

ORIGINAL
ARTICLEEffect of Intravenous Ketamine on Prevention of
Postoperative Shivering: A Comparison with Intravenous
PethedineMasomeh Tabari¹, Ghassem Soltani², Fariba Hooshmandi¹,
Shahram Amini²✉¹ Assistant Professor, Department of Anesthesiology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran;² Associate Professor, Department of Anesthesiology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

Received: 14 April 2014

Revised: 27 April 2014

Accepted: 30 April 2014

Abstract

Introduction: Postoperative shivering is one of the common problems following general anesthesia and may lead to multiple complications. This study aimed to compare the impact of Ketamine and Pethidine on postoperative shivering.

Methods: In a randomized clinical trial, one hundred and thirty-five patients undergoing elective abdominal surgery were recruited for the study. The patients were randomly divided to groups received Normal Saline, Ketamine or Pethidine at the end of surgery. The frequency of shivering was determined immediately after surgery, and at 10, 20, and 30 minutes, postoperatively.

Results: In zero time the rate of shivering was more severe than other times in the three groups. Also the rate of postoperative shivering was significantly less different in the pethidine and Ketamine groups than the Normal Saline group. However, no significant difference was seen between the pethidine and Ketamine groups.

Conclusions: The result of this study showed that exactly after operation, the rate of postoperative shivering was more severe than other times in 3 groups. Ketamine and Pethidine might reduce postoperative shivering with no significant difference.

Key Words: Postoperative shivering; Ketamine; Pethidine; general anesthesia

Introduction

Shivering is a common complication following surgery [1]. It is the rhythmic contraction of muscles with frequency of 4-8 Hertz [2]. It is the natural response of the body to central hypothermia with release of cytokines from surgical site. It can also occur because of pain

Almost all anesthetics impair autonomic control of body temperature. Its incidence ranges from 5% to 65% following general anesthesia and 30% with epidural anesthesia [3, 4]. However, the incidence appears to be less as more patients are kept normothermic and opioids are administered more frequently and in larger doses than in the past.

Shivering is an unpleasant postoperative feeling

© 2014 Journal of Surgery and
Trauma

Tel: +985614443041 (5533)

Fax: +985614440488

Po Box 97175-379

Email: jsurgery@bums.ac.ir

**✉ Correspondence to:**

Shahram Amini, Associate Professor, Department of Anesthesiology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, IR Iran;
Telephone Number: +98511-8525209
Email Address: aminish@mums.ac.ir

that might be associated with adverse effects especially in patients with poor myocardial reserve. Shivering decreases mixed venous oxygen saturation as a result of impaired cardiopulmonary function. In addition, postoperative shivering can increase oxygen consumption up to 5 times, might increase carbon dioxide production, minute ventilation, and hence, cardiac output even in healthy adults [5]. It is a potentially serious complication that increases oxygen consumption roughly 100% in proportion to intraoperative heat loss.

It might also be associated with increased blood pressure, intracranial pressure, metabolic rate, lactic acidosis, and postoperative surgical wound pain [6, 7].

Ketanserin, sufentanil, alfentanil, tramadol, physostigmine, clonidine, magnesium sulfate, Pethidine, dexamethasone, and doxaperam have been used for the treatment of postoperative shivering [8].

Among these, Pethidine is widely used as the first line therapy [9, 10]. However, it might result in nausea and vomiting, delayed gastric emptying, and increased length of recovery stay.

N-methyl-D-aspartate agonists including Ketamine can affect temperature regulation and might be effective for the management of shivering. Nevertheless, they are associated with some neuropsychological adverse effects including somnolence and hallucination.

The purpose of this randomized clinical trial was to compare Pethidine and Ketamine in the prevention of postoperative shivering in patients undergoing general anesthesia. The main outcome is to compare the incidence of postoperative shivering.

