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ARTICLE**A comparative study on the effects of warm intravenous fluids, intravenous pethidine, and combined warm intravenous fluids and humid-warm oxygen on hemodynamic parameters after general anesthesia in patients with shivering in the recovery room**Ayob Akbari<sup>1</sup>, Reza Abdi<sup>2✉</sup>, Somaye Jomefourjan<sup>3</sup>, Mojtaba Gholami<sup>4</sup><sup>1</sup> Medical toxicology and Drug Abuse Research Center(MTDRC), Birjand University of Medical Sciences, Birjand, Iran.<sup>2</sup> Assistant Professor of Orthopedics, Fellowship of Pediatric Orthopedics, Birjand University of Medical Science, Birjand, Iran<sup>3</sup> Surgery and Trauma Research Center, Birjand University of Medical Sciences, Birjand, Iran<sup>4</sup> MS in Nursing, Birjand University of Medical Sciences, Birjand, Iran

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**Abstract**

**Introduction:** Pethidine is commonly used to treat shivering after general anesthesia (GA), yet respiratory depression may subsequently occur. Warming methods such as warm fluids and/or humid-warm oxygen inhalation can reduce shivering after GA. This randomized clinical trial aimed to compare the effects of three different methods on the reduction of shivering and their hemodynamic and respiratory side-effects in patients undergoing abdominal surgery.

**Methods:** Eighty-seven patients undergoing abdominal surgery by GA were randomly assigned into three groups (two intervention groups versus the pethidine group). Patients in warmed intravenous fluids group received warmed ringer serum (38 °C). The patients in the combined warming group received warmed ringer serum (38 °C) and humid-warm oxygen, and patients in the pethidine group received intravenous pethidine only. The hemodynamic parameters of patients were collected and analyzed.

**Results:** The elapsed time of shivering in the warmed intravenous serum group, the combined warming group and the pethidine group were 7±1.5 min, 6±1.5 min, and 2.8±0.7 min, respectively, where the difference was statistically significant ( $P<0.05$ ). In the pethidine and combined warming groups, the pulse rate (PR) and systolic blood pressure (SBP) increased, whereas the diastolic blood pressure (DBP) decreased. As for the warmed intravenous serum group, pulse rate, DBP and SBP decreased ( $P>0.05$ ). The mean respiratory rate (RR) decreased in the pethidine group (from 16 to 15). The mean RR increased (from 16.2 to 16.8) in the combined warming groups, and the differences were statistically significant ( $p<0.05$ ).

**Conclusions:** The combined warming method reduces the shivering length, while the hemodynamic parameters (PR, BP) remain stable and respiratory depression does not occur. Therefore, it can be used to prevent hypothermia and reduce shivering after general anesthesia.

**Key Words:** Anesthesia; Meperidine; Intravenous; Combined; Hemodynamic; Shivering

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## Introduction

Some 60,000 medical interventions are performed under general anesthesia (GA) in the United States on a daily basis (1). Common postoperative problems after GA are nausea, vomiting and shivering. Less common but dangerous complications include heart attack, stroke, or death (2). Shivering in the recovery room is a common side-effect after GA. Approximately 5–65% of patients suffer from shivering (3). It can occur as frequently as 22% in Iran (4). Warming methods, opioids and many drugs are used to control shivering in the recovery room (5). Postoperative opioids may cause upper airway obstruction due to atonia in pharyngeal muscle or respiratory depression (6,7). The activation of opioid receptors induces analgesia, respiratory depression, sedation, euphoria, dysphoria, dizziness, cough reflex depression, decreased gastrointestinal motility, nausea, vomiting and urinary retention (6,8,9). Most opioids reduce sympathetic tone and enhance parasympathetic tone but may also induce bradycardia and/or hypotension (4,6).

One of the analgesic drugs commonly used to treat postoperative shivering is pethidine (3, 10). Pethidine has several side effects such as respiratory depression, nausea, vomiting and tachycardia (11-13). Humid-warm oxygen inhalation prevents hypothermia and shivering (5). Also, intravenous warmed fluids can have the same effects (14). In the present study, we compare the effects of three methods to reduce shivering including pethidine, warm intravenous fluids, and combined warm intravenous fluids with humid-warm oxygen inhalation. We also compare the side-effects of these three methods on hemodynamic parameters and respiratory rate.

