



A randomized controlled trial to compare the efficacy of pethidine and tramadol for postoperative shivering

Maria Arshad¹, Liaqat Ali², Aaifa Khalid¹,
Muhammad Nauman Ahmad³, Arshad Taqi⁴

ABSTRACT

¹Senior Registrar, Dept of Anesthesiology, Jinnah Hospital, Lahore (Pakistan)

²Associate Professor Allama Iqbal Medical College, Lahore (Pakistan)

³Professor of Anesthesiology, Sheikh Zaid Medical College, Lahore (Pakistan)

⁴Rashid Latif Medical College, Lahore (Pakistan)

Correspondence: Dr. Liaqat Ali, 419-Karim Block Allama Iqbal Town, Lahore (Pakistan); Phone: +923214364449; E-mail: aliliaqatdoc@gmail.com

Received: 25 Jul 2017

Reviewed: 14 Nov, 29 Nov 2017

Corrected: 16 Nov, 9 Dec 2017

Accepted: 9 Dec 2017

Objective: Postoperative shivering is common problem and it occurs in a large percentage of patients recovering from general or regional anesthesia, delaying recovery and discharge from hospital. Our objective was to compare the efficacy of pethidine and tramadol in the treatment of postoperative shivering in patients undergoing elective surgery under GA.

Methodology: This double blind randomized controlled trial was conducted from January to June 2014. By non-probability consecutive sampling method, a sample size of 40 patients in each group was used. Patients with fever, past history of convulsions, any neuromuscular abnormality, and those who received vasoconstrictors, adrenergic agonists, pethidine, tramadol, cold fluids or massive blood transfusion during surgery were excluded. Patients with postoperative shivering were randomly allocated in two groups using a lottery method. Patients in Group T received tramadol 1.0 mg/kg IV and patients in Group P received pethidine 0.5 mg/kg in 10 ml syringe slowly over 5 min. All patients were examined after 15 min of the start of intravenous drug to determine the efficacy of the drug.

Results: Tramadol appeared to be effective in 90% patients with postoperative shivering while pethidine was effective in 77.5 % patients ($p > 0.05$).

Conclusion: Both pethidine 0.5 mg/kg and tramadol 1.0 mg/kg given IV slowly over 5 min were effective in controlling post-anesthesia shivering following general anesthesia in majority of patients.

Key words: General anesthesia; Pethidine; Postoperative shivering; Tramadol

Citation: Arshad M, Ali L, Khalid A, Ahmad MN and Taqi A. A randomized controlled trial to compare the efficacy of pethidine and tramadol for postoperative shivering. *Anaesth Pain & Intensive Care* 2017;21(4):427-431

INTRODUCTION

Postoperative shivering is a common complication occurring in 5-65% of patients recovering from general anesthesia (GA) and 33% after regional anesthesia.¹ It is ranked as 6th most important problem of current anesthesiology practice.² Shivering may occur as thermoregulatory response to hypothermia, or muscle hyperactivity; however, in the postoperative period muscle activity may be increased even with normothermia, suggesting that mechanisms other than heat loss may contribute to the development of

shivering. These include uninhibited spinal reflexes, postoperative pain, decreased sympathetic activity, pyrogen release, adrenal suppression and respiratory alkalosis.³

Currently, pethidine is the most frequently used drug for the control of post anesthesia shivering. Its efficacy is reported to be 53-100%.^{3,4} Kappa-opioid receptors play an important role in the modulation of postoperative shivering.⁵ This explains the greater efficacy of pethidine compared with equi-analgesic doses of mu-receptor agonists such as morphine,

pethidine and tramadol for postoperative shivering

fentanyl, alfentanil and sufentanyl.⁶

Tramadol has a weak agonist effect on the mu receptor. It exerts a modulator effect on central monoaminergic pathways, inhibiting the neuronal uptake of noradrenaline (pain stimulant) and serotonin in spinal cord and encourages hydroxytryptamine secretion which affects body temperature regulation centre. It has less side effects like respiratory depression, nausea and vomiting than other μ -receptor agonists.⁶ Tramadol has been used to control postoperative shivering with reported efficacy of 66.66% – 82.5%. Tramadol has also been compared with pethidine but with inconsistent results.⁷ The rationale of our study was to compare the efficacy of pethidine and tramadol in controlling postoperative shivering after GA because of controversial results in previous studies regarding the efficacy of both drugs.^{2,7}

Our objective was to compare the efficacy of pethidine and tramadol in the treatment of postoperative shivering in patients undergoing elective surgery under GA. Our hypothesis was that tramadol was more effective than pethidine in the treatment of postoperative shivering.