Methods

After approval from ethics committee of Mashhad university of medical science (Ethic code: 2083241), 135 females with ASA (American Society of Anesthesiologists) class of I or II and age of 18 to 65 years scheduled for elective abdominal surgery at Qaem Hospital, Mashhad, Iran were recruited for a randomized double blind clinical trial. The patients and the investigators were blind to the study. They were randomly allocated (using randomization table) to receive either Pethidine 20 mg (n=45), Ketamine 0.5 mg/kg (n=46), or placebo (n=44) at the end of the surgery. Exclusion criteria were history of neuropsychological diseases, body mass index (BMI) more than 30, history of seizure, drug allergy, hypertension and any other

cardiovascular diseases, intraoperative blood component transfusion, and surgeries lasting more than 3 hours. After receiving midazolam 0.05mg/kg and fentanyl 2 g/kg, anesthesia was induced with propofol 2 mg/kg and atracurium 0.5mg/kg for endotracheal intubation. Anesthesia was maintained with propofol 70-100µg/kg/min and N2O 50% in oxygen. Fentanyl was given 0.02µg/kg/min. The room temperature and the intravenous fluids were kept between 22 to 24 centigrade degrees.

Postoperative shivering was assessed immediately after surgery, and at 10, 20, and 30 minutes using the following scales:

Grade 0: no shivering

Grade 1: slight fasciculation in the neck and face

Grade 2: visible shivering in more than one muscle group

Grade 3: shivering and movement throughout the body

We considered a difference in shivering frequency of 20% be clinically significant. A sample size of 34 was required to detect such a difference between the groups for a power of 90% at a significance level of 5%.

Using SPSS software for Windows, version 15 (SPSS Inc, Chicago, IL, USA), arithmetic mean and standard deviation values for different variables were calculated and statistical analyses were performed for each group. We used independent Student *t*-test and ANOVA to compare continuous variables exhibiting normal distribution, and Chi-square and Mann-Whitney *U* test for non-continuous variables. *P* value less than 0.05 was considered significant.

Results

135 patients completed the study. They aged from 18 to 60 years with mean age of 39±11.95 years and weight of 68.90±4.78kg. There was also no significant difference among the groups with respect to ASA class and duration of surgery (*p* values 0.07 and 0.1 respectively).

Shivering was more severe immediately after surgery in the three groups.

Immediately after surgery shivering with grade 0, 1, 2, and 3 in the Normal Saline group was seen in 27, 7, 5, and 5 cases, respectively, in the Pethidine group shivering with grade 0, 1, 2, and 3 was seen in 43, 1, 1, and 0 cases, respectively, and in the Ketamine group no one had shivering (grade 0). Using Post-hoc ANOVA (Tukey test) revealed that the difference was between the first and the second and third groups (*p* value<0.01). However,

Table 1: Frequency of shivering in groups under study at 10 minutes

	Normal Saline	Pethidine	Ketamine	P value
Grade 0	25	42	45	<0/001
Grade 1	9	1	1	<0/001
Grade 2	4	2	0	<0/001
Grade 3	6	0	0	<0/001

Data are presented as numbers

Table 2: Frequency of shivering in groups under study at 20 minutes

	Normal Saline	Pethidine	Ketamine	P value
Grade 0	29	44	46	<0/001
Grade 1	14	1	0	<0/001
Grade 2	1	0	0	<0/001
Grade 3	0	0	0	<0/001

Data are presented as numbers

Table 3: Frequency of shivering in groups under study at 30 minutes

	Normal Saline	Pethidine	Ketamine	P value
Grade 0	37	45	46	<0/001
Grade 1	7	0	0	<0/001
Grade 2	0	0	0	<0/001
Grade 3	0	0	0	<0/001

Data are presented as numbers

comparison of the Pethidine and Ketamine groups did not show significant difference (p value 0.15).

Shivering was seen more commonly in the Normal Saline than the other two groups at 10 minutes (table 1). Patients in the Normal Saline developed more shivering at 20 and 30 minutes, as well (tables 2, 3). In addition, frequency of shivering was similar in the Ketamine and Pethidine groups at all times.

Discussion

Our study revealed that intravenous Ketamine and Pethidine can decrease postoperative shivering with no significant difference.

Most anesthetics can decrease thermoregulation thresholds resulting in hypothermia in patients exposing to the operating room. Hypothermia may lead to shivering, prolonged drug action, coagulopathy, and decreased resistance to infection. Therefore, maintaining normal body temperature is pivotal for prevention of hypothermia and its complications.

Postoperative shivering increases recovery length of stay and cost and is an additional burden to both the patients and hospitals.

