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**Original Research Article**

# Comparison of tramadol and pethidine for control of shivering in regional anesthesia

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## ABSTRACT

**Background:** Shivering is a common problem faced by anaesthesiologists in the intraoperative as well as post-operative period. It occurs during both general anesthesia and regional anesthesia, but is more frequent and troublesome during regional anesthesia. There are many pharmacological and other methods to tackle this issue. Not many studies have compared between pharmacological agents that control shivering.
**Methods:** This randomized, prospective study conducted in 80 adult patients, was designed to explore the efficacy and potency of Tramadol in comparison to Pethidine for control of shivering under regional anesthesia. Patients received Tramadol or Pethidine in a dose of 0.5 mg/kg intravenously after the appearance of shivering. Disappearance and recurrence of shivering, sedation as well as haemodynamics were observed at scheduled intervals
**Results:** The complete disappearance of shivering took a mean 4.5 minutes in Tramadol group while 8 minutes in pethidine group (p value<=0.05). Tramadol was more potent than Pethidine with respect to control of shivering and its recurrence.
**Conclusions:** Intravenous Tramadol is qualitatively superior to Pethidine for control of shivering after regional anesthesia.

**Keywords:** Pethidine, Regional anesthesia, Shivering, Tramadol

## INTRODUCTION

Regional anesthesia is a safe and popular anaesthetic technique for various surgeries. But around 40-60% of patients under regional anesthesia develop shivering.[1]

Shivering can be very unpleasant and physiologically stressful for the patient. It increases the metabolic rate and oxygen consumption up to 100-600%. It can induce arterial hypoxemia and acidosis. It increases intraocular pressure and intracranial tension; causes stretch on suture lines. It interferes, with monitoring like electrocardiography, pulse oximetry and non-invasive blood pressure measurement. This could be detrimental to patients with low cardio respiratory reserve.[1]

The incidence of post-anaesthetic shivering is high in surgical patients. After obtaining the benefits of modern anesthesia, patients often report shivering as an unpleasant occurrence.[1]

Many physical and pharmacological interventions are used to decrease the incidence and to reduce the severity of post anaesthetic shivering. Non-pharmacological methods which use specialized equipment to prevent or to control shivering are expensive and are not practical in all clinical settings.[2]

Many pharmacological agents like Clonidine, Magnesium Sulphate, Amitriptyline, Urapidil, Dolasetron, Doxapram, are used to control shivering. These drugs have side effects like respiratory depression, bradycardia, hypo tension etc.[2]

Among the pharmacological interventions, Opioids like Pethidine and Tramadol are found effective in many studies. Tramadol has been used as analgesic for labor pain without adversely affecting mother or the newborn. With pharmacodynamic advantage of causing less respiratory depression and sedation, with its unique state of being a non-controlled drug, Tramadol has the potential use in controlling shivering and hence emerging as a new and safe drug to be used for treatment of post anaesthetic shivering.[3]

The objective of this study was to evaluate the safety and efficacy of Pethidine and Tramadol to control shivering in patients for surgeries under regional anesthesia and thereby to determine which of these pharmacological interventions serves best to achieve therapeutic effect with minimal side effect.

## METHODS

In the randomized controlled prospective study a total of 80 adult patients aged between 20-60 years, of ASA grade I or II undergoing various surgeries under regional anesthesia that subsequently developed shivering were included. Institutional Ethical Committee approval was obtained. Informed written consent was obtained by participating patients.

### *The patients were randomly divided into 2 groups*

- Group T- 40 patients who received 0.50 mg/kg Tramadol intravenously
- Group P- 40 patients who received 0.5 mg/kg Pethidine intravenously.

### *Inclusion criteria*

- Patients from either gender, aged between 20-60 years, of ASA grade I or II undergoing various surgeries under regional anaesthesia who developed shivering after anaesthesia
- Patients who gave a valid informed written consent.

