Tramadol and postoperative shivering in patients undergoing open and laparoscopic cholecystectomy under general anaesthesia

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Abstract

Background: For many years, shivering after anaesthesia has been recognised, and is one consequence of perioperative hypothermia. Shivering affects a number of physiological parameters. The aim of the study was to evaluate the severity of hypothermia after open and laparoscopic cholecystectomy, and to determine the efficacy of injection tramadol hydrochloride (HCl) in preventing postanaesthetic shivering.

Method: Eighty American Society of Anesthesiologists (ASA) Grade I and II patients scheduled to undergo either laparoscopic cholecystectomy, (Group A, n = 40) or open cholecystectomy (Group B, n = 40), were included in this randomised prospective study. Patients were further allocated randomly to two groups, to receive either tramadol 1 mg/kg (treatment group, Group A1 and B1, n = 40, 20 patients in each group), or the equivalent volume of normal saline (control group, Group A2 and B2, n = 40, 20 patients in each group), at the time of wound closure.

Results: Fall in temperature was significantly more in the laparoscopic cholecystectomy group (0.70°C and 0.81°C), than in the open cholecystectomy group (0.32°C and 0.275°C). The incidence of postanaesthetic shivering was comparable in the treatment groups (A1 and B1), but was significantly higher in the control groups (A2 and B2). Incidence of sedation was not significantly different between treatment and control groups.

Conclusion: Tramadol significantly reduced the incidence and severity of shivering, following open and laparoscopic cholecystectomy operations.

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Introduction

Postanaesthetic shivering is a common experience among patients recovering from general anaesthesia (GA). The incidence is estimated to be between 5-65%.[1] When a patient is subjected to GA, the autonomic thermoregulatory control is impaired.[2] Besides this, the cold environment of the operating room, cold intravenous fluids, cold and dry anaesthetic gases, exposure of body cavities, absence of muscular movements and subcutaneous vasodilatation, contribute to a fall in body temperature.

Cutaneous heat loss is mediated by the same four fundamental mechanisms that modulate heat transfer between any two substances: conduction, convection, radiation and evaporation.[3] Of all the heat loss mechanisms, radiation usually contributes the most.[4] Radiation is the transfer of heat from one surface to another via photons, and therefore does not depend on the temperature of the intervening air at all. Conduction is the direct transfer of heat from one surface to an adjacent surface. Heat transfer, in this case, is proportional to the difference in the surface temperatures, and insulation between them. Convection is the transfer of heat from one place to another by the movement of fluids (in physics, the term "fluid" means any substance that deforms under shear stress. It includes gases, liquids and plasma). Bulk motion of fluid enhances the heat transfer between the solid surface and the fluid.[5] It is well established that core hypothermia is more pronounced during large, than small, operations, with most of the difference presumably resulting from evaporative loss.[6] All these factors contribute to core hypothermia, which is implicated as the main cause of postanaesthetic shivering.

When core temperature falls by approximately 1°C, shivering occurs, and total body oxygen (O_2) consumption and carbondioxide (CO_2) production increase.[7] Shivering is an involuntary, oscillatory muscular activity that augments metabolic heat production.[8] Shivering is a very unpleasant experience for patients recovering from the comforts of modern anaesthesia, and is even worse than surgical pain.[9] This shivering has been variously described as "pentothal shakes", "halothane shakes", "postoperative spasticity" and "spontaneous postanaesthetic tremors". The use of these

imprecise terms displays our lack of complete understanding of the physiological mechanism behind the phenomenon.[10]

Shivering is a physiologically stressful condition that results in increased O_2 demand, an increase in intraocular and intracranial pressures, lactic acidosis, arterial hypoxemia, and other complications of sympathetic overactivity. Many studies have been carried out, using various pharmacological agents to overcome this ill effect of postoperative thermal discomfort. Some studies reported total abolition of postanaesthetic shivering by using tramadol,[11] while other studies found tramadol to be superior to pethidine in managing postanaesthetic shivering.[12,13]

Tramadol hydrochloride (HCl) is a synthetic opioid that prevents shivering by inhibiting the reuptake of norepinephrine, serotonine and dopamine. It also modulates the activity of the nucleus median raphe in the medulla acting centrally on the m opioid receptor, predominantly with minimal effect on the k-receptor.

