesthesiologists grade I & II patients aged between 18-35 years scheduled for elective LSCS under spinal anaesthesia who subsequently developed shivering intra operatively were selected. Equal number of patients were allocated to receive either clonidine 50µg (Gr C) or tramadol 50mg (Gr T). Grade of shivering, disappearance of shivering, haemodynamics and side effects were observed at scheduled intervals. The mean interval between the injection of drug and complete cessation of shivering was significantly earlier in group C than group T. Over all side effects were less in clonidine than tramadol, except sedation. It was concluded that clonidine is more effective in cessation of shivering than tramadol with fewer side effects.

**Key Words:** Clonidine, Tramadol, Post Spinal Anaesthesia Shivering, Lower Segment Cesarean Section.

## **Introduction:**

Elective lower segment caesarean section (LSCS) is widely performed under spinal anaesthesia. Shivering is known to be a frequent complication, reported in 40 to 70% of patients under going surgery under regional anaesthesia.<sup>1,2</sup> Shivering can double or even triple oxygen consumption and carbon di oxide production. Prospective randomized data suggest that high risk patients assigned to only 1.3 degree celsius core hypothermia were three times more likely to experience adverse myocardial outcomes.<sup>3</sup> It also causes arterial hypoxemia, lactic acidosis, increased intraocular pressure, increased intracranial pressure and interferes with pulse rate, blood pressure and electro cardiogram (ECG) monitoring.<sup>4,5,6</sup>

Though the mechanism of origin of shivering is not clear, various hypotheses have been proposed to explain it; pre-operative hypothermia is considered as the primary cause. Various pharmacological and non pharmacological methods have been proposed, of which tramadol<sup>7</sup> & clonidine<sup>8</sup> are the commonly used drugs to control shivering.

This prospective, double blind, randomized clinical study was designed to compare the anti shivering effect & side effects of clonidine and tramadol

in the treatment of post spinal shivering in patients under going elective LSCS.

## **Material and Methods:**

After obtaining permission of the ethical committee of college and written informed consent, 90 ASA I & II patients of age 18 - 35 years, scheduled for elective LSCS, who subsequently developed shivering intra operatively, under spinal anaesthesia, were enrolled by random allocation in this study and divided into two groups of 45 each.

Exclusion criteria included known hypersensitivity to clonidine and tramadol, hyper or hypothyroidism, cardio pulmonary, liver or renal disease, psychological disorder, blood transfusion during surgery, initial body temperature > 38°C or < 36°C.

Anaesthetist who were not involved in the study made the trial preparations and recorded group randomization separately. The anaesthetist conducting the case and recording the data were unaware of the preparation administered.

Subarachnoid block was given with inj. Bupivacaine 0.5% (12mg.) at L 3-4 interspace using 25 gauge whiteacre needle and blockage up to T 9-10 dermatome was achieved.

The parturients were randomly (envelop randomization) allocated to receive clonidine 50 µg (Gr C; n = 45) or tramadol 50 mg (Gr T; n=45). Parturients who developed grade 3 or 4 shivering for at least 3 minutes after spinal anaesthesia were included in the

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**Corresponding Author:** Dr. Saurabh Kulshrestha, Department of Anaesthesiology, Rama Medical College Hospital & Research Center, Mandhana, Kanpur - 209217 (U.P.)  
**Phone No.:** +91 9456716458  
**E-mail :** saurabhkulshrestha@yahoo.com

study. Both the drugs were given as slow IV bolus injection. Oxygen was administered to all the patients at a rate of 4 l/min. through venturi mask & patients were covered with drapes but not actively warmed, ambient temperature was maintained at 22-24°C. Intravenous fluids & drugs were administered at room temperature. Preloading was not done in both the groups as we did not want intravenous fluid to influence the onset of shivering mechanism. For the same reason no premedication was given.

Before beginning of spinal anaesthesia, standard monitoring procedure were established. Standard monitoring of pulse rate & oxygen saturation (spO<sub>2</sub>) was done continuously and noninvasive blood pressure (NIBP) & axillary body temperature were recorded before the commencement of surgery and there after at every 5 minutes for 1 hours and every 15 minutes for the rest of the observation period.