## Methods

This double-blind (participant and researchers) randomized trial is registered in the Iranian Registry of Clinical Trials (IRCT Code#2014012016278N1). Following similar studies, our study was conducted on 87 patients who tolerated abdominal surgery under GA in the Birjand-based Imam Reza Hospital in 2014. The patients were initially informed about the method of study after which consent forms were signed by them.

Induction method of anesthesia in all patients was the same, i.e., 3 µg/kg fentanyl, 2 mg/kg propofol and 0.5 mg/kg atracurium every 30 min. Maintenance of anesthesia in all the patients was

achieved by administration of 150 µg/kg/min propofol and 0.2 mg/kg atracurium every 30 min and 1 µg/kg fentanyl 1.5 h later to alleviate pain.

At the end of abdominal operation, the patients were randomly assigned into three groups. The first group received 0.4 mg/kg intravenous pethidine, room temperature serum (25.5 °C) and room temperature humid oxygen. The second group received 7 ml/kg warm ringer serum (38 °C), room temperature humid oxygen, and 3 ml of intravenous normal saline as placebo. The third group received combined 7 ml/kg warm ringer serum (38 °C), 8 liter/min humid warm oxygen (37 °C), and 3 ml of normal saline as placebo. All the patients were covered with a simple blanket in the recovery room.

Severity of shivering was assessed and recorded based on the following four- point scale:

Grade I: No shivering

Grade II: Mild shivering, slight facial and cervical muscle contraction

Grade III: Moderate shivering, obvious shivering in the head and neck, shoulders, and/or extremities

Grade VI: Severe shivering, obvious shaking all over the body (15)

The respiratory rate (based on chest movements during one minute) and hemodynamic parameters including pulse rate (PR from radial and based on monitoring), blood pressure (BP based on non-invasive monitoring) were assessed for 20 min postoperatively at three time intervals (0, 10, and 20 min after entry to the recovery room) (16). Inclusion criteria were 20 to 60 years of age; patient with shivering grades 2 or 3 (patient with the shivering-grade 4 needed immediate treatment and were excluded); American Society of Anesthesiologists' (ASA) class 1 and 2 patients (ASA1 patients: without any systemic disorder such as heart disorder, respiratory disorder, or endocrine disorder, and ASA2 patients, i.e., patients with a mild controlled systemic disease which does not limit their activities; patients with abdominal surgery under general anesthesia; duration of surgery between 1 and 3 h; preoperative normothermic patients that did not receive corticosteroids, nonsteroidal analgesics, antihypertensive drugs, antiepileptic drugs, blood and blood products; and patients without endocrine disorder, vascular disease, hypertension, ischemic heart disease, fever, drug addiction, obstructive pulmonary disease, and brain lesions according to their medical records. On the other hand, the exclusion criteria were ASA class 3 and 4; blood or blood products transfusion during surgery; and shivering grade 4.

The recovery temperature and humidity were measured and recorded using infrared thermometer (Beurer Medical FT60, ULM, Germany) and wall thermometer (Beurer Medical TFA, Wertheim, Germany). Data collection tools consisted of a questionnaire and a checklist of the recorded postoperative parameters. Patients and research colleagues that filled out the records were blind to the study. One supervisor anesthesiologist confirmed validity of the recording forms. Upon arrival of the patient into the recovery room, grade of shivering was determined and the hemodynamic parameters were recorded. Afterwards, the patients were randomly assigned into one of the three groups. The letter A, B and C were typed on 87 cards in equal numbers. Letter A represented the pethidine group, letter B represented the intravenous warm serum group, and letter C represented the combined serum and oxygen warm group. In the recovery room, the nurse colleague removed one card from the box, and the patients were allocated into the respective group. The logged card was not put back in the box anymore. The data were analyzed by ANOVA, repeated ANOVA test, least significant difference (LSD) test, Tukey test and repeated measurements in SPSS version 18. The significance level was considered as  $P < 0.05$ . The Ethics and Research Committee of Birjand University of Medical Sciences approved the study.

