

Pre-induction low dose pethidine does not decrease incidence of postoperative shivering in laparoscopic gynecological surgeries

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Abstract

Objectives: The incidence of shivering in patients undergoing a laparoscopic procedure is stated to be about 40%. A majority of laparoscopic gynecological procedures are taken up on an outpatient basis. Postoperative shivering may delay hospital discharge and is a common cause of discomfort in patients recovering from anesthesia.

Aims: To determine the effect of pre-induction, low-dose pethidine on postoperative shivering in patients undergoing laparoscopic gynecological surgeries.

Setting and Design: Sixty females between 25 and 35 years of age, of American Society of Anesthesiologists (ASA) class 1 and 2, were randomly divided into three groups of 20 patients each. Group I and II patients received i.v. pethidine 0.3 mg/kg and 0.5 mg/kg, respectively, while Group III received i.v. 0.9% normal saline just before induction of general anesthesia. Temperature of the Operating Room and the Post Anesthesia Care Unit was standardized and all fluids given during the study period were warmed to 37°C.

Materials and Methods: Temperature, measured with a tympanic membrane probe, was recorded preoperatively, after induction of anesthesia, on arrival at the Post Anesthesia Care Unit, and postoperatively at 15 minutes and 30 minutes. Shivering was graded (0 – 4 scale) at arrival of the patients to the PACU and every five minutes thereafter, up to 30 minutes.

Statistical Analysis: ANOVA, Chi-square test, Kruskal-Wallis ANOVA and Mann-Whitney U tests were used. A *P*-value of less than 0.05 was considered significant.

Results: Core body temperatures were statistically insignificant between groups at pre-induction, post-induction, and in the PACU (*P* > 0.05). At the end of surgery, shivering was present in 18 patients (30%). In groups I, II, and III, six (30%), three (15%), and nine (45%) patients shivered, respectively. The differences in incidence and grading of shivering among groups was found to be statistically insignificant (*P* > 0.05). The core body temperature of shiverers and non-shiverers were compared. In the PACU at 0, 15, and 30 minutes, the temperature among shiverers was significantly lower than that in the non-shiverers. Rescue drug i.v. pethidine 20 mg was given to patients with shivering grade ≥ 2 . None of the patients had shivering after 10 minutes.

Conclusions: Prophylactic pre-induction, low-dose pethidine does not have major role in preventing postoperative shivering.

Key words: Laparoscopy, pethidine, postoperative shivering

Introduction

Shivering is the rhythmic contraction of muscle groups with irregular intermittent periods of relaxation.^[1] Postoperative

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shivering is defined as an involuntary muscular activity, either generalized or localized to the neck, throat or jaw muscles after the patient gains consciousness. Postoperative shivering is a common cause of discomfort in patients recovering from anesthesia. The incidence of postoperative shivering varies between 5 and 65%.^[2] The incidence of shivering in patients undergoing laparoscopic procedures is stated to be about 40%.^[3]

Postoperative shivering may delay hospital discharge, as a majority of laparoscopic gynecological procedures are taken up on an outpatient basis. The mainstay treatment for postoperative shivering is pethidine, but its side effects, like sedation, postoperative nausea and vomiting (PONV), respiratory depression, and hemodynamic instability, which are dose-dependent, may delay hospital discharge.^[4] We

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hypothesized that pre-induction, low-dose pethidine, in outpatients undergoing gynecological laparoscopy, could prevent postoperative shivering.

Materials and Methods

Following the Institutional Review Board approval and after obtaining written informed consent, a prospective, randomized, double-blind, controlled study was conducted. The power of the study was calculated based on a study by Iqbal *et al.*, who reported that there was no shivering in 86% of the patients with use of the pethidine group, as compared to 30% in control group.^[5] Assuming the same result, our sample size came to be 16 in each group at a confidence interval of 95% and power of 85%. To increase the power of our study we enrolled 60 female patients, in the American Society of Anesthesiologists (ASA) class 1 and 2, between the ages of 25 and 35 years, undergoing gynecological laparoscopic procedures of approximately one hour duration, under general anesthesia (GA). The exclusion criteria for the study were:

1. Patients with any contraindication to the use of pethidine
2. Patients with any drug (sedative/narcotic) or alcohol dependence
3. Patients suffering from any febrile illness in the last week prior to surgery
4. Dehydrated, debilitated or malnourished patients

Patients were categorized into three groups using the Tippet's random chart:

- Group I ($n = 20$) i.v. pethidine 0.3 mg/kg (5 ml volume) just before induction of GA
- Group II ($n = 20$) i.v. pethidine 0.5 mg/kg (5 ml volume) just before induction of GA
- Group III ($n = 20$) i.v. 0.9% normal saline (5 ml volume) just before induction of GA (control group)

