ORIGINAL ARTICLE

A Comparative Study on the Effect of Tramadol and Pethidine on Postoperative Shivering

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ABSTRACT

Background: In most operating and recovery rooms, shivering is controlled by the use of humidifiers, warming blankets, and inhalation of humidified heated oxygen. The other alternative treatment modality is controlling the shivering by various drugs. Pethidine is a well known anti shivering medication. In recent years tramadol has been introduced for controlling postoperative shivering. The aim of this study was to compare the anti shivering effect of tramadol with pethidine.

Method: In this randomized, double blind study we evaluated 60 patients with ASA class I or II who developed postoperative shivering in recovery room. Half of them treated with pethidine 0.5 mg/kg (0.1ml/kg) and the others treated with tramadol 1 mg/kg (0.1ml/kg). We compared the efficacy of tramadol and pethidine, and the grade of shivering 5 minutes after injection of the drugs. The patients were categorized to three groups; completely improved, partially improved, and not improved (those who had no improvement after 15 minutes).

Results: In this study 16 out of the 30 patients (53.3%) in pethidine group improved completely. In tramadol group 20 out of the 30 patients (66.66%) improved completely. 6.66% of patients in tramadol group and 20% of patients in pethidine group had no improvement. Evaluating the data with Chi-Square test showed no significant difference between the two drugs in controlling post operative shivering (p=0.294).

Conclusion: There is no significant difference between tramadol and pethidine in controlling postoperative shivering. Both the drugs are effective in controlling the postoperative shivering.

Keywords: Postoperative shivering; Tramadol; Pethidine

INTRODUCTION:

The incidence of postoperative shivering has been reported to be 40%, but it is now appeared to be less because most of the patients are kept normothermic before operation and opioids are administered more frequently and in larger doses than previously. Postoperative shivering is a potentially serious complication, which leads to increased oxygen consumption. But there are various treatments such as warming the skin surface or using a variety of drugs.

In homeothermic species a thermoregulatory system coordinates the defenses against cold and heat to maintain internal body temperature within a suitable range, thus optimizing normal physiologic and metabolic function.

Shivering is an unpleasant and frequent complication in the postoperative period.[1-3]. The origin of postoperative shivering is unclear, various mechanisms have been proposed though.[4] The combination of anesthetic-induced thermoregulatory impairment and exposure to a cool environment can lead the patients towards hypothermia in operating and recovery rooms.

Shivering may happen as a thermoregulatory response to hypothermia. Muscle hyperactivity with tonic or clonic patterns and different frequencies has been reported.[3] In the post operative period, muscle activity maybe increased even with normothermia, suggesting that other mechanisms rather than heat loss and subsequent decrease in core temperature may contribute to the development of shivering. These mechanisms include uninhibited spinal reflexes, postoperative pain, decreased 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%.[3]

After the surgery, 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 prolonged postanesthesia care unit stay.[5] In addition, the quality of patients' recovery may also be influenced because of shivering and thermal discomfort.[6,7] 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 disturbing especially to mothers during labor and delivery.[4]

In most operating and recovery rooms, shivering is controlled by the use of humidifiers, warming blankets, and inhalation of humidified heated oxygen. The other alternative treatment modality is controlling the shivering by various drugs.

Pethidine is a well known antishivering medication. In recent years tramadol that can release 5-hydroxy tryptamine and stimulates receptors has been introduced for controlling postoperative shivering. Tramadol inhibits the reuptake of 5-HT, norepinephrine, and dopamine and facilitates 5-HT release. Despite different degrees of opioid-like characteristics in preclinical tests, tramadol is not significantly reversible by naloxone in human. In human volunteers a high dose of naloxone only partially reversed the antishivering effect of tramadol.[8]

Cerebral 2 adrenoreceptors are thought to play a role in the attenuation of postoperative shivering by tramadol.[1,7]

This study was designed to compare the effects of tramadol with pethidine in controlling post operative shivering.

MATERIALS AND METHODS:

In this prospective, double blind, randomized study we included 60 patients (ASA physical status I or II), who were scheduled for orthopedic surgery in Chamran Hospital affiliated to Shiraz University of Medical Sciences. The sample size calculation was based on assuming the power of 80% and α=0.05, which was determined after consultation with the statistician. The research committee of the University approved the ethical issues. Informed consents were obtained from all patients prior to operation. Sixty consecutive patients who developed shivering, either immediately or in the recovery room, following a general anesthesia were included in this study. Patients with myocardial insufficiency (New York Heart Association III or IV), cardiac arrhythmia, neuromuscular abnormalities, fever (T>37.5°C), age above 65 years and those who needed vasoconstrictors preoperatively, received $_2$ adrenergic agonists for long-term treatment, those with specific history of convulsions, alcohol, opium or psychotropic drug abuse and those who had received pethidine, tramadol, or overt cold fluids or blood products during the operation 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. A mixture of isoflurane (0.6% - 2% end-tidal), nitrous oxide 50% and oxygen 50% was used to maintain the anesthesia during the operation. Mechanical ventilation was used in all patients with endtidal carbon dioxide tension pressure at 30-36 mmHg. After surgery and extubation, the patients were transferred to the Post Anesthesia Care Unit (PACU).

