

# A Comparative Study Of The Effect Of Tramadol And Pethidine On Postoperative Shivering

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## Abstract

**Background :** Anesthesiologists attempt to keep perioperative normothermia for surgical patients. In most operating and recovery rooms , shivering is controlled by the use of humidifiers, warming blankets, and inhalation of humidified heated oxygen, however pharmacological control is an alternative treatment modality.

**Method :** In this randomized , double blind study we evaluated 60 patients with ASA class 1 or 2 , who developed postoperative shivering in recovery room. Half of them were treated with pethidine 0.5 mg/kg and others with tramadol 1 mg/kg. We compared the efficacy of tramadol with that of pethidine and the grade of shivering observed 5 minutes after injection of drug and categorized the patients to three groups; completely improved , partially improved and not improved that the last group had no improvement after 15 minutes .

**Results :** In this study 16 from 30 patients improved completely with pethidine ( 53.3% ) and 20 from 30, improved completely with tramadol (66.66% ). Besides 6.66% of tramadol group and 20% of pethidine group had no improvement. Evaluating this complex data with Chi-Square test showed no significant difference between two drugs in stopping post operative shivering (  $PV=0.294$  ).

**Discussion :** In this study we found that there is no significant difference in anti shivering effect of pethidine and tramadol although some papers believe that tramadol is superior and the others say that pethidine is most efficacious. This discrepancy could be due to difference in age of patients, duration of operation, core and room temperature in various studies.

**Conclusion ;** We concluded that tramadol is as effective as pethidine in subsiding shivering .

## INTRODUCTION

The incidence of postoperative shivering - like tremor reportedly is 40 percent , but it now appears to be less , because more patients are kept normothermic , and opioids are administered more frequently and in larger doses than previously. It is a potentially serious complication, increasing oxygen consumption and has various treatments ; skin surface warming and using a variety of drugs.

In recent years, tramadol that can release 5 \_ hydroxy tryptamin and stimulates receptors is introduced for subsiding postoperative shivering . Regarding this property, we compared tramadol with a well know anti shivering medication; pethidine, to find which one is superior for decreasing shivering.

In homeothermic species, a thermoregulatory system coordinates defenses against cold and heat to maintain internal body temperature within a narrow range, thus optimizing normal physiologic and metabolic function. The combination of anesthetic \_ induced thermoregulatory impairment and exposure to a cool environment makes most unwarmed surgical patients hypothermic. Although shivering is one consequence of preoperative hypothermia, and rarely the most serious it occurs frequently (i.e., 40\_60% after volatile anesthetic), and it remains poorly understood . Shivering is an unpleasant and frequent complication in the postoperative period (<sub>1,2,3</sub>: 1367\_1389) . The origin of postoperative shivering is unclear, various mechanisms have been proposed (<sub>4</sub>).

Shivering may happen as a thermoregulatory response to

hypothermia, or muscle hyperactivity with tonic, or clonic patterns and different frequencies have been reported (3). However in the post operative period, muscle activity maybe increased even with normothermia, suggesting that other mechanisms than heat loss and subsequent decrease in core temperature may contribute to the development of shivering. These include uninhibited spinal reflexes, postoperative pain, decrease sympathetic activity, pyrogen release, adrenal suppression, and respiratory alkalosis (3).

Shivering is an involuntary, oscillatory muscular activity that augments metabolic heat production. Vigorous shivering increases metabolic heat production up to 500-600% above base level. (3).

Surgical patients maybe admitted to the post anesthesia care unit with inadvertent hypothermia. Mild perioperative core hypothermia may increase the risk of wound infection, bleeding, cardiac complications, and a prolonged postanesthesia care unit state (3). In addition, the quality of a Patients recovery may also suffer because of shivering and thermal discomfort (6,7). Patients report that shivering is remarkably uncomfortable and some even find the accompanying cold sensation, worse than surgical pain (1). Moreover, shivering per se may aggravate post operative pain simply by stretching surgical incisions. Shivering also occasionally impedes monitoring techniques increases intraocular and intra cranial pressure, and is especially disturbing to mother during labor and delivery (4).

Potent antishivering properties have been attributed to numerous drugs. We discuss two of these drugs here; tramadol and pethidine.

Tramadol is an antishivering drug that inhibits the reuptake of 5-HT, Norepinephrine, and Dopamine and facilitates 5-HT release. Despite different degree of opioid like characteristics in preclinical tests, tramadol lacks significant naloxone reversibility in humans. In human volunteers a high dose of naloxone only partially reverses the anti shivering effect of tramadol (8).