The present study was conducted to determine the severity of hypothermia after open and laparoscopic cholecystectomy, to determine the efficacy of tramadol HCl in preventing postanaesthetic shivering, and to discover its other side-effects.

Method

After ethical committee approval and informed consent had been obtained, the study was conducted on 80 American Society of Anesthesiologists (ASA) Grade I and II adult male and female patients in the Department of Anaesthesiology and Intensive Care, Government Medical College, Jammu, India. Exclusion criteria included patients with a history of febrile illness in the last week, and those who had received narcotics or sedatives in the preoperative period. All patients were scheduled to undergo either laparoscopic (Group A) or open (Group B) cholecystectomy operations. Patients were further allocated randomly to two groups to receive either tramadol (1 mg/kg), namely the treatment group (Group A1 and B1, n = 40; 20 patients in each group), or the equivalent volume of normal saline, namely the control group (Group A2 and B2, n = 40; 20 patients in each group) at the time of wound closure. Detailed history of the patient, physical examination, systemic examination and relevant investigations were carried out.

Patients were prepared by eight hours preoperative fasting and overnight sedation with tab. alprazolam 0.25 mg. No premedication was administered to any of the patients. After the patients were brought into the operating room, the monitors were attached, and baseline values for pulse rate (PR), mean arterial pressure (MAP) and O_2 saturation were recorded. Preoxygenation was conducted with 100% O_2 using a face mask. Following that, induction of anaesthesia was carried out with thiopentone sodium 5 mg/kg intravenously (IV). Endotracheal intubation was facilitated using vecuronium bromide 0.1 mg/kg of body weight. After fixation of the endotracheal tube, the length of the temperature probe inserted into the nasopharynx was measured by nose-ear distance, defined as distance from the inner brim of the nostril to the tragus. Measurement of nasopharyngeal temperature at nose-ear distance had a high precision, and was unaffected by breathing or head turning. Nose-ear distance was anatomically closest to the brain base, and core temperature was recorded.[14] Anaesthesia was maintained using N_2O in O_2 (66%, 33%) along with isoflurane 0.5% and incremental doses of vecuronium bromide, as, and when, required. The temperature of the operating room was maintained between 22-24˚C. All fluids and drugs used were at room temperature. During anaesthesia, patients were covered with sheets, but not actively warmed. Perioperative analgesia was provided by using diclofenac sodium 1-1.5 mg/kg diluted in 100 ml of normal saline, and given IV over a period of 15 minutes just before induction of anaesthesia. Ventilation was maintained with appropriate minute volume. In patients undergoing laparoscopic surgery, the necessary changes were made in ventilation following pneumoperitoneum to maintain saturation between 98-100%.

At the time of wound closure, either tramadol 1 mg/kg, or the equivalent volume of normal saline was administered IV. At the end of the surgical procedure, nasopharyngeal temperature was again recorded, and residual neuromuscular block was reversed, using appropriate doses of. neostigmine and glycopyrrolate. All patients were given 28% oxygen by ventimask, and covered with a woollen blanket as per routine in the recovery room. Patients were observed in the recovery room for 30 minutes. PR, MAP, level of sedation, degree of postanaesthetic shivering, and occurrence of nausea and vomiting, were noted every five minutes by an observer who was unaware of the nature of the surgery. Shivering and sedation were assessed according to the gradings shown in Table I and II. Nausea and vomiting were treated using ondansetron 100 µg/kg IV. Shivering was controlled with tramadol 1 mg/kg.

Table I: Grades of shivering

Grade	Clinical signs
0	No shivering
1	Piloerection or peripheral vasoconstriction, but no visible shivering
2	Muscular activity (fasciculation) in only one muscle group
3	Muscular activity in more than one muscle group, but no generalised shivering
4	Shivering involving the whole body, with generalised shaking

Grading of the shivering was carried out by a scale similar to that validated by Crossley and Mahajan.[15]

Table II: Grades of sedation

Grade	Clinical signs
0	Alert
1	Arouse to voice
2	Arouse with gentle tactile stimulus
3	Arouse with vigorous tactile stimulus
4	No awareness

Statistical analysis

A sample size of approximately 40 in each group was needed to demonstrate the effectiveness of tramadol in reducing shivering by 50% (60% to 25%), with 95% confidence (α = 0.05), and the power of the study being 90%. Demographic profile, vital parameters, and surgical and anaesthetic variables were expressed as mean ± standard deviation. Mean results were compared using the analysis of variance (ANOVA) test. Changes in nasopharyngeal temperature were compared between the A1, B1; A2, B2; A1, A2; and B1, B2 groups using Student's t-test. The chi-square test was used for qualitative assessment, such as shivering and sedation. A p-value < 0.05 was considered statistically significant.