The patients were assigned to two groups to receive either pethidine 0.5mg/kg (0.1ml/kg) or tramadol 1 mg/kg (0.1ml/kg) intravenously over 90 seconds in case of shivering. Shivering scoring in this study was similar to that validated by Crossly et a[1,9] In this scaling system 0=no shivering, 1= piloerection or peripheral vasoconstriction but no visible shivering, 2= muscular activity in one muscle group, 3= muscular activity in more than one muscle group but no generalized shivering, and 4= the whole body shivering.

The postoperative inquiry of the patients and the shivering scores were assessed by an anesthesiologist and senior resident of anesthesiology who were blind to the patients' allocation in the PACU. The injections of tramadol (10mg/ml) and pethidine (5 mg/ml) were prepared in 10-ml syringes using a computergenerated random number list, and the syringes were labeled serially.

Neither the staff who monitored the patients nor were the patients aware of the group allocation. The code was broken at the end of the study. Only those patients with grades 3 or 4 of the shivering scaling system were treated. Drug efficacy was assessed on the basis of a sustained decrease in the grade of shivering by the anesthesiologist.

We evaluated all the patients 5 minutes after injecting the antishivering drug and categorized them to three groups; completely improved, partially improved, and those who did not respond to the drugs after 15 minutes (not improved). For those who did not respond to the first doses of the drugs after 15 minutes, other measures such as heat lamp and blanket were used. We also checked the patients for relapse of shivering but none of them who treated for shivering developed relapse.

RESULTS:

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

The number of patients who completely improved in 5 minutes after receiving tramadol was 20 (~67%). Eight out of the 30 patients in this group had partial improvement (~27%), and two (~7%) patients had no improvement even after 15 minutes. In the pethidine group, 16 out of the 30 patients (53%) improved completely after 5 minutes, eight (27%) patients had partial improvement, and six (20%) patients had no improvement.

Table 1: Patients characteristics

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

We evaluated these data with Chi-square test and there was no significant difference between tramadol and pethidine for control of post operation shivering (P=0.294) (Table 2).

Table 2: Number and percent of patients and degree of improvement after injection of pethidine or tramadol. (P value = 0.294)

	Shivering		
	Completely improved	Partially improved	Not improved
pethidine	16 (53.3%)	8 (26.66%)	6 (20%)
Tramadol	20 (66.66%)	8 (26.66%)	2 (6.66%)

Data are presented as meanstandard deviation.P values for comparison of all the variables in this table between the two groups were not significant.

No complications related to drugs such as nausea, vomiting, etc were detected.

DISCUSSION:

Shivering in post operative period can increase left ventricular systolic work index and oxygen consumption. It is therefore encouraging to find some simple and inexpensive interventions to treat this adverse effect of anesthesia and surgery.[4,10]

Shivering is a post anesthetic complication influenced by the type of anesthetic used during operation. Halothane, enflurane, and isoflurane are associated with high incidence of shivering (over 60%). Opioid and nitrous oxide based anesthesia have less incidence of shivering compared with that of halothane-based anesthesia.[11]

Post anesthesia shivering is often associated with 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. Likewise shivering is rarely associated with clinically important hypoxemia because hypoxia itself inhibits this response.[12,13]

Based on the previous studies, the most important risk factors for developing intraoperative hypothermia were the thermal status of the patient before surgery, the size and age of the patient, the ambient operating room 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, katanserin, clonidine, propofol, physostigmine, and nefopam. Opioids are the most extensively used drugs to control shivering. Amongst the opioids, pethidine is the most efficacious.[14]

Evidence suggested that Kappa-opioid receptors play an important role in the modulation of post operative shivering.[11] 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 receptors, for which it has a low affinity. They also believed that the effect of tramadol on 5-HT3, which can activate descending inhibitory pathways to produce anti nociception might be more important than its effect on adrenergic receptors.[11]

In 1999 Jhi-joung Wang reported that the response rate with pethidine was 83-93%.(16) On the other hand in Bhatnagar study, the response rate to pethidine was only 80% after 49 minutes and more than 50% of patients who received pethidine suffered a recurrence of shivering within 10 minutes of the initial response.[11]

Bhatnagar et al also showed that the number of patients who improved within 10 minuets of receiving tramadol was significantly higher than those who received pethidine (12/15 v 4/15, $P<0.05$).[11]

Dewitt et al in 1997 reported that post operative shivering stopped after 1-2mg/kg tramadol injection in 100% of their patients. But in Bhatnagar study response rate to tramadol injection was only 80%.[17]

Finally, Dewitte et al in 2002 showed that the shivering to vasoconstriction slope ratio of pethidine was greater than tramadol (1.85 v 1.40), suggesting a special anti shivering action. Dewitte also explained that anti-shivering properties correlate with vasopressor response to drugs that was +344 for pethidine and +346 for tramadol that were very close to each other.[1,8]

In our study we found that there was no significant difference between tramadol and pethidine for reducing postoperative shivering ($P=0.294$).