All patients were premedicated with oral diazepam 0.1 mg/kg 45 minutes before the procedure. In the operating room, the standard five-lead electrocardiography (ECG), non-invasive blood pressure (NIBP), and pulse oximetry were attached and the baseline hemodynamic parameters were noted. A baseline intravenous normal saline infusion was started. All fluids used were warmed to 37°C before infusion. Temperature of the operating room (OR) and Post Anesthesia Care Unit (PACU) were kept constant between 21 and 22°C, with constant humidity, by centrally air conditioning and laminar flow. An anesthesiologist, blinded to the drug and group allocation, administered the study drug. Anesthesia was induced with a sleep dose of i.v. thiopentone and tracheal intubation was facilitated with i.v. vecuronium 0.1 mg/kg.

Fentanyl 1.5 $\mu\text{g}/\text{kg}$ i.v. was given as intraoperative analgesia. Ventilation was controlled and anesthesia maintained with isoflurane in a mixture of oxygen and nitrous oxide (30 : 70). All patients were covered with one layer of surgical drapes over the chest, arms, thighs, and calves during the operation and one cotton blanket over the entire body, postoperatively. No other warming device was used. Intraoperative monitoring included heart rate (HR), NIBP, oxygen saturation (SpO_2), and end tidal CO_2 concentration (EtCO_2). After completion of the procedure, the residual neuromuscular blockade was reversed with i.v. atropine 20 $\mu\text{g}/\text{kg}$ and neostigmine 50 $\mu\text{g}/\text{kg}$. The postoperative shivering was graded (0 – 4 scale) at arrival of the patients to the PACU and every five minutes thereafter, up to 30 minutes. Scores were assessed by an unbiased observer in the PACU, who was blinded to the test group. Shivering was grading using the following scale:^[6]

Grade	Clinical Signs
0	No shivering
1	Piloerection, but without visible muscular activity
2	Visible muscular activity confined to one muscle group
3	Visible muscular activity confined to more than one muscle group
4	Gross muscular activity involving the entire body

Temperature monitoring was carried out with a tympanic membrane probe [Instant thermometer HM3, Braun, Theromoscan Inc., San Diego, USA; Error $\pm 0.1^\circ\text{C}$ ($\pm 0.2^\circ\text{F}$)] preoperatively, after induction of anesthesia, at arrival to PACU, and 15 minutes and 30 minutes postoperatively. Rescue i.v. pethidine 20 mg was administered if shivering lasted > 5 minutes, was clinically distressing shivering or shivering was $>$ grade 2. Occurrence of adverse effects (sedation, PONV, hemodynamic instability, oxygen desaturation, respiratory depression), if any, were noted.

The demographic data, hemodynamic parameters, SpO_2 , EtCO_2 , temperature, and duration of anesthesia among the groups were compared using analysis of variance (ANOVA) followed by unpaired *t*-tests where required. Intergroup categorical data (incidence of shivering, PONV, and number of patients receiving rescue pethidine) were analyzed using the Chi-square test. The grades of shivering were analyzed using Kruskal-Wallis ANOVA by ranks, followed by Mann-Whitney U tests if required. Intragroup data was assessed by paired *t*-tests. A *P*-value of < 0.05 was considered significant.

Results

Sixty patients were enrolled in the study and all completed the study. Patients in the three groups were comparable in relation to their age and body weight [Table 1]. The mean duration of surgery was 50.75 ± 3.78 minutes in group I, 57.25 ± 5.44

minutes in group II, and 54.00 ± 4.47 minutes in group III, and the difference was not statistically significant. HR, NIBP, SpO₂, and EtCO₂ were comparable in all the groups with no statistically significant difference.

Tympanic membrane temperatures measured pre-induction, post-induction, and in the PACU were compared using ANOVA and no statistically significant difference was observed [Table 2 and Figure 1]. After induction, the mean tympanic membrane temperature fell in all three groups. The maximum fall in temperature was seen at arrival in PACU. In group I, the fall in temperature was $0.83 \pm 0.58^\circ\text{C}$, in group II $0.74 \pm 0.45^\circ\text{C}$, and in group III $0.78 \pm 0.64^\circ\text{C}$. There was no significant difference in the fall of temperature among the three groups. Gradual rewarming occurred thereafter, for up to 30 minutes. Temperatures of shiverers and non-shiverers were compared using ANOVA. At pre-induction and post-induction both shiverers and non-shiverers were comparable. In the PACU at 0, 15, and 30 minutes, temperature among the shiverers was significantly lower than among the non-shiverers ($P < 0.05$) [Table 3 and Figure 2].

