Original Research

The Effect of Intravenous Ketamine and Pethidine on The Incidence of Shivering in Patients Undergoing Tonsillectomy Surgery: A Double-Blind Randomized Clinical Trial Study

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Abstract

Background: Postoperative shivering is a common complication after general anesthesia. Given that shivering is an unpleasant feeling and experience for the patient, its prevention is of particular importance for the treatment team. Despite the use of various medications, postoperative shivering is still seen with high prevalence.

Method: In this double-blind randomized clinical trial study, 224 patients undergoing tonsillectomy surgery with ASA I and II who were hospitalized in Shahid Mohammadi Hospital, Bandar Abbas in 2024 were included in the study. The patients were divided into three groups using a random number table; ketamine, pethidine, and control. The volume of the syringe for administering the drugs was the same in all three groups. After extubation, the incidence of shivering in recovery was assessed and recorded by the anesthesiologist.

Results: The obtained results show that compared to others, divorced teenagers had significantly higher fear, behavioral avoidance, social avoidance, physiological discomfort and total social anxiety index. There was no statistically significant difference between obsessive beliefs and its factors in divorced teenagers and others.

Conclusion: The results of the present study showed that the use of pethidine showed better performance in reducing side effects by significantly reducing the incidence of shivering. These findings emphasize that the appropriate choice of drug can help improve the patient experience and reduce unpleasant complications after surgery.

Keywords: Ketamine, Pethidine, Shivering, Tonsillectomy.

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Introduction

Postoperative shivering is a common complication after general or regional anesthesia with a prevalence of 5-65% or an average of 40% (2-1). Postoperative shivering is a phenomenon that is temperature regulated (a physiological response to anesthesia that causes central hypothermia), or is caused by the release of cytokines through the surgical procedure (3-4). Various mechanisms have been described for the occurrence of postoperative shivering. Postoperative shivering is usually, but not always, associated with hypothermia; therefore, one of the mechanisms for the occurrence of postoperative shivering is thermoregulatory mechanisms (5). Several methods, both pharmacological and non-pharmacological, have been proposed to prevent the occurrence of this complication (6). Non-pharmacological methods mainly include keeping the patient warm with various methods, and pharmacological methods that are most commonly used include; the use of drugs such as clonidine, pethidine, tramadol-pethidine and nefopam is (7). Given that shivering is an unpleasant feeling and experience for the patient, its prevention is of particular importance for the treatment team (8). Pethidine is the main drug for the treatment or prevention of shivering (9-11), which controls shivering by acting on K receptors and directly affecting the thermoregulatory center, and its beneficial role has been proven in many studies, but it has side effects such as respiratory depression, nausea, vomiting and hallucinations (12). Ketamine is a phencyclidine derivative that acts primarily as an NMDA receptor antagonist. Ketamine produces hemodynamically stable anesthesia through central sympathetic stimulation without affecting respiratory function (13). Ketamine, a competitive NMDA receptor antagonist, has been reported to have an inhibitory effect on postoperative shivering (14-15). However, the use of ketamine can cause psychomimetic side effects, such as drowsiness or hallucinations, and despite experimental studies in animals, the use of ketamine in humans has yielded variable results (16). Talebi et al. compared the effects of pethidine and ketamine in preventing shivering after tonsillectomy in children. The results of the present study showed that there was no significant difference between the ketamine and pethidine groups in terms of the prevalence of postoperative shivering during recovery, but given the higher incidence of complications in the ketamine group, pethidine is still considered a more appropriate choice (17). Despite the use of various drugs, postoperative shivering is still seen with a high prevalence. Therefore, the present study was conducted to compare the effects of intravenous ketamine and pethidine on the incidence of shivering in patients undergoing tonsillectomy.

Method

In this double-blind randomized clinical trial, 224 patients undergoing tonsillectomy with ASA I and II who were hospitalized in Shahid Mohammadi Hospital, Bandar Abbas in 2024 were included in the study. The sampling method was carried out by convenient randomization using a random number table. After approving the plan and obtaining the code of ethics from the ethics committee, patients voluntarily entered the study if they had informed consent from their parents. Inclusion criteria included; patients with ASA I and II and patients aged 6 to 15 years. Patients were excluded from the study if they had a history of neurological disease, a history of epilepsy, heart diseases, a history of taking neuroleptics, coagulation problems, and were allergic to pethidine or ketamine. Patients were divided into three groups; ketamine, pethidine, and control based on a random number table. The demographic characteristics of the patients including; age, gender, height, and weight were recorded. The method of induction and maintenance of anesthesia was the same in all patients. To induce anesthesia in all patients, midazolam at a dose of 0.05 mg/kg, fentanyl at a dose of 2 μg/kg, propofol at a dose of 2 mg/kg, and atracurium at a dose of half an mg/kg were administered intravenously and under monitoring. The time of administration of the desired drugs in all three groups was immediately after the end of the operation and before the removal of the endotracheal tube. Thus, the first group was injected with pethidine at a dose of half an mg/kg intravenously in a volume of 2 cc, the second

