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COMPARISON OF TRAMADOL AND ONDANSETRON IN PREVENTION OF POSTOPERATIVE SHIVERING AFTER LAPAROSCOPIC CHOLECYSTECTOMY

Dr Hira Saeed[1], Dr Taoseef Ahmed[2*], Dr Ayesha Arshad[3], Dr Syed Sajjad Raza Kazmi[4], Muhammed Naeem[5], Dr Asif Hussain[6], Dr Nimra Usman[7]

[1]Senior Registrar, MBBS, FCPS, FJMU, Sir Gangaram Hospital Lahore, Pakistan
[2*]MBBS, FCPS, Assistant Professor Anaesthesia, Fatima Jinnah Medical University Lahore, Pakistan
[3]MBBS, FCPS, Assistant Professor Anaesthesia, King Edward Medical University, Lahore, Pakistan
[4]MBBS, MCPS, FCPS, FIPM, Associate Professor of Anesthesia, Rashid Latif Medical College, Lahore, Pakistan
[5]Assistant Professor, MBBS, MCPS, FCPS, Fatima Jinnah Medical University Lahore, Pakistan
[6]MD, FCPS Anaesthesia, FJMU/SGRH Lahore, Pakistan
[7]Evercare Hospital, Lahore, Pakistan

***Corresponding author:** Dr Taoseef Ahmed,
*Email: drtauseef07@gmail.com

ABSTRACT

Background

Shivering as a post-operative complication after laparoscopic cholecystectomy is common which usually manifests itself in increased metabolic demands and discomfort of patients. Proper prevention plays an important part in the increased favorability of the recovery outcomes. Other drugs which have a potential effect in reducing shivering are Tramadol (an opioid analgesic drug) and Ondansetron (a 5HT3 antagonist mainly used for nausea) among others. This comparison of efficacy for postoperative shivering preventing by the two drugs aims at guiding clinicians for the best pharmacologic management for improved patient care and perioperative safety in minimal-invasion surgeries.

Methods

This randomised controlled trial was conducted in the Department of Anaesthesiology, Sir Ganga Ram Hospital, Lahore, over a period of six months, from 1st April to 30th September 2020, following approval of the study protocol. In total, 92 patients who were in the age group 20 to 70 and any gender were randomly assigned to the two study groups. In one group, patients got ondansetron given through IV and in the other group, patients received tramadol the same way for preventing shivering after surgery. Grade II or greater postoperative shivering within 30 minutes of extubation was the major outcome observed. Written consent was provided by all the study participants before they took part in the research.

Results

The average age among participants was 41.5 years with a standard deviation of 14.3 years. A higher number of females were included in the study, reflected by a male-to-female ratio of 1:2.1. Obesity was identified in 18 patients (19.6%). According to the American Society of Anesthesiologists (ASA)

physical status classification, 47 individuals (51.1%) were categorized as class I, and 45 (48.9%) as class II. Postoperative shivering occurred in 20 patients (21.7%) who underwent laparoscopic cholecystectomy under general anesthesia. A significantly lower incidence of shivering was observed in those administered tramadol compared to those given ondansetron (8.7% vs. 34.8%; p = 0.002). This trend remained consistent across different patient subgroups when stratified by age, sex, body mass index, and ASA classification.

CONCLUSION: The study has compared the effectiveness of intravenous tramadol and ondansetron in patients who followed general-anesthesia and it was found that tramadol is better than ondansetron in the prevention of postoperative shivering and this difference in effectiveness is seen regardless of age, gender, body mass index and American Society of Anesthesiologists (ASA)groups. These findings are indicative that tramadol can eventually be the agent of choice in preventing shivering in the future practice of anesthesia.

KEY WORDS: General Anesthesia, Post-Operative Shivering, Tramadol, Ondansetron

Introduction

Post operative shivering is a clinically troubling interference that is often described by patients as even more painful than post operative pain. Its pathophysiology is not clearly known, but some of the speculated mechanisms are thermoregulatory activation, autonomic dysregulation, inhibited spinal reflexes, sympathetic hyperactivation, adreno-cortical suppression, and respiratory alkalosis [1, 2]. As opposed to the earlier assumption, shivering can also occur in normothermic patients and its prevalence after general anaesthesia has been suggested as 45 % [3]. The effects of postoperative shivering are high oxygen consumption, increased oxygen demand, cardio-vascular stress, haemorrhage, infection and risk of lactic acidosis. It can also interfere with monitoring modalities and reduce patient comfort [4–6]. Among the neurotransmitter systems implicated, the serotonergic pathway plays a key role in thermoregulation. Serotonin antagonists like ondansetron may reduce postoperative shivering by lowering the thermoregulatory threshold [5,7,8].