Postoperative shivering was noted and graded according to a scale by an unbiased observer. At the end of anesthesia,

Table 1: Demographic data of the study groups (Mean ± SD)

Parameters	Group I (n = 20)	Group II (n = 20)	Group III (n = 20)
Age (years)	29.90 ± 3.38	30.10 ± 3.89	28.65 ± 3.67
Weight (kgs)	51.35 ± 8.31	54.20 ± 8.85	53.00 ± 8.49

Table 2: Comparison of tympanic membrane temperature (°C) among the three groups (Mean ± SD)

Time	Group I (n = 20)	Group II (n = 20)	Group III (n = 20)
Pre-induction	36.34 ± 0.60	36.53 ± 0.52	36.38 ± 0.62
Post-induction	35.94 ± 0.51	35.99 ± 0.54	35.91 ± 0.65
PACU			
0 minute	35.51 ± 0.53	35.78 ± 0.54	35.60 ± 0.52
15 minutes	35.75 ± 0.56	35.94 ± 0.48	35.79 ± 0.49
30 minutes	36.13 ± 0.46	36.30 ± 0.39	36.20 ± 0.33

PACU = Post anesthesia care unit

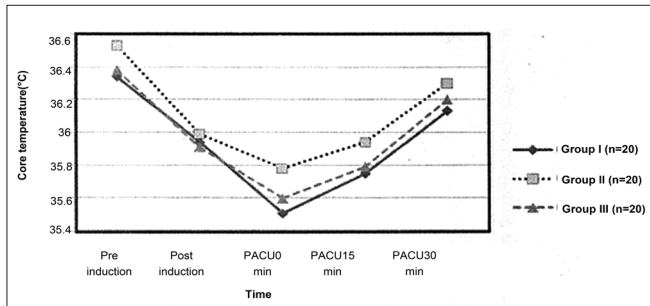


Figure 1: Comparison of core body temperature between the study groups at different time intervals

shivering was present in 18 out of 60 patients (30%). In group I, six patients (30%) had shivering: Out of them one had shivering grade II, two grade III, and three grade IV. In group II, three patients (15%) had shivering: Out of whom one had shivering grade II, one grade III, and one grade IV. In the control group, nine patients (45%) had shivering: Out of whom two had shivering grade II, six grade III, and one grade IV. All patients having shivering grade ≥ 2 were given the rescue drug (i.v. pethidine 20 mg). No patient had shivering after 10 minutes. The difference in incidence of shivering among the three groups was found to be statistically not significant by the Chi square test ($P > 0.05$). Shivering grades among the three groups were comparable using Kruskal Wallis ANOVA by rank, followed by the Mann-Whitney U tests, which found them to be statistically not significant ($P > 0.05$) [Table 3].

In groups I, II, and III, three, three, and four patients had PONV, respectively. PONV responses of all the patients in the three groups were measured and compared using the Chi square test. No statistical significant difference was observed ($P > 0.05$).

Discussion

Post-anesthetic shivering is associated with increased oxygen consumption, carbon dioxide production, increased cardiac output, tachycardia, and hypertension.^[7] Shivering may interfere with monitoring.^[8] It leads to patient discomfort and

Table 3: Comparison of core body temperature (°C) between shiverers and non-shiverers (Mean ± SD)

Time	Shiverers (n = 18)	Non-shiverers (n = 42)
Pre-induction	36.30 ± 0.59	36.76 ± 0.59
Post-induction	35.77 ± 0.63	36.02 ± 0.52
PACU		
0 minute	35.27 ± 0.62*	35.67 ± 0.59*
15 minutes	35.47 ± 0.42*	35.98 ± 0.47*
30 minutes	35.98 ± 0.38*	36.30 ± 0.40*

* $P < 0.05$, PACU = Post anesthesia care unit

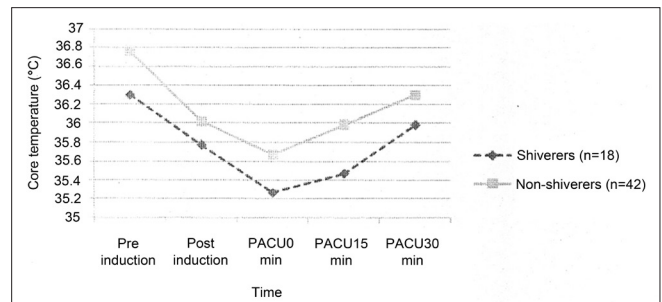


Figure 2: Comparison of core body temperature between shiverers and non-shiverers

may delay discharge from hospital. Prevention of postoperative shivering should be considered mandatory.