Results

Demographic profile and preoperative vital parameters were similar in all the groups (p-value = not significant) (see Tables III and IV).

Table III: Demographic variables in different groups (mean ± standard deviation)

	A1	A2	B1	B2
Age (years)	36.65 ± 3.2	36.35 ± 2.91	35.65 ± 2.66	35.20 ± 3.01
Sex (male:female)	5:15	5:15	5:15	5:15
Weight (kg)	56.65 ± 3.45	55.60 ± 4.69	56.70 ± 4.07	56.70 ± 4.37

p-value = not significant; p-value > 0.05

Table IV: Preoperative vital parameters and duration of surgery (mean ± standard deviation)

	A1	A2	B1	B2
Heart rate (beats/minute)	91.7 ± 5.65	92 ± 4.10	91.20 ± 5.22	91.45 ± 4.85
Mean arterial pressure (mmHg)	92.4 ± 2.70	92.15 ± 2.62	91.80 ± 2.42	91.55 ± 2.42
SPO_2 (%)	98.85 ± 1.26	98.75 ± 1.12	98.57 ± 1.21	98.60 ± 1.27
Duration surgery[a] (minutes)	115 ± 28.47	110 ± 29.30	95 ± 26.20	90 ± 25.30
Duration of anaesthesia[a] (minutes)	125 ± 28.29	120 ± 30.20	105 ± 22.50	96 ± 25.60

a = p-value = significant; p-value < 0.05

However, duration of surgery and anaesthesia was significantly longer in the laparoscopic cholecystectomy surgery group, in comparison to the open cholecystectomy surgery group (p-value < 0.05) (see Table IV). There was a significant (p-value < 0.05) fall in nasopharyngeal temperature in the laparoscopic cholecystectomy group, namely 0.7 °C ± 0.23 (Group A1) and 0.81 °C ± 0.31 (Group A2), whereas it was 0.32°C ± 0.14 (Group B1) and 0.275 °C ± 0.27 (Group B2) in the open cholecystectomy group (see Table V). The difference in fall in temperature between the laparoscopic and open cholecystectomy groups was found to be statistically significant (p-value < 0.05).

Table V: Variations in nasopharyngeal temperature (°C) (mean ± standard deviation)

	A1	A2	B1	B2
Preoperative	36.425 ± 0.22	36.52 ± 0.21	36.845 ± 0.20	36.90 ± 0.35
Postoperative	35.63 ± 0.28	35.70 ± 0.23	36.525 ± 0.25	36.62 ± 0.36
Difference	0.70 ± 0.23	0.81 ± 0.31	0.32 ± 0.14	0.275 ± 0.27

p-value = significant; p-value < 0.05 (statistically significant fall in temperature in the laparoscopic and open cholecystectomy groups)

Shivering

The incidence of shivering was highly significant (p-value < 0.001) in the control group (A2 and B2), as compared to the treatment group (A1 and B1). The incidence of shivering was comparable in the treatment group (A1 and B1) (see Table VI). Grade 3 or 4 shivering was not seen in the study group.

Table VI: Incidence and severity of postoperative shivering

Grade	A1	A2	B1	B2
0	16 (80%)	4 (20%)	17 (85%)	6 (30%)
1	4 (20%)	12 (60%)	3 (15%)	11 (55%)
2	0 (0 %)	3 (15%)	0 (0%)	2 (10%)
3	0 (0%)	1 (15%)	0 (0%)	1 (5%)
4	0 (0%)	0 (0%)	0 (0%)	0 (0%)

p-value < 0.0001: extremely statistically significant (Fisher's Exact Test). Highly significant incidence of shivering in control groups as compared to treatment groups

Sedation

The incidence of sedation was not significantly different between the treatment (A1 and B1) and the control group (A2 and B2). Deep sedation (Grades 3 and 4) was not noted in any of the patients in this study (see Table VII). All patients remained haemodynamically stable, and no respiratory depression was noted in any patient during the study period. Nausea and vomiting were noted in slightly greater frequency in treatment group patients, but the difference between the treatment and control groups was insignificant, and was easily treated with ondansetron 100 µg/kg IV.

