

# Comparison of Pethidine and Tramadol for the Control of Shivering in Patients undergoing Elective Surgery under Spinal Anesthesia

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## ABSTRACT:

**Introduction:** Shivering is a common problem faced by an anesthesiologist during intraoperative as well as in postoperative period. It is a frequent, unpleasant, and undesirable complication occurring after sub-arachnoid block (SAB), secondary to vasodilation as a result of sympathetic blockade. The incidence of shivering has been reported to be about 36-85% after SAB. The present study was designed to compare the efficacy of pethidine and tramadol on reducing postoperative shivering following sub-arachnoid block and to compare their adverse effects. **Methods:** This randomized, experimental study was conducted in patients undergoing surgery under sub-arachnoid block over a four months period. Patients were randomized into Group P (receiving pethidine) or Group T (receiving tramadol). Patients received either tramadol or pethidine in a dose of 0.5mg/kg intravenously after the appearance of shivering. Disappearance of shivering as well as hemodynamics were observed at scheduled intervals. **Result:** Shivering score was significantly lower in Group P at 10, 15, 20, and 30 min compared to Group T. Similarly, nausea/vomiting and dizziness were also lower in Group P but sedation score was higher. **Conclusion:** Pethidine provide better anti-shivering effect than tramadol with less side effect in terms of nausea and vomiting but more sedation.

**Keywords:** adverse effects • pethidine • shivering • spinal anesthesia • tramadol

## INTRODUCTION:

Shivering can be defined as spontaneous, rhythmic, oscillatory, tremor-like muscular hyperactivity which occurs as a physiological stressful response to core hypothermia in an attempt to raise the metabolic heat production. It is a frequent, unpleasant, and undesirable complication occurring

after sub-arachnoid block (SAB), secondary to vasodilation due to sympathetic blockade. Shivering occurs mainly in hypothermic patients but may also occur in normothermic.<sup>1</sup> The incidence of shivering has been reported to be about 36-85% after SAB.<sup>2</sup> Shivering has detrimental effects like interference in monitoring of pulse rate, blood-pressure (BP), and ECG, increase in oxygen consumption, catecholamine secretion, carbon dioxide production, metabolic rate by 400%, intra-ocular pressure (IOP), intra-cranial pressure (ICP), and lactic acid production. Increase in heart rate, cardiac output and BP may cause problem in patient with low cardiac and pulmonary reserve.<sup>3</sup> Shivering also contribute to increased wound pain, delayed healing, and delay discharge from post-anesthetic care unit.<sup>4</sup> The present study was designed to compare the efficacy of pethidine and tramadol on reducing postoperative shivering following sub-arachnoid block and to compare their adverse effects.

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## METHODS:

This double blind, randomized controlled study was carried out at Anesthesiology department at Lumbini Medical College Teaching Hospital after approval from Institutional Review Committee (IRC-LMC) from August 2015 to November 2015. ASA I and II patients belonging to either sex, aged between 18 and 65 years, undergoing elective orthopedic, lower abdominal, or urological surgery under spinal anesthesia were enrolled in the study. Patients who refused to participate or with neuromuscular diseases, psychological disorders, recent history of febrile illness, hypo or hyperthyroidism, cardiopulmonary disease, an initial body temperature  $>38^{\circ}\text{C}$  or  $<36^{\circ}\text{C}$ , a known history of alcohol or substance abuse, or receiving vasodilators and medications likely to alter thermoregulation were excluded from the study. Patients who required blood transfusion during surgery were also excluded.

Following a detailed pre-anesthetic examination, preoperative investigations including complete blood picture, renal function tests, liver function tests, and coagulation profile were sent and report assessed. All patients were premedicated with 0.25 mg tablet of alprazolam the previous night of surgery. Informed written consent was obtained from the participants.

On arrival in the operating theatre, an intravenous line was opened with a 18G cannula in the dorsal aspect of either one of the hands. Lactated Ringer solution, warmed to  $37^{\circ}\text{C}$ , was infused at 10 ml/kg/hr over 30 min before spinal anesthesia. The infusion rate was then reduced to 6 ml/kg/h. Heart rate, mean arterial pressure (MAP), and peripheral oxygen saturation were recorded using standard noninvasive monitors before intrathecal injection and there after at 0, 5, 10, 15, 20, 25, and 30 minutes. Body temperature was monitored with a mercurial thermometer at the start of spinal anesthesia and during treatment of shivering. The temperature of the operating room was between  $21\text{-}23^{\circ}\text{C}$ .