### *Exclusion criteria*

- Patients with significant cardiovascular, renal, hepatic, respiratory or neurological diseases
- Patients with fever, thyroid disease, obesity
- Patients With known hypersensitivity to Tramadol or Pethidine
- Patients on long term Phenothiazine's and MAO inhibitors.

### *Anesthetic management*

Ambient temperature was noted. Baseline vital parameters were recorded. A standard double layered blanket was used to cover the chest and upper limb of the patient. All the pre-loading fluids and drugs were given at room temperature. Oxygen at rate of four liter/min was administered through face mask to all the patients

Monitoring of Blood Pressure (BP), pulse oximetry, ECG, was done throughout the procedure. After pre-medication in the form of ondansetron IV, baseline preoperative axillary temperature was noted in all the patients. Central neuraxial blockade (Spinal, Epidural, Combined Spinal and Epidural) or peripheral neural blockade was given according to the surgical procedures.

Patients who developed shivering after the regional block were included in the study. A total of 80 cases fitting the above criteria were studied. They were randomly divided into one of the two groups.

### *Parameters compared*

Shivering was graded as follows. Modified Crossley and Mahajan scale was used to assess the degree of shivering.[4]

- Grade 0- No shivering
- Grade 1- Muscular activity involving only one muscle group
- Grade 2- Muscular activity involving two or more than two muscle groups, but not involving whole body
- Grade 3- Shivering involving entire body, bed shaking.

The drug was administered by another anesthetic personnel who was blinded to whether the drug contains Pethidine or Tramadol. The same person assessed the effect of the drug administration based on the format provided.

All the patients were assessed for shivering grades, its disappearance, hemodynamic status, and complications if any.

Patients were observed at intervals of 1 min till 5 minutes, and thereafter at 10,20, 30, 45, and 60 minutes. Baseline Pulse rate, BP, SPO2, Respiratory rate, and temperature was noted, and also during shivering, and thereafter the drug administration at regular intervals.

Recurrence of shivering was also noted and an additional dose of either Tramadol or Pethidine in a dose of 0.25 mg/kg IV was given in respective groups.

Attending anesthesiologist recorded the time of disappearance of shivering from the time of administration of the drug either Tramadol or Pethidine.

Sedation characteristics were noted and graded according to the Ramsay's sedation score.

Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Number (%).

Significance is assessed at 5 % level of significance. Student's T Test has been used to find the significance of study parameters between two groups of patients, Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

## RESULTS

**Table 1: Demographic data.**

| | Group T | Group P | P value |
|---|---|---|---|
| Age | 37.7±12.7 | 40.1±13.5 | 0.06 |
| Weight | 57.9±11.4 | 60.6±11.2 | 0.08 |
| Sex F/M | 13/27 | 17/23 | 0.6 |
| ASA grade 1:2 | 31:9 | 33:7 | 0.8 |

There was no significant difference in the age, sex and weight distribution between the two groups. Samples were matching by ASA grading also. Analysis was done by chi square test.

***Haemodynamics***

**Table 2: Heart rate characteristics (beats per minute).**

| Time (minutes) | Group T (n=40) | Group P (n=40) | P-value |
|---|---|---|---|
| 0 | 83.5±6.0 | 83.2±5.7 | 0.8 |
| 1 | 88.1±8.4 | 89.2±8.6 | 0.5 |
| 2 | 89.8±9.2 | 95.1±8.8 | 0.0* |
| 3 | 86.1±9.2 | 90.0±8.6 | 0.5 |
| 4 | 84.9±10.1 | 85.0±10.1 | 0.9 |
| 5 | 82.3±9.3 | 82.0±9.0 | 0.8 |
| 10 | 79.9±9.1 | 79.2±8.8 | 0.7 |
| 20 | 77.6±8.3 | 77.8±7.8 | 0.9 |
| 30 | 76.8±7.5 | 76.2±6.8 | 0.5 |
| 45 | 76.4±6.7 | 75.4±6.5 | 0.7 |
| 60 | 74.5±7.0 | 74.8±6.3 | 0.6 |

*Statistically significant at 0.05 level.