METHODOLOGY

Operational Definitions:

Shivering was defined as readily detectable tremors of face, jaw, head, trunk and extremities lasting longer than 15 seconds, occurring in patients after recovery from GA.

Grading of shivering was done as follows and was declared on the basis of clinical examination:

Grade 0: No shivering

Grade 1: One or more of the following: Piloerection, peripheral vasoconstriction, peripheral cyanosis with, 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

Efficacy was determined in terms of improvement in grade of shivering. The drug was considered effective if there was improvement in shivering of at least two grades from baseline within 15 min of starting IV drug injection.

Both drugs were independent variables while control

of shivering was dependent variables.

This double blind randomized control trial was conducted from January to June 2014 at the Department of Anesthesiology, Sheikh Zaid Hospital Lahore. By a consecutive (non-probability) sampling method a sample size of 80 was used based on previous studies which indicated 53.5% efficacy of pethidine³ and 83.5% efficacy of tramadol⁷ for the control of shivering after GA, with 95% confidence interval, 5 % level of significance and 80% power. The WHO sample size calculator was used.

All patients who underwent elective surgery under GA and developed shivering postoperatively of grade 2, 3 or 4 were included. Patients were ASA – 1 and II classification, between age group 18-60 years and of either gender.

Following patients were excluded from the study; patient with fever or allergy to any of the study drug, any neuromuscular abnormality on history, those who had received vasoconstrictors and adrenergic agonists on medical records, and past history of convulsions. Patients who received pethidine, tramadol, cold fluids (fluids without warming) or massive blood transfusion (≥ 3 transfusions or blood loss more than 50% of total blood volume intraoperatively) or who had temperature $< 36.5^{\circ}$ C at extubation were also excluded.

After approval from hospital ethical and research committee, all patients meeting the inclusion criteria were recruited from the outpatient. The purpose and benefits of the study were explained to all and they were assured that the study was done for research and informed consent was taken.

All the patients were subjected to detailed anesthesia assessment. Anesthesia technique was standardized using propofol 2 mg/kg, atracurium 0.5 mg/kg, ketorolac 0.5 mg/kg, nalbuphine 0.1 mg/kg, isoflurane 2% with oxygen and air. The trachea of all patients was intubated with an endotracheal tube. Ringer lactate was used for intra-operative fluid management and operating room temperature was kept at 20° C. Oxygen saturation, heart rate and blood pressure was monitored and oxygen was provided to all patients through facemask at 5 L/min in the recovery room. First 80 patients who developed shivering after recovery from anesthesia in recovery room were included in the study. They were randomly allocated in two groups of 40 each by lottery method. Grade of shivering was assessed by a senior anesthesiologist who was blinded to the drug used. Drugs were made by a primary anesthetist in 10 ml syringes. All

patients were blinded to the drug used for the control of shivering.

Patients in Group T were given IV tramadol 1 mg/kg slowly over 5 min and patients in Group P were administered IV pethidine 0.5 mg/kg slowly over 5 min. All patients in both the groups were re-examined after 15 min of the start of intravenous drug and grade of shivering was re-assessed. The drug was considered efficient if there was improvement in shivering by 2 grades.

All the above mentioned information was recorded on a pre-designed proforma. Strict exclusion criteria were followed to control confounders and bias in the study results. No patient dropped out. Sedation, nausea and vomiting were also noted in both groups.

Data Analysis Procedure: Data were analyzed by using SPSS version 20. Quantitative variables like age were described as mean \pm SD. Categorical variables like gender and efficacy were described as frequencies and percentages. Chi square test was used to compare the efficacy in both the groups while keeping $p < 0.05$ as significant.

RESULTS

A total of 80 patients were included in the study (40 in each group). There was no statistical difference of age and gender between the two groups (Table 1).

No significant respiratory depression was noted in any patient. Tramadol was effective in controlling shivering in 36 (90%) patients and pethidine in 31 (77.5%) patients ($p = 0.13$). The baseline grades of shivering and 15 min after administration of study drugs is shown in Table 2 and 3.

The difference was not statistically significant. Two patients in pethidine group developed nausea, but this did not need any further treatment.