Cerebral 2 adrenoreceptors are thought to play a role in the attenuation of post operative shivering by tramadol (1,7).

Meperidine decreases the shivering threshold almost twice as much as the vasoconstriction threshold. This is in distinct contrast to other analgesic and sedative drugs, including propofol, Dexmedetomidine and Midazolam, and to general anesthetic (1). The gain and maximum intensity of shivering

remain unchanged during both Alfentanil and Meperidine administration. These results thus demonstrate that the special antishivering effect of Meperidine is primarily mediated by disproportionate reduction in the shivering threshold (1,2).

### **MATERIALS AND METHODS**

In this prospective, double blind, randomized study we included 60 patients (ASA physical status I or II), scheduled for orthopedic surgery. Institutional ethics committee clearance and informed consent from all patients were obtained prior to operation. It was explained that if shivering were to occur post operatively one of the two study drugs would be given to control it. The first sixty consecutive patients who developed shivering, either immediately or in the recovery room, following a general anesthetic, were included in this study. Patients with myocardial insufficiency (New York Heart Association III or IV), cardiac arrhythmia, muscle disease, Parkinson disease, fever ( $T > 37.5^{\circ}\text{C}$ ), needing vasoconstrictors perioperatively and received 2 adrenergic agonists for long term treatment, age above 65 years and those who had received pethidine or tramadol intra operatively were excluded from the study. General anesthesia was induced by thiopental (5mg/kg) accompanied by Midazolam (0.1 mg/kg) and Morphine (0.1 mg/kg) as premedication.

Atracurium (0.8 mg/kg) was given to facilitate orotracheal intubation. Intraoperatively, a mixture of halothane (0.6% - 1.5% end-tidal), nitrous oxide 50% and oxygen 50% was used to maintain anesthesia. Mechanical ventilation was used in all patients with end-tidal carbon dioxide tension pressure at 30-36 mmHg. After surgery and extubation, patients were transferred to the post anesthesia Care unit (PACU).

The post operative inquiry of patients and the evaluation of patients shivering score were assessed by an anesthesiologist and senior resident of anesthesiology in the PACU and injections of tramadol 10mg/ml and pethidine 5 mg/ml were prepared in 10ml syringe using a computer-generated random number list, and the syringe labeled serially. Patients received 0.1 ml/kg of the assigned drug intravenously over 90 seconds.

Neither staff monitoring the patient nor the patients were aware of group allocation. The code was broken at the end of the study period. Drug efficacy was assessed on the basis of a sustained decrease in the grade of shivering.

We evaluated all patients 5 minutes after injecting antishivering drug and categorized them to three groups; completely improved, partially improved and not improved , that the last group was patients who didn't response to any drug even after 15 minutes.

## RESULTS

There were no statistical inter-group differences in age, weight, pulse rate, respiratory rate, BP and duration of operation in this study. There was a female preponderance in both groups. (Table No.1) .

**Figure 1**

Table 1: patient Characteristics

	Gender		Age	Weight	Pulse Rate	Mean BP	Duration of operation
	M	F					
Pethidine(N:30)	5	25	30.5±3	60±3	84±4	80±10	95min±20
Tramadol(N:30)	6	24	35.2±2	54±4	87±4	84±11	105min±15

The number of patients who stopped shivering (completely improved) with in 5 minutes of receiving tramadol was 20 from 30 (66.66%), 8 from 30 had partial improvement (26.66%) , and 2 from 30 had no improvement (6.66%) even after 15 minutes. In the pethidine group, 16 from 30 (53.33%) improved completely after 5 minutes, 8 from 30 had partial improvement (26.66%) and 6 from 39 had no improvement (20%) .

We evaluated these data with chi square test and there was no significant difference between tramadol and pethidine for post operation shivering control; (Pv=0.294). (Table No.2).

**Figure 2**

Table 2: Percent of shivering improvement with pethidine or tramadol.

	SHIVERING		
	Completely improved	Partially improved	Not improved
pethidine	16/30 53.3%	8/30 26.66%	6/30 20%
Tramadol	20/30 66.66%	8/30 26.66%	2/30 6.66%

## DISCUSSION

Shivering, as nausea or vomiting , never becomes chronic and it is unlikely to kill a patient. However, in shivering post operative patients, left ventricular systolic work index and oxygen consumption index may be increased . It is therefore encouraging that some simple and inexpensive interventions are effective in the treatment of this adverse effect of anesthesia and surgery (4,9).