There is no statistically significant difference in HR between the two groups except at second minute where Tramadol has significant advantage over Pethidine for maintaining the heart rate. Analysis was done by independent T test. The two groups maintained heart rate within 15% of basal value.

P value is significant for the tramadol group for stopping shivering. Tramadol has significant advantage over Pethidine for stopping shivering. Analysis was done by independent T test.

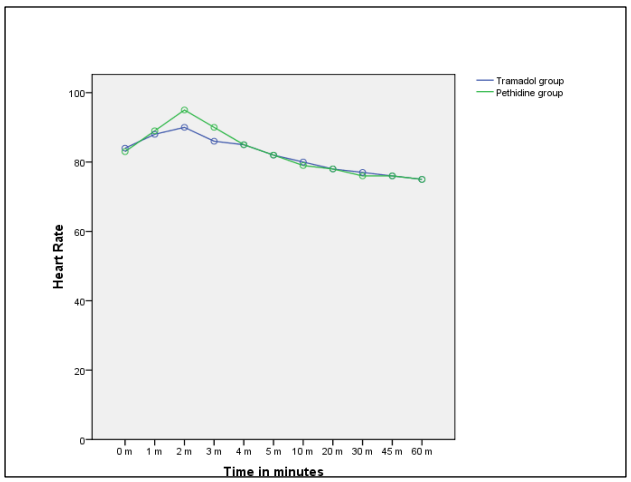


**Figure 1: Comparison of heart rate between the two groups of patients.**

Sedation characteristics are significant at 5 minutes and 10 minutes for Pethidine i.e.; Pethidine causes more sedation tramadol at 5 and 10 minutes. Analysis was done by independent T test.

**Table 3: Time at which shivering stopped (in minutes).**

| Incident | Group T (n=40) | Group P (n=40) | 'P' value |
|---|---|---|---|
| Shivering stopped | 4.58±.5.9 minutes | 8.02±5.15 minutes | 0.018* |

*Statistically significant at 0.05 level.

P value is significant at 5, 10 and 30 minutes. Tramadol has significant advantage over Pethidine for stopping shivering early i.e., at 5 and 10 minutes post shivering. Also, it is useful for preventing an early recurrence at 30 minutes.

**Table 4: Mean sedation characteristics (according to Ramsay's sedation scoring).**

| Time in minutes | Group T (n=40) | Group P (n=40) | P-value |
|---|---|---|---|
| 1 | 2.0 | 2.0 | |
| 2 | 2.0 | 2.0 | |
| 3 | 2.0 | 2.0 | |
| 4 | 2.0 | 2.0 | |
| 5 | 2.0 | 2.1±.035 | 0.01* |
| 10 | 2.0 | 2.1±0.3 | 0.04* |
| 20 | 2.0 | 2.0 | |
| 30 | 2.0 | 2.0 | |
| 45 | 2.0 | 2.0 | |
| 60 | 2.0 | 2.0 | |

**Table 5: Control of shivering.**

| Time (minutes) | Group T (n=40) | Group P (n=40) | P- value |
|---|---|---|---|
| 1 | 0 | 0 | |
| 2 | 0 | 0 | |
| 3 | 5 (12.5%) | 2 (5%) | 0.216 |
| 4 | 15 (37.5%) | 9 (22.5%) | 0.111 |
| 5 | 40 (100%) | 21 (52.5%) | 0.000* |
| 10 | 40 (100%) | 34 (85%) | 0.013* |
| 20 | 40 (100%) | 40 (100%) | |
| 30 | 40 (100%) | 35 (87.5%) | 0.027* |
| 45 | 35 (87.5%) | 31 (77.5 %) | 0.189 |
| 60 | 40 (100%) | 40 (100%) | |

*Statistically significant at 0.05 level.