Grading of shivering was done as follows<sup>9</sup>:

Grade 0: No shivering

Grade 1: One or more of the following: Piloerection, peripheral vasoconstriction, peripheral cyanosis without other cause, but without visible muscle activity.

Grade 2: Visible muscle activity confined to one muscle group

Grade 3: Visible muscle activity in more than one muscle group

Grade 4: Gross muscle activity involving the whole body

Patients who developed either grade 3 or 4 of shivering were included in the study. The attending anaesthetist recorded the time in minutes at which shivering started after spinal anaesthesia (onset of shivering), severity of the shivering, time of disappearance of shivering (in minutes) and response rate (shivering ceased after treatment in 15 minutes). Duration of surgery was noted and duration of spinal anaesthesia was recorded by assessing spontaneous recovery of sensory block using pin prick method and observing spontaneous movement of limbs in the post operative period. If shivering did not subside by 15 minutes, the treatment was considered to be not effective. Recurrence of shivering was also noticed until the patients left the operation theatre. Patients who did not respond or in whom recurrence of shivering occurred were treated with additional dose of clonidine (0.5 µg / kg IV) or tramadol (0.5 mg/kg IV) in the respective groups if required. Side effects like nausea, vomiting, bradycardia (<50/Min), Hypotension

(> 20 % of baseline), dizziness and sedation score were recorded. Sedation score was assessed with a four point scale as follows:<sup>10</sup>

1. Awake and alert.
2. Drowsy, responsive to verbal stimuli.
3. Drowsy, arousable to physical stimuli.
4. Unarousable.

Bradycardia, hypotension and vomiting were treated with atropine, mephenteramine and metaclopramide, respectively, in titrated doses when required. Statistical analysis was done using suitable statistical software and student t test and chi- square test were applied for the interpretation of results. A *p* value < 0.05 was considered statistically significant.

## Results:

Ninety parturients who experienced shivering of grade 3 and 4 after spinal anaesthesia during caesarean section were included in the study. Parturients characteristic in respect of age, weight, duration of surgery, volume of intravenous fluid administered and duration of spinal block were comparable (Table I).

Shivering disappeared in 43 ( 95.5%) patients who received clonidine and 41 ( 91.11%) who received tramadol (Table II).

Severity of shivering was unchanged in 2 (4.5%) patients of group C and 4 ( 8.8%) patients of group T. Two parturients in group C ( severity of shivering unchanged) and 7 parturients ( 4- severity of shivering unchanged ; 3 recurrence of shivering ) in group T were given rescue doses of clonidine or tramadol respectively.

The mean interval between the injection of drug (clonidine and tramadol) and the complete cessation of shivering was  $2.59 \pm 0.66$  minutes in clonidine group &  $5.11 \pm 0.08$  minutes in tramadol group, the difference was statistically significant ( $p > 0.0001$ ). Complication rates were significantly higher in group T than in group C (Table III). Nausea, vomiting & dizziness were higher in group T while more patients of group C were sedated than group T.

Bradycardia occurred in 3 patients of group C and 1 patients of group T. In group C, 5 patients suffered from hypotension and 3 patients complained of dry mouth, both of which were not present in group T.

Table I : Demographic data of patients.

Parameter	Group	
	C (n =45)	T (n =45)
Age (years)	32.81 $\pm$ 3.52	31.47 $\pm$ 3.63
Wt. (kg)	63 $\pm$ 9.6	64 $\pm$ 8.9
Duration of surgery (Min.)	58.91 $\pm$ 10.15	60 $\pm$ 7.20
IV Fluids (ml)	2130.76 $\pm$ 200.12	2111.35 $\pm$ 207.12
Duration of Spinal Block ( Min.)	128.60 $\pm$ 9.21	125.87 $\pm$ 8

Table II : Post-spinal anaesthesia shivering and responses.

Parameter	Group		p-value	Significance
	C (n =45)	T (n =45)		
Onset of shivering (Min.)	6.8 $\pm$ 3.2	6.4 $\pm$ 3.4	0.43	N.S.
Severity of shivering (Grade)	3.1 $\pm$ 0.07	3.3 $\pm$ 0.04	0.31	N.S.
Time interval from treatment to cessation of shivering (Min.)	2.59 $\pm$ 0.66	5.11 $\pm$ 0.08	>0.0001	H.S.
Response Rate ( % )	43 (95.5%)	41 ( 91.11%)	-	-
Recurrence of shivering ( % )	Nil	3 (6%)	-	-

(N.S. - non significant , H.S. - highly significant)

Table III: Complications in both groups.