DISCUSSION

The results of our study did not show a statistically significant difference between the efficacy of pethidine and tramadol in controlling postoperative shivering. Dhimar and colleagues

found tramadol and pethidine to be equally effective as well. However, tramadol stopped shivering sooner than pethidine. At 5 min tramadol was effective in all patients, while pethidine was effective in 51% of the cases. Pethidine was effective in all patients at 20 min. They also found the recurrence rate of shivering to be lower in tramadol group and more nausea vomiting in pethidine group. Tramadol was declared qualitatively superior by the authors of this study but it was conducted in patients receiving regional anesthesia and dose of pethidine was 1mg/kg.⁴

In another study of 150 patients, tramadol 1 mg/kg and 2 mg/kg were associated with 4% and 2% shivering respectively after GA while 48% patients experienced shivering in placebo group. There was no statistically significant difference of adverse events between two doses of tramadol.⁸ Talakoub and colleagues found that tramadol 0.5 mg/kg and pethidine 0.5 mg/kg were equally effective for the control of shivering after caesarean section under regional anesthesia. However time to control shivering was significantly less with tramadol. Tramadol was associated with a higher incidence of somnolence, nausea and vomiting.⁹

A Seifi et al. also found pethidine and tramadol equally effective in treating post anesthesia shivering in patients recovering from GA³. Sharma and

Table 1: Demographic parameter of patients

Variables	Group P	Group T	Statistics
Mean age (y)	36.57 \pm 9.86	37.05 \pm 9.95	$p > 0.05$
Sex F	16	19	35 (43%) $p > 0.05$
M	24	21	45 (56.3%) $p > 0.05$

Table 2: Baseline grade of shivering before study drug administration [Data given as n (%)]

Baseline grade of Shivering	Treatment groups		Total
	Tramadol	Pethidine	
2	9 (22.5)	5 (12.5)	14 (17.5)
3	17 (42.5)	17 (42.5)	34 (42.5)
4	14 (35)	18 (45)	32 (40)
Total	40 (100)	40 (100)	80 (100)

Table 3: Grade of shivering after 15 min of study drug administration

Baseline grade of Shivering	Treatment groups		Total
	Tramadol	Pethidine	
0	26 (65)	22 (55)	48 (60)
1	10 (25)	9 (22.5)	19 (23.75)
2	2 (5)	3 (7.5)	5 (6.25)
3	2 (5)	6 (15)	8 (10)
Total	40 (100)	40 (100)	80 (100)

pethidine and tramadol for postoperative shivering

colleagues, however, found pethidine to be more effective than tramadol at 10, 15, 20 and 30 min while there was no statistically significant difference at 5 and 25 min after giving study drugs. Pethidine was associated with more sedation and tramadol caused significant nausea and vomiting.¹⁰

We used 1.0 mg/kg tramadol and 0.5 mg/kg pethidine; this is in contrast with Sharma¹⁰ who used 1.0 mg/kg pethidine to demonstrate the superiority of pethidine in controlling shivering. Side effects of pethidine in higher dose are likely to preclude its use in clinical setting.

Shivering increases oxygen consumption as much as 5 folds, decreases arterial oxygen saturation and has been shown to correlate with an increased risk of myocardial ischemia, angina and wound pain. Shivering increases metabolic rate up to 400%.¹¹ Postoperative shivering may delay hospital discharge and is a common cause of discomfort in patients recovering from anesthesia.¹² Different drugs like pethidine, fentanyl, morphine, ketamine, tramadol, granisetron, clonidine and dexmedetomidine have been tried to control postoperative shivering.^{1,3,13,14} Tramadol is a relatively safer drug than pethidine regarding sedation and respiratory depression^{6,8,15} while controversial regarding nausea and vomiting with both drugs.^{6,9,10}

Our study has some limitations; the effect was measured at only one time i.e. 15 min post anesthesia, therefore we cannot comment on the efficacy of drugs before or after this period. We did not measure the temperature of our patients postoperatively, duration of anesthesia and type of surgery; all of which could introduce a bias in the results. Doses of the drugs were also selected arbitrarily, keeping in view their safety profile and doses used in clinical settings. We

demonstrated a trend towards greater efficacy with tramadol but this did not reach statistical significance. This could be due to a Type II error.

There are a few unanswered questions; Onyekwulu and colleagues demonstrated the superiority of 0.5 mg/kg over 0.25 mg/kg tramadol in controlling shivering after cesarean sections, a comparison of 0.5 mg/kg with 1.0 mg/kg would help in determining an effective dose that reduces the side effects of tramadol while effectively controlling shivering.¹⁶ A larger study may unmask a true difference in the effect of two agents, which was not evident in our study. Effect of body temperature on control of shivering needs further studies as well as recurrence of shivering after the initial success in treatment.

Pethidine being the most frequently used drug for postoperative shivering¹⁷ is not consistently available in all the places owing to its status as a controlled narcotic drug. Besides, its unfavorable side effect profile is a deterrent to its use in all settings. A search for an alternative that is readily available and has a better safety profile makes tramadol a likely candidate. Its efficacy is comparable to pethidine in the studies conducted so far.