Comparison of Pethidine, granisetron, and Normal Saline in laparoscopic surgery showed that Pethidine and granisetron could dramatically decrease postoperative shivering with no significant difference [10].

A number of studies showed the same result of efficacy of Pethidine and Ketamine in preventing postoperative shivering [11-15].

Similar to our study, Ketamine has been effective in preventing shivering after prostate [16] and general surgeries [17].

Application of Ketamine and Pethidine in children after tonsillectomy showed the same result with no significant difference between the two drugs [18].

In contrast, Pazuki et al revealed that Pethidine could better reduce postoperative shivering after cesarean section [19].

In another survey, it was reported that Pethidine and dexamethasone were similar in reducing shivering after abdominal surgery [20].

In addition to common drugs used, many researchers have used tramadol [21, 22], clonidine [23], dexamethasone [24], dexmedetomidine [25], acupuncture [26], ondansetron [27, 28], and

hydrocortisone [29] successfully for prevention of postoperative shivering.

Conclusions

In conclusion, we demonstrated that shivering is more common immediately after surgery and intravenous Pethidine and Ketamine can significantly and similarly reduce postoperative shivering.

Acknowledgements

We would like to thank the personnel of the operating room and surgical ward at Qaem hospital for their contribution to this study.

References

1. Bock M, Bauer M, Rösler L, Sinner B, Motsch J. Dolasetron and shivering. A prospective randomized placebo –controlled pharmacoeconomic evaluation. *Anaesthesist*. 2007; 56(1): 63-6.
2. Macario A, Weinger M, Carney S, Kim A. Which clinical anesthesia outcomes are important to avoid? The perspective of patients. *Anesth Analg*. 1999; 89(3): 625-8.
3. Dabir SH, Radpey BAZ, Parsa T. Evaluation of the incidence of postane-sthesia shivering. *Journal of Iranian Society Anaesthesiology and Intensive Care*. 2006; 28(1): 60-9.
4. Eberhart LH, Döderlein F, Eisenhardt G, Kranke P, Sessler DI, Torossian, et al. Independent risk factors for postoperative shivering. *Anesth Analg*. 2005; 101(6): 1849-57.
5. Zhang Y, Wong KC. Anesthesia and postoperative shivering: its etiology, treatment and prevention. *Acta Anaesthesiol Sin*. 1999; 37(3): 115-20.
6. Buggy DJ, Crossley AW. Thermoregulation, mild perioperative hypothermia and postoperative shivering. *Br J Anesth*. 2000; 84(5): 615-28.
7. Kiekkas P, Pouloupoulou M, Papahatzi A, Souleles P. Effects of hypothermia and shivering on standard PACU monitoring of patients. *AANA J*. 2005; 73(1): 47-53.
8. Miller RD (eds). *Anesthesia*, 5th ed. Philadelphia: Churchill Livingstone; 2005.
9. De Witte JL, Kim JS, Sessler DI, Bastanmehr H, Bjorksten AR. Tramadol reduces the sweating vasoconstriction and shivering thresholds. *Anesth Analg*. 1998; 87(1): 173-9.
10. Iqbal A, Ahmed A, Rudra A, Wankhede RG, Sengupta S, Das T, et al. Prophylactic Granisetron Vs Pethidine for the Prevention of Postoperative Shivering: a Randomized Control Trial. *Indian J Anaesth*. 2009; 53(3): 330-4.
11. Hosseinzadeh H, Aidi M, Kolahdozan Kh. Comparison of efficacy of two methods for post operating shivering (Pethidin & Doxapram) in increasing the arterial oxygen saturation (SaO₂). *Pharmaceutical Sciences*. 2003; 9(1): 29-37. [Persian]
12. Rafiei MR, Hashemi SJ, Davodabadi AH, Adibhajibaghri M. The Study of Effects of Tramadol and Pethidine for Post Operative Shivering after Spinal Anesthesia for Inguinal Hernia Repair in Shahid Beheshti Hospital of Kashan During 18 Months. *Iranian Journal of Surgery*. 2006; 14(2): 0-0. [Persian]
13. Javaherforoosh F, Pipelzadeh M, Namazi M. Effect of Oral Clonidine on Post Operative Nausea and Vomiting in Gynecological Laparoscopic Surgery. *Armaghane-danesh, Journal of Yasuj University of Medical Sciences*. 2008; 13(2): 19-27. [Persian]
14. Entezariasl M, Isazadehfar KH, Mohammadian A, Khoushbaten M. Comparison the effect of ondansetron and meperidine in the prevention of postoperative shivering after general anesthesia. *Journal of Iranian Society Anaesthesiology and Intensive Care*. 2008; 30(62): 23-32.
15. Khosravi A, Moein Vaziri MT. Effect of Dexamethasone on reducing postoperative shivering. *Journal of Iranian Society of Anaesthesiology And Intensive Care*. 2002; 21(35-36): 17-21.
16. Al-Khaled H, Al-Kaabneh A. Intraoperative ketamine for the prevention of shivering post-trans urethral resection of prostate. *Journal Royal Medical Service*. 2006.13 (2): 30-3.
17. Begum R, Islam R, Sarker PC, Karmakar KK, Alam AM. Prophylactic Use of Ketamine Hydrochloride for Prevention of Post Operative Shivering. *Journal of the Bangladesh Society of Anaesthesiologists*. 2008; 21(1):29-35.
18. 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. *Anesthesiology and Pain Official Journal of ISRAPM*. 2012; 2(6): 25-29. [Persian]
19. Pazoki Sh, Noroozi A, Shadman AH. Comparison effect of different doses of Ketamine with Pethidine in reducing postoperative shivering after cesarean section. *Arak Medical University Journal*. 2009; 12(2): 9-16. [Persian]
20. Khoshrang H, Parvizi A, Haddadi S, Heidarzadeh A. Comparing the Effect of Pethidine, Dexamethasone and Placebo on Preventing Post-operation Shivering. *Zahedan Journal of Research*