Parameter	Group	
	C (n =45)	T (n =45)
Nausea	0	30(66.60%)
Vomiting	0	11(24.40%)
Bradycardia	3 (6.66%)	1 (2.22%)
Hypotension	5 (11.11%)	0
Dizziness	0	22 (49.00%)
Dry Mouth	3 (6.66%)	0
Sedation score		
1	30 (66.66)	40 ( 88.88%)
2	15 ( 33.33%)	5 (11.11%)

## Discussion:

Hypothermia during central neuraxial blockade is common<sup>11</sup> and can be nearly as severe as that observed during general anaesthesia.<sup>12</sup> There are three principal reasons for hypothermia under spinal anaesthesia. First, spinal anaesthesia leads to an internal redistribution of heat from the core to peripheral compartment,<sup>13</sup> secondary to sympathetic block and peripheral vasodilation. Second, loss of thermoregulatory vasoconstriction below the level of the spinal block leads to increased heat loss from the body surfaces. Third, there is altered thermoregulation under the central neuraxial block, characterized by a decrease in shivering thresholds. In addition rapid administration of cold intravenous fluids contributes to the development of shivering.

Treatment modalities include covering the patient with blankets, application of radiant heat and warming the operating room.<sup>14</sup> The use of warm local anaesthetic solution or warm intravenous fluids has met with various degrees of success.<sup>15</sup> Various pharmacological treatments like IV opioids, alfentanil, pethidine<sup>16</sup> nalbuphine and meperidine<sup>17</sup> opioid analgesic tramadol<sup>18</sup> and 5HT antagonists ondansetron,<sup>19</sup> have been used. Our study was designed to compare efficacy of clonidine, an  $\alpha_2$  agonist with that of tramadol, a non opioid analgesic for control of shivering after spinal anaesthesia in patients undergoing LSCS.

Clonidine is a centrally acting selective  $\alpha_2$  agonist. Clonidine exerts its anti shivering effects at three levels : Hypothalamus, locus coeruleus and spinal cord. At the hypothalamic level, it decreases

thermoregulatory threshold for vasoconstriction and shivering, because hypothalamus has high density of  $\alpha_2$  adrenoceptors and hence is effective in treating the established post anaesthetic shivering.<sup>20,21</sup> It also reduces spontaneous firing in locus coeruleus – a pro-shivering centre in pons. At the spinal cord level, it activates the  $\alpha_2$  adrenoceptors and release of dynorphine, norepinephrine and acetylcholine. The depressor effects of these neurotransmitters at the dorsal horn modulate cutaneous thermal inputs.<sup>22</sup>

Tramadol is an opioid analgesic with opioid action preferably mediated via  $\mu$  (mu) receptor with minimal effect on kappa and delta binding sites; tramadol also activates the monomeric receptor of the descending neuraxial inhibiting pain pathway. The anti shivering action of tramadol is probably mediated via its opioid or serotonergic and noradrenergic activity or both.<sup>23,24</sup>

In the present study, it was observed that clonidine is as effective as tramadol in treating post spinal shivering, but the time interval from the commencement of treatment to cessation of shivering is quite less with clonidine than with tramadol ( $p > 0.0001$ ).

The response rate was also higher in the clonidine group than in tramadol group but difference was not statistically significant ( $p = 0.03$ ).

In the present study, incidence of nausea, vomiting and dizziness was higher in tramadol group while sedation was higher in clonidine group. Three patients of group T had recurrence of shivering in post operative period, while no patients in clonidine group suffered recurrence.

Bradycardia occurred in 3 patients of group C and 1 patients of group T. While hypotension was more common in group C. On overall analysis, higher complication rate were noted in group T patients compared to group C.

The limitation of this study is that core body temperature was not measured.

## Conclusion:

Clonidine 50  $\mu$ g and tramadol 50mg both are effective in treating post spinal anaesthesia shivering in patients under going LSCS however the side effects were fewer with clonidine. The more frequent incidence of side effects of tramadol may limit its use as an anti shivering drug.

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