Patients were randomized into one of the group (Group T or Group P) according to a list of computer generated random numbers. Group T would receive tramadol in a dose of 0.5 mg/kg and Group P would receive pethidine in a dose of 0.5 mg/kg. The anesthetists conducting the case and recording the data were unaware of which group the patient belonged to. A prepared solution of either tramadol or pethidine in a 10 ml syringe, labeled

as 'anti-shivering agent' at strength of 10 mg/ml was handed over to the anesthetists. This solution was to be given in a dose of 0.5 mg/kg if shivering occurred. All the patients were assessed for shivering grades, its disappearance, hemodynamic status, and complications if any.

Neuraxial anesthesia was instituted at either  $L_{3-4}$  or  $L_{4-5}$  interspaces using three ml (15 mg) of hyperbaric bupivacaine 0.5% using a 25 gauge Quincke spinal needle, blocking up to  $T_{9-10}$  dermatome. Supplemental oxygen was given via a face mask at a rate of three l/min during the operation. All patients were covered with one layer of surgical drapes over the chest thighs and calves during the operation and one cotton blanket over the entire body after the operation.

All cases were screened for shivering, if any, and graded with a five point scale validated by Crossly and Mahajan.<sup>5</sup>

- 0 = No shivering.
- 1 = Piloerection or peripheral vasoconstriction but no visible shivering.
- 2 = Muscular activity in only one muscle group.
- 3 = Muscular activity in more than one muscle group but not generalized.
- 4 = Shivering all over the body.

Gradation of Sedation was done as follow:

- 0 = Awake
- 1 = Drowsy
- 2 = Asleep but arousable
- 3 = Asleep but not arousable

If shivering occurred, it was graded and recorded and 'anti-shivering agent' was given. If shivering persisted for 15 minutes at grade three or above, it was termed as 'severe shivering' and rescue treatment with the second dose of same amount of the same drug was done.

Side-effects such as nausea and vomiting and dizziness were recorded. If patient developed nausea and vomiting, metoclopramide 10 mg was administered by intravenous route.

Data was analyzed with statistical software SPSS version 16.0 (Illinois, Chicago). Demographic data and vital parameters were expressed as mean and standard deviation (*SD*). All the categorical data were analyzed using chi-square test or Fisher exact test. Scale variables were compared using independent t-test, and ordinal variables were analyzed using Wilcoxon rank sum test. *P* value of  $<0.05$  was considered statistically significant

**RESULT:**

Eighty patient were included in the study. There were 44 (55%) in Group P and 36 (45%) in Group T. There was no significant difference between two group with respect to age, sex and duration of anesthesia (Table 1). There was no clinically significant respiratory depression in any of the patient. Intraoperative saturation was within normal range throughout in both the groups. All patient were normothermic during our procedure. A patient in Group T was excluded as he was found mentally unsound.

Shivering was significantly lower in Group P compared to Group T at 10, 15, 20, and 30 minutes (Table 2). Pethidine is likely to be superior in controlling shivering compared to tramadol.

Patients were more sedated in Group P at 5, 15, 20, 25, and 30 minutes as compared to Group T and this difference was statistically significant (Table 3).

In Group P, out of 44 patients, only two (4.5%) experienced nausea or vomiting; whereas, in Group T, 27 (77%) experienced nausea or vomiting. Nausea or vomiting was significantly more common in Group T as compared to Group P ( $X^2[N=79, df=1] = 44.2, p=0.001$ ).

In Group P, five (11.4%) patient experienced dizziness whereas in Group T, 16 (45.7%)

Table 3: Perioperative sedation score at different time interval.

Time min	Group P Mean rank	Group T Mean rank	Statistics
0	40	40	$W=1400, p=1$
5	32.17	49.8	$W=1744.5, p=0.04$
10	37.66	41.86	$W=1318, p=0.3$
15	35.27	43.76	$W=1234.5, p=0.04$
20	34.77	44.16	$W=1217, p=0.02$
25	29.44	53.21	$W=1862.5, p=0.001$
30	35.27	43.76	$W=1234.5, p=0.001$

$W = Wilcoxon rank sum value$

patient experience dizziness. This difference was statistically significant ( $X^2[N=79, df=1] = 11.79, p=0.001$ ). Patients receiving tramadol are more likely to experience dizziness.