## Results

According to chi-square and ANOVA tests, the age, gender, length of surgery, and the temperature of recovery room were similar in the three groups ( $P > 0.05$ ) (Table 1). Based on the chi-square test, the shivering mean length in the pethidine, warmed intravenous serum group and the combined warming group were 2.8 min, 7 min, and 6 min, respectively, where the difference was statistically significant ( $P < 0.05$ ) (Table 2). None of the patients had shivering at the 10th and 20th minutes of intervention; the diastolic and systolic BP and RR difference in the three groups at arrival to the recovery room were not significant ( $P > 0.05$ ) (Table 2).

Based on the ANOVA and Tukey test, the PR difference after 10 minutes in the two intervention

groups (group 2 and 3) and (group 1 and 2) were not significant ( $p > 0.05$ ). However, the difference between pethidine group and combined warming group (groups 1 and 3) was significant ( $P < 0.05$ ) (Table 2).

After 20 minutes, the PR differences between all groups were significant ( $P < 0.05$ ) (Table 2). This means that all the groups induce tachycardia. After 10 and 20 minutes, the Tukey test showed that the differences between systolic BP changes in the two intervention groups and the pethidine group were not significant ( $P > 0.05$ ) (Table 2). In the pethidine group, based on the repeated ANOVA test and the LSD test, the means of PR at 0, 10, and 20 min after entry into the recovery room were significant ( $P < 0.05$ ) (Table 2). However, the diastolic and systolic BP values at three time intervals were not significantly different ( $P > 0.05$ ) [Table 2].

In the warmed intravenous serum group, according to the repeated ANOVA test and the LSD test, the systolic BP at three time intervals were not significantly different ( $P > 0.05$ ) (Table 2). However, the LSD test showed diastolic BP and PR differences at three time intervals were statistically significant ( $P < 0.05$ ) (Table 2).

In the combined warming group, based on the repeated ANOVA test and the LSD test, the systolic and diastolic BP values at the three time intervals (i.e., 0, 10, and 20 min after entry into the recovery room) were not statistically significant ( $P > 0.05$ ) (Table 2). However, the LSD test showed that the PR difference at the three time intervals were significantly different ( $P < 0.05$ ) (Table 2).

Concerning RR, based on Tukey test, the difference between pethidine and warmed intravenous serum was statistically significant ( $P < 0.05$ ) (Table 2). However, the difference between combined warming group and combined pethidine and warmed intravenous serum group was not significant ( $P > 0.05$ ) (Table 2). The Tukey test showed that the respiratory rate in the pethidine group at the three time intervals decreased ( $P < 0.05$ ), while it increased in the combined warming group ( $P < 0.05$ ). Nonetheless, the respiratory rate in the warmed intravenous serum group at the three times did not change ( $P > 0.05$ ) (Table 2).

**Table 1: Comparison of some characteristics of participants in the three groups**

Variables	Pethidin group Mean (SD)	Warmed intravenous group Mean (SD)	Combined warming group Mean (SD)	P-value
Age (years)	51.4(15.2)	51.0(9.6)	53.3(12.2)	0.751
Gender				
female (N(%))	9(31%)	14(49%)	15(51%)	0.234
male (N(%))	20(69%)	15(51%)	14(49%)	
Length of surgery (min)	37.7(12)	43.0(10)	40.0(10.0)	0.140
Temperature of recovery room (°C)	23.0(0.84)	23.03(0.82)	23.03(0.83)	0.980
Humidity of recovery room (%)	34.5(1.2)	33.8(1.7)	33.7(1.8)	0.159