CONCLUSION

This study found IV tramadol 1mg/kg administered over 5 min to be equally effective in controlling post anesthesia shivering compared to IV pethidine 0.5 mg/kg administered over 5 min.

Conflict of interest: No conflict of interest of any author in this study

Authors' contribution:

MA. Conduct of study and literature research
LA. Manuscript writing and literature research
AK. Conduct of study
MNA. Manuscript concept and review of data.
AT. Manuscript review and editing

REFERENCES

1. Elvan EG, Uzan S, Karabulut E, Coskun F, Aypar U. Dexmedetomidine and postoperative shivering in patients undergoing elective abdominal hysterectomy. *Eur J Anaesthesiol.* 2008 May;25(5):357-64. doi: 10.1017/S0265021507003110. [PubMed]
2. Bhukal I, Solanki SL, Kumar S, Jain A, Pre-induction low dose pethidine does not decrease incidence of postoperative shivering in laparoscopic gynecological surgeries. *J Anaesthesiol Clin Pharmacol.* 2011;27(3): 349–353. [Free full text]
3. Seifi A, Avestimehr S, Mowla A, Kamalipour H. A comparative study of the effect of tramadol and pethidine on postoperative shivering. *The Internet Journal of Anesthesiology.* 2008;16(2) DOI: 10.5580/1817. [Free full text]
4. Dhimar AA, Patel GM, Swadia VN. Tramadol for Control of Shivering (Comparison with pethidine). *Indian J Anaesth.* 2007;51(1):28-31. [PubMed] [Free full text]
5. Burks LC, Aisner J, Fortner CL, Wiernik PH, Meperidine for the treatment of shaking chills and fever. *Arch Intern Med* 1980;140(4):483-488. [PubMed]
6. Bhatnagar S, Saxena A, Kannan TR, Punj J, Panigrahi M, Mishra S. Tramadol for postoperative shivering. A double-Blind comparison with pethidine. *Anaesth Intensive care* 2001;29:149-154. [PubMed] [Free full text]
7. Angral R, Wani AA, Kapoor BB. Tramadol and postoperative shivering in patients undergoing open and laparoscopic cholecystectomy under general anaesthesia. *South Afr J Anaesth Analg* 2012;18(2): 111-14. [Free full text]
8. Mathews S, Al Mulla A, Varghese PK, Radim K, Mumtaz S. Postanaesthetic shivering-- a new look at tramadol. *Anaesthesia*, 57, 4, 2002, pp 394-8. [PubMed] [Free full text]
9. Talakoub R, Noori Meshkati Sh. Tramadol versus meperidine in the treatment of shivering during spinal anaesthesia in cesarean section. *JRMS*, 11, 3, 2006, pp 151-155. [Free full text]
10. Sharma M. Kharbuja K, Khadka B, Comparison of pethidine and tramadol for the control of shivering in patients undergoing elective surgery under spinal anaesthesia. *Journal of Lumbini Medical College.* 2016;4(2):64-7. [Free full text]
11. Iqbal A, Ahmed A, Rudra A, Sengupta S, Das T, Roy D et al. Prophylactic Granisetron Vs Pethidine for the Prevention of Postoperative Shivering: A Randomized Control Trial. *Indian J Anaesth.* 2009;53(3):330–334. [PubMed] [Free full text]
12. Daniel I. Sessler. Perioperative Thermoregulation. In: Silverstein J, Rooke A, Reves, JG, McLeskey CH, editors. *Geriatric anesthesiology*. 2nd ed. New York (NY): Springer; 2007. p107-122.
13. Norouzi M, Doroodian MR, Salajegheh S. Optimum dose of ketamine for prevention of postanesthetic shivering; a randomized double-blind placebo-controlled clinical trial. *Acta Anaesthesiol Belg.* 2011;62(1):33-6. [PubMed]
14. Shukla U, Malhotra K, Prabhakar T. A comparative study of the effect of clonidine and tramadol on post-spinal anaesthesia shivering. *Indian J Anaesth.* 2011;55(3): 242–246. [Free full text]
15. Javaherforoosh F, Akhondzadeh R, Aein KB, Olapour A, Samimi M. Effects of Tramadol on shivering post spinal anaesthesia in elective cesarean section. *Pak J Med Sci* 2009;25(1):12-17. [Free full text]
16. Charuluxananan S, Trakulthong C, Areejunthawa J, Kooanantkul J, Jarukasetporn C, Patradul C, et al. Pharmacological treatment of post-anesthetic shivering: A systematic review and meta-analysis. *Asian Biomedicine.* 2009;3(4):351-363. [Free full text]