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group with ketamine at a dose of half a mg/kg intravenously in a volume of 2 cc, and the third group (control group) with normal saline in a volume of 2 cc. The volume of the syringe for administering the drugs was the same in all three groups. After extubation, the occurrence of shivering during recovery was evaluated and recorded by the anesthesiologist. Data analysis was performed using SPSS software version 21 and descriptive statistics (mean, standard deviation, number and percentage) and inferential statistical tests (Chi-square and ANOVA) at a significance level of $P<0.05$.

Results

The study population consisted of 224 participants who were divided into three groups (control, ketamine, pethidine). Demographic and clinical characteristics of the participants in the three groups were compared. The results showed that there was no significant difference in gender distribution between the groups (P=0.180) (Table 1).

Analysis of variance (ANOVA) showed that there was no significant difference in age between the three groups (P=0.3490). The mean age of the control group (7.99 ± 3.53 years) was not significantly different from the ketamine group (7.52 ± 3.11 years) and the pethidine group (7.24 ± 2.81 years). Pairwise comparisons after performing the Tukey test and the Bonferroni correction also showed no significant difference between the groups. The majority of patients in all groups did not experience shivering (83.8% in the control group, 88% in the ketamine group, and 96.0% in the pethidine group). There was a significant difference in the incidence of shivering between the groups (P=0.049). The results indicated that the pethidine group had the lowest incidence of shivering (4.0%), which was lower than the ketamine and control groups.

Discussion

Extubation of the patient is an essential procedure in anesthesia when endotracheal intubation is required, as well as in the intensive care unit, when mechanical ventilation support is required. Extubation, which is performed safely in most cases, can cause significant challenges and complications. Complications associated with tube removal can be severe and lead to major complications and mortality (18). Further investigation of the incidence of postoperative shivering in patients undergoing tonsillectomy with different anesthetic drugs showed that there was a significant difference in the incidence of shivering between the groups (p=0.049). The results indicated that the pethidine group had the lowest incidence of shivering (4.0%), which was lower than the ketamine and control groups. Rahimi et al. in their study compared the pharmacological effect of pethidine with ketamine, Alfentanil and Sufentanil used during anesthesia in the treatment of shivering after anesthesia as a suitable alternative to pethidine in cases where its use is prohibited. According to the reported results, no significant difference was observed between the studied groups in relation to shivering (19). These findings are different from the present study. The reasons for this difference can be attributed to the different time of administration of the studied pethidine. Pazoki et al. in their study compared the effect of different doses of ketamine and pethidine in reducing shivering after elective cesarean section. Based on the results reported, the reduction in the amount and severity of shivering in the pethidine group was greater than in the ketamine group at 5 mg/kg, indicating that pethidine is better than ketamine (20). These findings are similar to the present study.

In a study by Hasannasab et al. on the prophylactic effect of doxapram, ketamine, and meperidine on postoperative shivering conducted on 120 patients aged 20 to 45 years under general anesthesia, 20 mg of meperidine was injected intravenously in the first group, 0.25 mg/kg of ketamine in the second group, and 0.25 mg/kg of doxapram in the third group immediately before wound closure. One patient (5.2%) in the meperidine group, three patients (5.7%) in the ketamine group, and four patients (10%) in the doxapram group experienced postoperative shivering. This study showed that meperidine, ketamine, and doxapram are equally effective in preventing postoperative shivering (21). These findings are similar to the present study because in the present study, both ketamine and pethidine were effective in reducing shivering, but the effectiveness of pethidine was reported to be greater. In a study

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by Bhukal and colleagues on the effect of pethidine on the prevention of postoperative shivering in 60 women aged 25 to 35 years undergoing laparoscopic gynecological surgery, pethidine 0.3 mg/kg was administered intravenously in the first group, pethidine 0.5 mg/kg in the second group, and normal saline was administered intravenously just before induction of anesthesia. Six patients (30%) in the first group, three patients (15%) in the second group, and nine patients (45%) in the third group experienced postoperative shivering. This study showed that low doses of pethidine do not play a significant role in preventing postoperative shivering (22). In the present study, pethidine was administered intravenously at a dose of half an mg/kg in a 2 cc bath and showed significant efficacy in reducing shivering.