Ondansetron, a selective 5-HT3 antagonist widely used to prevent postoperative nausea and vomiting, has shown some efficacy in reducing shivering [8]. Tramadol works by acting on μ-opioid receptors, blocking the reuptake of norepinephrine and serotonin and it can also influence the area in the brain that maintains normal body temperature [9,10]. Tramadol produces fewer side effects than other opioid agonists [11]. Some research compares how effective these drugs are at preventing shivering; however, the results are mixed. In the first, 10% of people receiving tramadol were reported to shiver, whereas 16.7% of those on ondansetron experienced it [12]; it was also 8.1% and 16.6%, according to the second study [13]; compared to the third, where the rates became 26% and 34% [14].

Given the limited and inconsistent data, particularly within the local context, this study aims to compare the efficacy of tramadol and ondansetron in preventing postoperative shivering in patients undergoing laparoscopic cholecystectomy, to inform future anaesthetic practice.

Methods

This was a randomised controlled trial conducted in the Department of Anaesthesiology, Sir Ganga Ram Hospital, Lahore, over a six-month period from 1st April to 30th September 2020, following ethical approval. A total of 92 patients undergoing elective laparoscopic cholecystectomy under general anaesthesia were enrolled using non-probability purposive sampling. The sample size (46 patients per group) was calculated at 95% confidence level and 80% power, assuming postoperative shivering incidences of 34% for the ondansetron group and 10% for the tramadol group, based on previous studies [12,14].

Inclusion criteria comprised patients aged twenty to seventy years, of both genders, with ASA physical status I or II. Patients were excluded if they had hypersensitivity to the study drugs, ASA

status III or IV, perioperative fever, cardiovascular, renal, hepatic, or thyroid disease, required blood transfusion, or were haemodynamically unstable.

Informed consent was secured from all participants prior to their inclusion in the study. Preoperative evaluations were carried out a day before the scheduled surgery. Standard monitoring protocols included electrocardiography (ECG), heart rate, pulse oximetry,non-invasive blood pressure, and capnography. Participants were randomly assigned to one of two groups: Group A received 8 mg of intravenous ondansetron (diluted to 5 ml), and Group B was given intravenous tramadol at a dose of 0.5 mg/kg (also diluted to 5 ml). Both medications were administered slowly over a one-minute period. The study design was double-blind, with the anesthesiologist responsible for evaluating postoperative shivering blinded to the treatment allocation.

Preoxygenation was performed with 100% oxygen for 3–5 minutes. Premedication included midazolam 2 mg and nalbuphine 6 mg IV. Anaesthesia induction was standardised with propofol 2mg/kg and atracurium 0.5 mg/kg, followed by endotracheal intubation. Maintenance was achieved using 50% oxygen, 50% nitrous oxide, and isoflurane (1.0–1.2 MAC). Fluid management followed the 4-2-1 rule with pre-warmed Ringer's lactate. Extubation and reversal were done once patients were fully awake. Postoperative shivering was assessed for 30 minutes following extubation. Data were recorded using a structured proforma.

SPSS version 23.0 was used for analysing data. Age and body mass index (BMI) were summarized using mean values and standard deviations, whereas categorical variables such as gender, ASA classification, and the occurrence of shivering were reported as frequencies and percentages. The chi-square test was employed to evaluate differences in shivering between the two groups, with a p-value of ≤ 0.05 considered statistically significant. To account for potential effect modifiers, the data were stratified based on age, BMI, gender, and ASA classification, followed by the application of post-stratification chi-square analysis.

RESULTS

Among the patients, ages ranged from 20 to 70 and the average age was 41.5±14.3 years. Over half (53 patients or 57.6%) of the patients were between 20 and 44 years old and 39 patients (42.4%) were 45 years old or older. About 30 (32.6%) of the patients were male and 62 (67.4%) were female, with a male to female ratio of 1:2.1. Patients in the study had BMIs ranging from 22.2 Kg/m2 to 34.5 Kg/m2, with a mean of 27.3±3.4 Kg/m2 and 18 patients (19.6%) were obese. 47 patients (51.1%) were considered ASA class I, while the remainder, 45 (48.9%), were ASA class II. A summary of the findings is available in Table :1.

The two study groups were found to be comparable with respect to mean age ($p = 0.948$), mean BMI ($p = 0.776$), and the distribution of subgroups based on age ($p = 0.833$), gender ($p = 0.656$), BMI ($p = 0.599$), and ASA classification ($p = 0.835$), as detailed in Table 2. Postoperative shivering occurred in 20 patients (21.7%) who underwent laparoscopic cholecystectomy under general anesthesia. The incidence of shivering was significantly lower among patients who received tramadol compared to those who were administered ondansetron (8.7% vs. 34.8%; $p = 0.002$), as presented in Table 3. Upon stratification, this significant difference persisted across various subgroups categorized by age, gender, BMI, and ASA status, as shown in Table 4.