The better response to tramadol in Bhatnagar's study might be due to the duration of operations. Their cases were undergone extensive head and neck surgery for malignancy, which lasted 8-10 hours, but the operations in our study were about 1-2 hours.

The second reason for discrepancy in the results of our study with the other ones can be due to the temperature of operation room and the core temperature. Macario et al reported that the second highest risk factor (after neonatal period) for postoperative shivering is ambient temperature in operating rooms and the core temperature.[5]

None of the patients in this study had adverse effects due to either pethidine or tramadol, although pethidine has been considered to be associated with

more postoperative nausea, vomiting, sedation, and respiratory depression.

In conclusion, pethidine 0.5 mg/kg and tramadol 1mg/kg are effective to control postoperative shivering during the first 15 minutes after injection. And tramadol can decrease postoperative shivering as efficiently as pethidine.

REFERENCES:

1. Dewitte J,sessler DI. perioperative shivering . Anesthesiology 2002 96:467-84.
2. Dewitte J, deloof T, Deyelder j , Housmans Pr. Tramadol in the treatment of post anesthetic shivering .Acta anesthesiol scand ;1997 41:506-10.
3. Sessler Daniel I,temperture monitoring . In : Roland D.Miller, Anesthesia;6th edition ; Churchill livingstone, Philadelphia, USA ;2005.
4. Kranke P, Tberhart LU, Roewer N , Tramer Mr. .Pharmacological treatment of post operative shivering .A quantitative systematic review of randomized controlled trials .Anesth Analg 2002 94:453-60.
5. Macario A, Dexter F. What are the most important risk factors for a patients developing intraoperative hypothermia .Anesth Analg 2002 ; 94:215-20.
6. Buggy Dy, crossley AWA . Thermoregulation , mild perioperative hypothermia and post anaesthetic shivering. Br J Anaesth 2000;84:615-28.
7. Piper swen N , Rohm . K. D, Maleck W. H et al . Dolasetion for preventing postanesthetic shivering. Anesth Analg 2002 ; 94:106-11.
8. De witte JL, Kim J-s , Sessler DI, Bastan mehr H, Bjorksten AR. Tramadol reduces the shivering , vaso constriction and sweating threshold. Anesth Analg 1998;87:173-9.
9. Crossly AW, Mahajan RP. The intensity of postoperative shivering is not related to auxiliary temperature. Anesthesia 1994; 49(3):205-7
10. Bilotta F , Pietropaoli P, La RosaI et al . Effects of shivering prevention on haemodynamic and metabolic demands in hypothermic postoperative neurosurgical patients. Anaesthesia 2001 ; 56:514-9.
11. Bhatnagar S, Saxena A , Kannan TR, Punj J, Panigrahi M , Mishra S. Tramadol for post operative shivering .A double-Blind comparison with pethidine. Anaesth Intensive care 2001;29:149-154.
12. Frank SM, Fleisher LA, olson KF, Gorman RB , Higgins MS, Breslow MJ, Sitzmann JV, Beattie C . Multivariate determinants of early post operative oxygen consumption in elderly patients . Anesthesiology1995;83:241-9.
13. Iwashita H , Matsukawa T, ozaki M, Sessler DI ,Imamura M, Kumazawa T . Hypoxemia decreases the shivering threshold in rabbits anesthetized with 0.2 MAC isoflurane . Anesth Analg 1998;87:1408-11.
14. Burke HH , Aisner J , Fortner CL, Wiernik PH, Meperidine for the treatment of shaking chills and fever . Arch Intern Med 1980;140: 483-488.
15. Alfonsi P , Sessler DI, Dumanoir B et al . The effects of meperidine and sufentanil on the shivering threshold in post operative patients. Anesthesiology 1998; 89: 43-48.
16. Jhi-Joung Wang , Shung Tai Ho , Shih Chun Lee et al . A comparison among naluphine, meperidine and placebo for treating post anesthetic shivering . Anesth Analg 1999;88:686-689.
17. Dewitte J, Deloof T , Veyleder J De , Housmans PR . Tramadol in the treatment of post anaesthesia shivering . Acta Anaes thesiol scand 1997;41:506-510.