Discussion

Body temperature is usually controlled by a negative feedback system in the hypothalamus that integrates information from the whole body. Approximately 80% of this thermal input is derived from core body temperature. The hypothalamus coordinates increase in heat production (non-shivering and shivering thermogenesis), as well as an

Table VII: Incidence and severity of sedation in postoperative period (as percentage)

Grade	A1	A2	B1	B2
0	14 (70%)	16 (80%)	13 (65%)	15 (75%)
1	6 (30%)	4 (20%)	7 (35%)	5 (25%)
2	0 (0%)	0 (0%)	0 (0%)	0 (0%)
3	0 (0%)	0 (0%)	0 (0%)	0 (0%)
4	0 (0%)	0 (0%)	0 (0%)	0 (0%)

p-value = not significant; p-value > 0.05

increase or decrease in heat loss by causing cutaneous vasodilatation or vasoconstriction respectively, as needed to maintain normothermia.

The fundamental tremor frequency on the electromyogram in humans is near 200 Hz. A slow 4-8 cycles/minute waxing and waning pattern modulates this basal frequency. Shivering aggravates postoperative pain by stretching of the surgical incision, and increases the incidence of surgical bleeding, wound infection and longer hospital stay.

After an initial rapid fall in core temperature, a slow and linear reduction in temperature occurs, due to core-to-peripheral redistribution. Finally, core temperature stabilises, and virtually remains unchanged. The fall in temperature varies from 0.5-1.5°C during the first hour. Some studies reported a fall in temperature of 2.8 ± 0.5°C after three hours,[16] whereas others reported less of a fall in temperature, namely 1.3°C after two hours.[17] In our study, the fall in temperature was significantly more in the laparoscopic surgery group (p-value < 0.05), because of the convection effect produced by cool CO_2 (20.1°C) flow inside the peritoneal cavity.[18] However, the duration of anaesthesia was also significantly longer in the laparoscopic surgery group (p-value < 0.05), as compared to the open surgery group (see Table IV). Therefore, the greater fall in temperature may be due to the longer duration of anaesthesia in the laparoscopic group.

The incidence of shivering was 80% (Group A2) and 70% (Group B2), though nasopharyngeal temperature was never below 35.5°C. However, the incidence of shivering in the treatment group of patients (A1 and B1) was significantly less (p-value < 0.05) (see Table VI).

Earlier studies have also shown good results with tramadol, using different doses. De Witte et al used tramadol in a dose of 3 mg/kg of body weight.[11] Mathews et al also reported the use of a low dose of tramadol in treating postanaesthetic shivering, and found tramadol to be superior to pethidine without any incidence of severe side-effects.[1] The researchers used tramadol in a dose of 1 mg/kg, and found that 80% of the patients stopped shivering within 10 minutes of administration of the drug. Dhimar et al found that shivering disappeared in one minute with tramadol 1 mg/kg, and in five minutes in the case of pethidine 1 mg/kg.[19] Enakshi et al observed that tramadol 1 mg/kg can safely prevent postoperative shivering following open and laparoscopic cholecystectomy, without increasing the side-effects.[20] Others have reported that tramadol 2 mg/kg had the best combination of anti-shivering and analgesic efficacy, without excessive sedation and significant side-effects.[13] In these studies, the researchers used opioids for perioperative analgesia, which, in themselves, result in anti-shivering effects, but we used diclofenac sodium IV for perioperative analgesia. That is why the incidence of shivering was slightly more than in previous studies.

In our study. tramadol hydrochloride 1 mg/kg IV was given at wound closure, and postoperative shivering was effectively prevented in 82.5% (see Table VI) of patients, in both study subgroups A1 and B1. No respiratory depression was seen in any of the patients in the treatment group. Shivering of Grades 2 to 4 was not observed in any of the patients. In a few cases, nausea and vomiting in the postoperative period were easily treated with ondansetron 100 µg/kg. No other side-effects were seen during the observation in the recovery room.

In conclusion, tramadol hydrochloride is effective and safe in preventing postoperative shivering following open and laparoscopic cholecystectomy, with minimum side-effects in a dose of 1 mg/kg.

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