## DISCUSSION

Regional anesthesia is emerging as safe and popular technique both in elective and emergency situations in the modern anesthesia practice. Incidence of post anesthesia shivering is high.[5]

Shivering continues to be a common problem faced by the anaesthesiologist during intra operative and post-operative periods. Shivering occurs both during general and regional anesthesia. Unfortunately, there is no gold standard drug or definitive strategy drawn in management of this commonly encountered problem. Shivering is a very unpleasant experience for the patients receiving comforts of modern anesthesia. At times, it is described as a sensation worse than surgical pain. It is uncomfortable to the patients as well as to the operating room personnel, especially during regional anesthesia.[5,6]

The exact mechanism of development of post anesthesia shivering is not known. Many hypotheses like, perioperative heat loss, stress, the direct effect of certain anaesthetics, hypercapnia and hypoxia, uninhibited spinal reflexes, pain, early recovery of spinal reflex activity and sympathetic over activity have been suggested.[3,6]

Physical methods of active and passive warming systems, warming of inspired air, warming systems for IV fluids, blood and its products are tried in many studies; these methods require use of specialized equipment, which is not economically feasible and practical in all clinical settings.[1]

Pharmacological methods are cost effective when compared to physical methods. There is no single gold standard drug for treatment of shivering. Pethidine and Clonidine are most commonly studied drugs. Clonidine is associated with bradycardia and hypotension, and Pethidine is associated with nausea and vomiting and respiratory depression.[1,3] Tramadol is a novel analgesic; it has Opioid effect mediated via the mu-receptor, with minimal effect on kappa and delta receptors. Tramadol inhibits 5- HT3 reuptake and promotes its release. It also inhibits synaptosomal noradrenaline reuptake.[7]

Electro physiologic, neurophysiologic and neuro-pharmacologic experiments in animals have established the role of Noradrenaline and 5HT3 in the control of body temperature. Activation of nucleus Raphe Magnus, where 5-HT3 acts as a neurotransmitter has inhibitory effect on shivering. It is thus possible that anti-shivering effect of Tramadol is mediated by its effect on these receptors. So, many authors have postulated that, Tramadol is likely to have better clinical utility as an anti-shivering drug when compared to Pethidine, whose anti-shivering effect is postulated to be mediated through kappa receptors.[7] With its pharmacodynamic advantage in causing less respiratory depression and sedation, with its unique status of not being a controlled drug, it has potential use in the control of shivering in the obstetric suite, because it is more convenient and, theoretically, safer than Pethidine.[3]

Tramadol and Pethidine are approximately equipotent with respect to analgesia. The minimum effective dose of Pethidine for control of shivering is found to be 0.35 mg/kg. Although the anti-shivering and analgesic effects of these two agents may be mediated via different receptors, it is postulated that Tramadol may control shivering at doses < 1 mg.kg -1.[3,8]

Many studies have demonstrated the usefulness of Tramadol in control of shivering; studies have also demonstrated that, Tramadol is more effective in treatment of shivering when compared to other drugs like Pethidine and amitriptyline.[3,6,8] Different doses of Tramadol from 0.2 mg/kg to 3mg/kg were used to control postoperative shivering in different studies.[8-10] There was statistically significant difference between the time of stopping of shivering between group T when compared to group P. The mean time or stopping shivering in the present study for group T was 4.5 minutes and 8.0 minutes for Pethidine.

Dhimar A et al conducted a study on 60 ASA grade 1 and grade 2 patients who developed shivering after regional anesthesia, they compared the effect of Tramadol 1mg/kg with Pethidine 1 mg/kg.[1,8] They concluded Tramadol is superior to Pethidine in control of shivering. In their study, the mean response time for Tramadol group was 1 min and 3 minutes for Pethidine. In the present study, there was an increase in the response time in both of the two groups of drugs.