A number of physical methods have been used to alleviate shivering, which includes; forced-air patient warming systems, radiant heaters, complex humidifiers, intraoperative double-draping, maintaining OR and PACU temperature at more than 25°C, and providing an extra blanket and heated humidified oxygen delivery in the PACU.^[2] The mainstay of treatment of postoperative shivering is, however, pharmacological. A wide range of drugs like pethidine,^[9-11] other opioids (fentanyl, alfentanil, and sufentanil),^[12] doxapram,^[13] clonidine,^[14] ketanserin,^[14] and dexmedetomidine^[11,15] are reported to be effective in preventing and suppressing established shivering. Pethidine has been used both intraoperatively and postoperatively for prevention and treatment of shivering. In a majority of adults 25 mg pethidine i.v. is effective in treating postoperative shivering.^[10] Half life of i.v. pethidine is four to six hours and it can be used prophylactically in short or medium duration surgeries. It may, however, potentiate the sedative, PONV, respiratory, and hemodynamic effects of the opioids given perioperatively, and can lead to delayed discharge from the PACU.

In the present study, all the groups have been comparable in respect to age and body weight. Controversy exists regarding the relationship between post-anesthetic shivering and age. Some reports suggest that relatively younger patients are more prone to develop post-anesthetic shivering^[16,17] but Vaughan *et al.* observed that geriatric patients were prone to hypothermia and shivering.^[7]

The mean duration of surgery in all the three groups was 50 – 60 minutes. Goold^[17] observed shivering to be more frequent when the duration exceeded 30 minutes, while Moir *et al.*^[16] found this critical duration to be more than one hour. On the other hand, Holderaft *et al.*^[18] could not find any relation between the two. Harrison *et al.*^[19] in their study observed that mean core body temperature fell by 2.1°F when volatile anesthetic agents were used and 1°F when intravenous anesthetic agents were used.

In the present study, shivering was correlated with the all in tympanic membrane temperature. The patients who shivered had a significantly lower temperature in the PACU than those who did not shiver. John *et al.*^[20] found a greater fall in intraoperative temperature in patients who subsequently shivered. However, there are many reports, which found no correlation between the fall in temperature and shivering. Liem *et al.*^[21] found no correlation between a fall in body temperature and the incidence of shivering. Similarly, Baxendale *et al.*^[22]

did not find any significant difference in the core temperature between patients who shivered and those who did not.

Neither the incidence nor the grades of postoperative shivering differed significantly among the three groups. Stephen *et al.*^[23] reported an incidence of 5%, whereas, Pauca *et al.*^[9] found the incidence to be 62.67%. The incidence of shivering in our study was in the middle of the overall range mentioned in contemporary literature.^[1,9,18,23] Our study agreed with the work of Moir,^[16] who reported the incidence of postoperative shivering after GA to be 29.6% .

Rescue drug (i.v. pethidine 20 mg) was administered to a total of 18 study patients who had shivering grade >2. The shivering stopped in five to ten minutes after giving 20 mg i.v. pethidine. In all these cases there was no recurrence of shivering within the study period of 30 minutes. Wrench *et al.*^[6] found that 26 patients, out of 30 patients, stopped shivering within 10 minutes of administration of i.v. pethidine 20 mg.

The HR either remains unchanged or increases slightly in laparoscopic procedures.^[24] With pethidine the HR may increase slightly.^[25] In the present study, the HR remained stable and showed a similar trend in all the groups. In laparoscopic surgeries, blood pressure is elevated because of the increase of systemic vascular resistance.^[24] Blood pressure is normally unaffected, but sometimes it may fall after administration of pethidine.^[25] In the present study, in all the groups, the blood pressure remained within normal range at all monitored levels. During gynecological laparoscopic procedures in patients under controlled ventilation, EtCO₂ progressively increases to reach a plateau 15 to 30 minutes after starting CO₂ insufflation.^[24] Oxygen saturation remained within 98 and 100% in all three groups of patients.

There was no significant difference among all the three groups in terms of incidence of PONV. No other detrimental effects of pethidine like sedation and respiratory depression were noted in any patient during routine postoperative monitoring.

The limitations of our study were that we measured tympanic membrane temperature once at pre-induction and thereafter at completion of surgery, for a mean duration of 50 minutes of the surgical procedure. Shivering was also measured for a 30-minute period only. The postoperative pain score was not measured, which may have influenced non-thermoregulatory pain and affected the shivering threshold. Pethidine had a half life of four to six hours, and the mean surgical time in our study was 50 minutes. Inefficacy of pethidine in preventing post-anesthetic shivering was possibly due to early administration of the drug. Dosing of pethidine just before completion of surgery might have a role in the prevention of post anesthetic shivering.

Conclusions

We found a 30% incidence of postoperative shivering, but found no statistically significant difference in the incidence and grade of shivering among patients administered pre-induction pethidine and those who were not. After induction, body temperature fell in all patients and the lowest temperature was seen at arrival in the PACU. There was no difference in the degree of fall of temperature among the three groups. The patients who shivered had significantly lower temperatures in the PACU than those who did not shiver. We could not demonstrate the potential role of prophylactic low-dose pethidine in preventing postoperative shivering.

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