A study by Ayatollahi et al. compared the prophylactic use of pethidine and ketamine to prevent post anesthetic shivering and was conducted on 120 patients aged 20 to 50 years who were under general anesthesia for endoscopic sinus surgery. In the first group, meperidine 0.4 mg/kg, in the second group, ketamine 0.3 mg/kg, in the third group, ketamine 0.5 mg/kg, and in the fourth group, normal saline was administered to the patient 20 minutes before the end of the surgery. In the first group (pethidine), no patients had post anesthetic shivering, in the second group (ketamine 0.3), three patients, in the third group (ketamine 0.5), and in the placebo group, nine patients had post anesthetic shivering. The difference between the first three groups and the normal saline group was significant, but the difference between the first three groups was not significant. The rate of hallucinations was lower in the lower-dose ketamine group than in the higher-dose ketamine group (23). These findings are similar to the present study. It seems that multiple mechanisms are effective in producing or at least inhibiting postoperative shivering, and perhaps the effects of pethidine in reducing shivering can be attributed to its non-opioid effects in addition to its effect on kappa receptors, and perhaps the reason for the effect of ketamine on reducing shivering is also due to the non-opioid effects of this drug (24-25).

Conclusion

The results of the present study showed that the use of pethidine showed better performance in reducing side effects by significantly reducing the incidence of shivering. These findings emphasize that appropriate drug selection can help improve the patient experience and reduce unpleasant complications after surgery.

Limitations:

This study had limitations that should be considered in interpreting the results. First, the sample size was relatively small, which may have limited sufficient statistical power to detect some subtle differences. Second, the study focused only on patients undergoing tonsillectomy, and the results may not be generalizable to other surgeries or clinical populations. These limitations could affect the validity and generalizability of the results.

Recommendations:

To improve future studies, it is suggested that the sample size be increased to provide higher statistical power to detect significant differences. Also, conducting similar studies in other types of surgeries and diverse populations could help in the generalizability of the results. Assessing the impact of individual factors such as pain tolerance and different responses to medications could also provide more accurate insights. Including a longer follow-up period to examine the long-term effects of medications on postoperative complications is also essential. Finally, the use of more sophisticated tools to measure complications and outcomes could increase the precision of the findings.

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Authors Contributions:

The author contributed to the data analysis. Drafting, revising and approving the article, responsible for all aspects of this work.

Ethical Consideration

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References

1. Dal D, Kose A, Honca M, Akinci SB, Basgul E, Aypar U. Efficacy of prophylactic ketamine in preventing postoperative shivering. B J of Anaesth; 20058(5): 1-4.
2. Bahattaeharya PK, Bhatlacharya L, Jain RK, Agarwal RC. Post anaesthesia shivering. Indian J of Anaesthesia; 200347(2): 88-93.
3. Mathews S, Al Mulla A, Varghese PK, Radim K, Mumtaz S. Postanaesthetics shivering a new look at tramadol. Anesthesia 2002,57: 394-8.
4. Powell RM, Buggy DJ. Ondansetron given befor induction of anesthesia reduce shivering after general anesthesia. anesth analg 2000:90:1423- 1427.
5. Lopez MB. Postanaesthetic shivering - from pathophysiology to prevention. Rom J Anaesth Intensive Care. 2018 Apr;25(1):73-81.
6. Kamran, Z., Nazemroaya, B. 'The intravenous injection of pethidine and dexmedetomidine in the prevention of cesarean postoperative shivering under spinal anesthesia: A double-blind clinical trial', The Iranian Journal of Obstetrics, Gynecology and Infertility. 2022; 25(6), pp. 52-60.
7. Jain A, Gray M, Slisz S, Haymore J, Badjatia N, Kulstad E. Shivering treatments for targeted temperature management: a review. The Journal of Neuroscience Nursing 2018; 50(2):63.
8. Heidari SM, Sabzeali M. Preemptive Effect of Pethidine, Ketamine and Ondansetron on Post-Operative Shivering in Patients undergoing Abdominal Surgery with General Anesthesia. J Isfahan Med Sch 2016; 34(371): 90-7
9. Malekshoar, M., Vatankhah, M., Rasekh Jahromi, A., Ghasemloo, H., Mogharab, F., Ghaedi, M., Abiri, S., Taheri, L., Roostaei, D., Kalani, N., Hatami, N., Sadeghi, S. E. Shivering control in women under spinal anesthesia: A narrative review on the role of drugs. The Iranian Journal of Obstetrics, Gynecology and Infertility, 2021; 24(7): 61-69.
10. Sessler DI. Temperature regulation and monitoring. In: Miller RD, Editor. Miller's anesthesia. Philadelphia, PA: Elsevier Health Sciences; 2010. p. 1533-57.
11. Kelsaka E, Baris S, Karakaya D, Sarihasan B. Comparison of ondansetron and meperidine for prevention of shivering in patients undergoing spinal anesthesia. Reg Anesth Pain Med 2006; 31(1): 40-5.
12. Wrench IJ, Cavill G, Ward JE, Crossley AW. Comparison between alfentanil, pethidine and placebo in the treatment of post-anaesthetic shivering. Br J Anaesth 1997; 79(4): 541-2
13. Shetabi H, Naghibi K, Peyman A, Norouzi H. Comparison of the effectiveness of intranasal ketamine compared with intravenous ketamine in controlling pain during cataract surgery. Tehran Univ Med J 2022; 80 (8) :642-649
14. 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.
15. Gecaj-Gashi A, Hashimi M, Sada F, Salihu S, Terziqi H. Prophylactic ketamine reduces incidence of postanaesthetic shivering. Niger J Med 2010;19(3): 267-70
16. Minville V, Fourcade O, Girolami JP, Tack I. Opioid induced hyperalgesia in mice model of orthopedic pain: preventive effect of Ketamine. Br J Anesth 2010;104(2):231-8.
17. Talebi H, Kamali A, yazdi B, Salehjafari N, Reihani Z, Hendodari N et al . Comparing the efficacy of low dose ketamine versus pethidine in controlling shivering after tonsillectomy surgery. JAP 2012; 2 (4) :25-29