**DISCUSSION:**

Perioperative shivering is one of the most unwanted and common complication after spinal anesthesia. There are various explanation for hypothermia and shivering during SA; it leads to an internal redistribution of heat from core to peripheral compartment secondary to sympathetic block and peripheral vasodilation, loss of thermoregulatory vasoconstriction below the level of spinal block leads to increased heat loss from body surface, and there is altered thermoregulation under SA. Other factor like cold temperature of operation theatre, rapid infusion of cold fluids, and cold anesthetic drugs. There are various pharmacological and non pharmacological modalities of prevention and treatment like covering patient with blankets, application of radiant warmer, warming the operating rooms, use of warm fluids, and drugs like alfentanil, fentanyl, nalbuphine, ondansetron, meperidine, and tramadol.<sup>6-11</sup> Pharmacological intervention dose not reduce body temperature but resets the shivering to a lower level there by decreasing shivering and its episode

Tramadol hydrochloride, an opioid receptor agonist drugs, have a modulatory effect on central monoaminergic pathways and thus inhibits the neuronal uptake of noradrenaline/serotonin which resets the body temperature regulation centre.<sup>12-14</sup> Pethidine is an opioid derivative frequently used for post spinal shivering. Pethidine combines with mu and kappa receptors and is responsible for anti-shivering action.<sup>15</sup> Pethidine also act directly on thermoregulatory center and not only through activation of receptors.<sup>16</sup>

Table 1: Demographic parameter of patient

Variables	Group P	Group T	statistics
Age in yr mean (SD)	40.23 (13.24)	37.54 (13.96)	$t=0.88, df=77, p=0.4$
Sex	M=27 F=17	M=17 F=18	$X^2=1.29, p=0.26$
Duration of anesthesia in min mean (SD)	50.9 (12.4)	47.5 (11.7)	$t=1.24, df=77, p=0.22$

Table 2: Perioperative shivering score at different time interval

Time min	Group P Mean rank	Group T Mean rank	Statistics
0	41.97	37.53	$W=1313.5, p=0.3$
5	42.86	36.4	$W=1274.0, p=0.1$
10	31.67	50.47	$W=1766.0, p=0.001$
15	32.84	48.12	$W=1636, p=0.001$
20	30.97	48.12	$W=1797, p=0.001$
25	36.67	44.19	$W=1546, p=0.9$
30	31.78	50.33	$W=1761.5, p=0.001$

$W = Wilcoxon rank sum value$

In the present study, we compared the efficacy of pethidine and tramadol for shivering management after spinal anesthesia in patients under going elective surgeries. We found pethidine to be more effective than tramadol for controlling shivering. In contradiction to our finding, Zahedi H. et al. and Singh SN. et al. found tramadol to be more effective than pethidine for controlling post-spinal shivering. However, they used tramadol in higher dose at one mg/kg against 0.5 mg/kg used by us and gave general anesthesia to most of the cases.<sup>14,17</sup>

Complication rates for nausea and vomiting and for dizziness were higher in Group T compared to Group P whereas more patients were sedated in Group P than in Group T. Findings of our study was similar to that by Gangoupadhya et al. who reported higher incidence of vomiting with tramadol.<sup>18</sup> There are various studies on tramadol and they have documented that side effects of tramadol is dose dependent and more likely to occur if loading dose

is higher.<sup>19-21</sup>

This study had a small sample size. Future studies should contain a large sample size. Another limitation was that the present study included short duration surgeries. The anti-shivering effect of pethidine and tramadol needs to be evaluated in surgeries of longer duration where chances of developing hypothermia are more. We could not measure core body temperature the procedure is uncomfortable and unacceptable in patient with SA.

## CONCLUSION:

Pethidine controls shivering better than tramadol, and it produces less dizziness and nausea and vomiting. However, it produces more sedation than tramadol. Thus, pethidine is a safe and effective agent for controlling shivering associated with spinal anesthesia.

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