Shivering is a post anesthetic complication influenced by the

type of anesthetic used . Halothane, enflurane and isoflurane are associated with a high incidence of shivering (over 60%) .Opioid and nitrous oxide based anesthesia is associated with an incidence only half that of halothane \_ based maintenance of anesthesia (10).

Post anesthesia shivering is often preceded by core hypothermia but can occur with normothermia at the end of surgery (6). Equipment to maintain normothermia is effective in preventing shivering , but may be expensive and is not practical in all settings. Because shivering intensity is markedly reduced in elderly and frail patients, it is unlikely that shivering itself provokes serious adverse outcomes in these patients and shivering is rare in elderly patients . Likewise shivering is rarely associated with clinically important hypoxemia because hypoxia itself inhibits this response (11,12).

Morbid cardiac outcomes associated with mild perioperative hypothermia appear to be mediated by a mechanism more subtle than shivering , perhaps the associated marked increased in plasma catecholamine concentrations (13) . We hypothesized on the basis of review of the literature , that the most important risk factors for a patients developing intra operative hypothermia were the thermal status of the patient before surgery, the size and age of the patient the ambient O.R. temperature, the size of the surgical incision and the presence of neuropathy ( 5).

Many drugs have been used to treat shivering , including opioids , Doxapram , Tramadol , Ketanserin, Clonidine, Propofol, physostigmine and Nefopam,with opioids being the most extensively evaluated. Amongst the opioids, Pethidine has been found to be most efficacious ; Burke.L et al published in 1980 (14). Evidence suggested that Kappa-opioid receptors play an important role in the modulation of post operative shivering (10).This explains the greater efficacy of pethidine compared with equi\_analgesic doses of Mu-receptor opioid agonists such as Morphine , Fentanyl, Alfentanil and sufentanil (10,15).

Bhatnagar and Saxena believed that the analgesic potential of tramadol is mediated weakly through its effect on the Mu-opioid receptor, for which it has a low affinity and besides they published in 2001 that of greater importance maybe its effect on 5-HT3 and nor adrenergic receptors , with activation of descending inhibitory pathways producing anti nociception(10).

In 1999 Jhi-joung Wang published that the response rate

with pethidine is 83 to 93% (<sub>16</sub>). In the other hand in Bhatnagar study, the response rate to pethidine was only 80% after 49 minutes and more than 50% of patients receiving pethidine suffered a recurrence of shivering within 10 minutes of the initial response(<sub>10</sub>).

Bhatnagar et al also showed that the number of patients who stopped shivering within 10 minutes of receiving Tramadol was significantly higher than after pethidine (12/15 Vs 4/15,  $P < 0.05$ ) (<sub>10</sub>).

Dewitt et al in 1997 published that shivering stops 100% after 1-2mg/kg Tramadol injection and after that Bhatnagar in India found a lower percentage (80%) in response to tramadol (<sub>17</sub>).

Finally, Dewitte et al in 2002 showed that the shivering to vasoconstriction slope ratio of pethidine is greater than Tramadol (1.85 Vs 1.40), suggesting a special anti shivering action. Dewitte also explained in his paper that anti shivering properties correlate with vasopressor response to drugs that is +344 for pethidine and +346 for tramadol that are very close to each other. (<sub>18</sub>).

In our study we found that there is no significant difference between tramadol and pethidine for reducing post operative shivering ( $P = 0.294$ ). As you can see in literature some papers believe that pethidine is the most efficacious antishivering medication and the others say that tramadol is superior to pethidine, though Dewitte published that they have nearly similar properties on postoperative shivering.

That the better response of patients to tramadol in Bhatnagar study may be due to duration of operations since their cases were extensive head and neck surgery for malignancy that had undergone eight to ten hours, but our operations were between one to two hours.

Although no correlation could be demonstrated between core temperature and grade of shivering, we believe that core temperature may be an important factor influencing the rate of increase of temperature rise during shivering. Further research is required to understand the relation between core temperature and rate of temperature rise.

Thus the second reason for discrepancy in different studies can be due to operation room and core temperature in our study and the others; as Macario et al said that the second highest rated risk factor (after Neonatal period as a risk factor) for post operative shivering is ambient OR temperature and core temperature (<sub>5</sub>). None of the patients

in this study had adverse effects due to either pethidine or tramadol, however pethidine is considered to be associated with more postoperative nausea, vomiting, sedation and respiratory depression.

In conclusion, pethidine 0.5 mg/kg is as effective as tramadol 1mg/kg for post operative shivering during the first 15 minutes after injection, but tramadol is associated with less hemodynamic disturbances and less sedation or other side effects.

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