Talakoub et al studied the effect Tramadol 0.5 mg/kg and Pethidine 0.5 mg/kg on post anaesthetic shivering in parturient under spinal anesthesia. In their study, time of cessation of shivering from the time of drug administration was 2.5 minutes for Tramadol and 5.0 minutes for Pethidine. The time taken for cessation of shivering in the present study is comparable though slightly higher than the above study.[6] Bhatnagar et al in

their study administered Tramadol at 1mg/kg and Pethidine at 0.5 mg/kg IV for post anaesthetic shivering. They found that the number of patients who stopped shivering in 10 minutes were significantly higher in Tramadol group when compared to Pethidine group. This study is also comparable to the present study.[7]

The vital parameters like SBP, DBP, SPO2, body temperature did not show any significant change with the administration of Tramadol. There was a significant increase in the HR in the Pethidine group in the second minute but this is a known characteristic of Pethidine. Studies have found that administration of Tramadol 0.2mg/kg to 3 mg/kg does not affect the hemodynamic and other vital parameters of the patients. One of the limitations of the present study is that core temperatures of the patients were not measured.

In the present study, it was found that recurrence of shivering present in both groups, but in the Pethidine group recurrence was seen as early as 30 minutes whereas it was 45 minutes with Tramadol. Since Tramadol does not cause significant respiratory depression, it can be safely used in management of recurrence of shivering. The probable reason for recurrence of shivering could be result of low concentration of the active drug, when hypothermia is still persisting and individual variations in the core temperature. Till date it is not clear whether higher shivering grades require higher doses of the drug.[3]

This study did not control tightly the various factors which might influence the incidence of shivering, like the temperature of drugs and intravenous fluids and temperature of the operating room. However, this should not have affected the validity of comparisons. First, the current study focused on the response after treatment, rather than the incidence of shivering. Second, by randomization, the two study groups had been subjected to a similar degree of influence of these factors.

Patients receiving Pethidine intravenously for control of shivering during regional anesthesia were more sedated at five minutes after injection, although there was no difference in level of consciousness at later intervals.

Some patients developed recurrence of shivering after initial control. Further studies are indicated to compare these two agents directly to substantiate these possible differences. Synergism in the anti-shivering properties of these two agents is also possible, as their effects are likely mediated via different receptors.

## CONCLUSION

From the findings of the study it can be concluded that Tramadol in a dose of 0.5mg/kg iv is an effective dose of Tramadol for control of shivering in patients undergoing regional anesthesia and it is better than Pethidine for the same.

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## REFERENCES

1. Aditi AD, Mamta GP, Swadia VN. Tramadol for control of shivering, a comparison with Pethidine. Indian J Anesthesia. 2007;51:28-31.
2. Bhattacharya PK, Bhattacharya L, Jain RK, Agarwal RC. Post anesthesia shivering a review. Indian J Anesthesia. 2003;47:88-93.
3. Chan AM, Ng KF, Tong EW, Jan GS. Control of shivering under regional anesthesia in obstetric patients with Tramadol. Can J Anesthesia. 1999;46:253-8.
4. Alfonsi P. Post anaesthetic shivering. Drugs. 2001;61:2193-2205.
5. Atashkhoyi S, Negar S. Effect of Tramadol for prevention of shivering after spinal anesthesia for caesarean section. Res J Biol Sci. 2008;3:1365-9.
6. Talakoub R, Noorimeshkati S. Tramadol versus Pethidine in the treatment of shivering in cesarean section. JRMS. 2006;11:151-5.
7. Bhatnagar S, Saxena A, Kannan TR, Punj J, Panigrohi M, Mishra S. Tramadol for postoperative shivering A double blind comparison with Pethidine. Anesthesia Intensive Care. 2001;29:149-54.
8. Sajedi P, Khalili G, Kyhanifard L. Minimum effective dose of Tramadol in the treatment of post anesthetic shivering. JRMS. 2008;13:75-9.
9. Mohta M, Kumari N, Tyagi A, Sethi A, Agarwal, D, Singh M. Tramadol for prevention of post anaesthetic shivering: a randomized double-blind comparison with Pethidine. Anesthesia. 2009;64:141-6.
10. Trekova NA, Buniatian AA, Zolicheva NIu. Tramadol hydrochloride in the treatment of postoperative shivering Anesteziol Reanimatol. 2004;5:86-9.

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