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18. Cavallone LF, Vannucci A. Extubation of the difficult airway and extubation failure. Anesth Analg. 2013;116(2):368–83.
19. Rahimi M, Golparvar M, Naghibi Kh, Ghomi A. Comparing Alfentanil, Sufentanil, Ketamine and Pethidine for Prevention of Postanesthetic Shivering: A Randomized Placebo Controlled Clinical Trial. J Isfahan Med Sch 2015; 33(324): 212-20
20. Pazoki S, Noroozi A, Shadman A H. Comparison effect of different doses of Ketamine with Pethedine in reducing postoperative shivering after cesarean section. J Arak Uni Med Sci 2009; 12 (2) :9-16
21. Hasannasab B, Banihashem N, Khoshbakht A. Prophylactic effects of doxapram, ketamine and meperidine in postoperative shivering. Anesthesiology and Pain Medicine. 2016; 6(1):e27515.
22. Bhukal I, Solanki SL, Kumar S, Jain A. Pre-induction low dose pethidine does not decrease incidence of postoperative shivering in laparoscopic gynecological surgeries. Journal of Anaesthesiology, Clinical Pharmacology. 2011; 27(3):349-53.
23. Ayatollahi V, Hajiesmaeili MR, Behdad Sh, Gholipur M, Abbasi HR. Comparison of prophylactic use of meperidine and two low doses of ketamine for prevention of post-anesthetic shivering: A randomized double-blind placebo controlled trial. Journal of Research in Medical Sciences. 2011; 16(10):1340-6.
24. Sagir O, Gulhas N, Toprak H, Yucel A, Begec Z, Ersoy O. Control of shivering during regional anaesthesia: prophylactic ketamine and granisetron. Acta Anaesthesiol Scand 2007; 51(1): 44-9.
25. Asl ME, Isazadefar K, Mohammadian A, Khoshbaten M. Ondansetron and meperidine prevent postoperative shivering after general anesthesia. Middle East journal of anaesthesiology. 2011 Feb 1;21(1):67-70.

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Tables

Table 1: Comparison of demographic and clinical characteristics of patients undergoing tonsillectomy surgery between control, ketamine, and pethidine groups

Group	Girl	Boy	P
Control	43 (57.5%)	31 (42.5%)	0.180
Ketamine	47 (62.7%)	28 (37.3%)	
Pethidine	36 (48%)	39 (52%)	

Table 2: Incidence of postoperative shivering in patients undergoing tonsillectomy surgery between control, ketamine, and pethidine groups

Group	Shivering	P
Control	12 (16.2)	0.049
Ketamine	9 (12.0)	
Pethidine	3 (4.0)	
Total	24 (10.7)	

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