- in Medical Sciences (Tabib-e-Shargh). 2007; 9(3): 155-61. [Persian]
21. Heidari SM, Rahimi M, Soltani H, Hashemi SJ, Shabahang S. Premedication with oral tramadol reduces severity of postoperative shivering after general anesthesia. *Adv Biomed Res.* 2014; 3: 64.
 22. Yousuf B, Samad K, Ullah H, Hoda MQ. Efficacy of tramadol in preventing postoperative shivering using thiopentone or propofol as induction agent: A randomized controlled trial. *J Anaesthesiol Clin Pharmacol.* 2013; 29(4): 521-5.
 23. Jabbary Moghaddam M, Ommi D, Mirkheshti A, Dabbagh A, Memary E, Sadeghi A, Yaseri M. Effects of clonidine premedication upon postoperative shivering and recovery time in patients with and without opium addiction after elective leg fracture surgeries. *Anesth Pain Med.* 2013; 2(3): 107-10
 24. Entezariasl M, Isazadehfah K. Dexamethasone for prevention of postoperative shivering: a randomized double-blind comparison with pethidine. *Int J Prev Med.* 2013; 4(7): 818-24.
 25. Kim YS, Kim YI, Seo KH, Kang HR. Optimal dose of prophylactic dexmedetomidine for preventing postoperative shivering. *Int J Med Sci.* 2013; 13; 10(10): 1327-32.
 26. Shoar S, Esmaeili S, Khorgami Z, Naderan M, Shoar N. Efficacy of acupuncture in prevention of postoperative anaesthesia-related shivering. *Acupunct Med.* 2013; 31(1): 120-1.
 27. Entezari Asl M, Isazadehfah Kh, Akhavanakbari G, Khoshbaten M. The effect of ondansetron in prevention of postoperative shivering after general anesthesia in gynecological surgery. *Iran Red Crescent Med J.* 2012; 14(5): 316-7.
 28. Asl ME, Isazadehfah K, Mohammadian A, Khoshbaten M. Ondansetron and meperidine prevent postoperative shivering after general anesthesia. *Middle East J Anesthesiol.* 2011; 21(1): 67-70.
 29. Pawar MS, Suri N, Kaul N, Lad S, Khan RM. Hydrocortisone reduces postoperative shivering following day care knee arthroscopy. *Can J Anaesth.* 2011; 58(10): 924-8.