**Table2: Comparison of hemodynamic parameters of three groups(between and within) and elapsed time of shivering**

Variables	Group 1 Mean (SD)	Group 2 Mean (SD)	Group 3 Mean (SD)	P-value
PR0(arrival to R.R)	77.6(3.3)	77.2(4.1)	77.5(3.9)	0.990
PR1(after 10min)	83.7(5.4)	78.4 (4.4)	80.2 (5.0)	0.012
PR2(after 20min)	90.0(12.7)	82.8(9.8)	88.2(11.8)	0.001
p	0.000	0.012	0.001	
Systolic Bp 0	118(12.2)	122.5(10.6)	121.2(11.0)	0.411
Systolic Bp 1	116.0(23.0)	131.0(24.0)	122.0(9.0)	0.471
Systolic Bp 2	120.0(11.0)	119.0(22.0)	124.0(9.7)	0.385
P	0.351	0.701)	0.245	
Diastolic BP 0	73.0(10.8)	77.0(10.2)	76.0(13.5)	0.410
Diastolic BP 1	71.0(12.0)	70.0(9.0)	71.0(13.0)	0.815
Diastolic BP 2	71.0(12.0)	71.5(11.5)	74.0(12.0)	0.010
P	0.101	0.010	0.151	
RR 0	16.0(1.4)	17.1(1.3)	16.2(1.3)	0.341
RR 1	14.8(1.5)	16.8(1.3)	16.5(1.4)	0.000
RR 2	15.2(1.2)	15.6(4.5)	16.8(1.3)	0.010
P	0.023	0.123	0.029	
elapsed time of shivering	2.8(0.7)	7.0(1.5)	6.0(1.5)	0.000
0=arrival to recovery room. 1=after 10min. 2=after 20min				

## Discussion

In our study, we compare a pair of non-pharmacological methods including warmed intravenous fluids and combined warming (warmed intravenous fluids with humid-warm oxygen) with a pharmacological method (pethidine as the routine treatment) in terms of hemodynamic parameters in shivering patients (17). The patients are considered to be stable hemodynamically after opioids administration; however, minor bradycardia might occur (18). Nevertheless, a review of the related articles shows that pethidine induces different hemodynamic effects, most typically, tachycardia and hypotension (18,19). Our study shows that pethidine was better than the two intervention groups in controlling shivering although it has various effects in hemodynamic parameters in comparison with the non-

pharmacological methods. In the pethidine and combined warming groups, the mean of PR increased. In warmed intravenous fluid, PR decreased a little, which is agreeing with T. Flacke's findings showing that pethidine induces tachycardia (18). In the study of Mildh, when a minimum of 112.5 mg of pethidine was administered intravenously, PR and mean arterial pressure (MAP) increased (20). However, consistent with this study, the effect was not significant as compared with the morphine group. Also, when 187.5 mg of pethidine was infused as 3-hour infusion, MAP remained stable, whereas PR reduced significantly with first injection (20) which it is in contrast to our finding. These finding show that if the pethidine dose was increased, bradycardia happened.

In the study of Hamunen (1993), no changes in PR or MAP were noted when pethidine was given postoperatively to children (21). In the study of Tarkkila et al (1998), insignificant decreases in PR and MAP occurred after pethidine administration (22). In the present study, the mean of systolic BP in the warmed intravenous serum decreased, while it decreased in the pethidine and combined warming groups. Moreover, the mean of the diastolic BP in the three groups were decreased although those changes were not statistically significant ( $P > 0.05$ ).

According to the study of Leena Mildh, respiratory rate did not decrease 5 minutes after one I.V. Bolus of 112.5 mg pethidine. However, during the 3-hour infusion of 187.5 mg pethidine, respiratory rate decreased ( $P < 0.05$ ) (20). In a study by Tarkkila et al (1998), the bolus dose of pethidine 0.6 mg/kg decreased the respiratory rate (22). This finding is in line with our findings where pethidine decreased the respiratory rate.

## Conclusions

The combined warming method can be used in patients undergoing abdominal surgery to prevent hypothermia and reduce shivering. Hemodynamic parameters were stable and respiratory depression does not occur in this method compared to the pethidine group. It is convenient, easy, and cost-effective. However, it seems that a larger random control trial is needed to establish the priority of combined method in comparison to the pethidine conventional method.

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**Conflict of Interest:** none declared

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