Table 1: Baseline Characteristics of Study Population

Characteristics	**Participants n=92**
Age (years)	41.5±14.3
● **20-44 years**	53 (57.6%)
● **45-70 years**	39 (42.4%)
Gender	
● **Male**	30 (32.6%)

● **Female**	62 (67.4%)
BMI (Kg/m^2)	27.3±3.4
● **Non-obese**	74 (80.4%)
● **Obese**	18 (19.6%)
ASA Class	
● **Class-I**	47 (51.1%)
● **Class-II**	45 (48.9%)

Table 2: Baseline Characteristics of Study Groups

n=92

Characteristics	Tramadol n=46	Ondansetron n=46	P-value
Age (years)	41.6±12.9	41.4±15.7	0.948
● **20-44 years**	26 (56.5%)	27 (58.7%)	0.833
● **45-70 years**	20 (43.5%)	19 (41.3%)	
Gender			
● **Male**	14 (30.4%)	16 (34.8%)	0.656
● **Female**	32 (69.6%)	30 (65.2%)	
BMI (Kg/m^2)	27.2±3.4	27.4±3.4	0.776
● **Non-obese**	36 (78.3%)	38 (82.6%)	0.599
● **Obese**	10 (21.7%)	8 (17.4%)	
ASA Class			
● **Class-I**	24 (52.2%)	23 (50.0%)	0.835
● **Class-II**	22 (47.8%)	23 (50.0%)	

Chi-square test, Independent sample t-test, Observed difference was statistically insignificant

Table 3: Comparison of Post-Operative Shivering in Patients undergoing Laparoscopic Cholecystectomy receiving Tramadol versus Ondansetron

n=92

Post-Operative Shivering	Tramadol n=46	Ondansetron n=46	P-value
Yes	4 (8.7%)	16 (34.8%)	0.002*
No	42 (91.3%)	30 (65.2%)	
Total	46 (100.0%)	46 (100.0%)	

*Chi-square test, * observed difference was statistically significant*

Table 4: Comparison of Post-Operative Shivering across Various Subgroups of Patients undergoing Laparoscopic Cholecystectomy receiving Tramadol versus Ondansetron

n=92

Subgroups	Tramadol n=46	Ondansetron n=46	P-value
Age			
● **20-44 years**	2/26 (7.7%)	9/27 (33.3%)	0.021*
● **45-70 years**	2/20 (10.0%)	7/19 (36.8%)	0.047*
Gender			
● **Male**	1/14 (7.1%)	6/16 (37.5%)	0.050*
● **Female**	3/32 (9.4%)	10/30 (33.3%)	0.021*
BMI			

● **Non-obese**	3/36 (8.3%)	13/38 (34.2%)	0.007*
● **Obese**	1/10 (10.0%)	3/8 (37.5%)	0.163
ASA Class			
● **Class-I**	2/24 (8.3%)	8/23 (34.8%)	0.027*
● **Class-II**	2/22 (9.1%)	8/23 (34.8%)	0.038*

*Chi-square test, * observed difference was statistically significant*

DISCUSSION

Shivering is a common complication observed after both regional and general anesthesia [1,2]. While patients often find it highly discomforting, it also poses clinical concerns due to its association with increased oxygen consumption [3]. Although hypothermia is frequently identified as a contributing factor, shivering can also occur during the perioperative period in patients who maintain normal body temperatures [2,3]. The precise underlying mechanisms remain poorly understood. However, factors such as pain and the abrupt cessation of opioids—especially those with a short duration of action—have been suggested as potential causes [1,3].

Despite the limited understanding of postoperative shivering, a universally accepted gold standard for its prevention and management has yet to be established [4]. The primary approach remains the prevention of perioperative hypothermia. Although several treatment options are available, most are based on empirical practices rather than solid evidence [5]. Existing guidelines for managing shivering are generally of low quality and lack consistency [3,5]. Intravenous ondansetron is commonly administered to surgical patients to reduce the incidence and severity of postoperative shivering [6–8]. However, recent studies have suggested that intravenous tramadol may offer superior efficacy compared to ondansetron, challenging the conventional approach and advocating its use in future practice [9–14]. Nevertheless, the current body of evidence remains inconclusive and conflicting [12–14], and a lack of region-specific research further underscores the need for the present study.

The objective of this study was to compare the frequency of postoperative shivering between tramadol versus ondansetron in patients undergoing laparoscopic cholecystectomy.

In the current study, the mean age of patients undergoing laparoscopic cholecystectomy was recorded as 41.5 ± 14.3 years. This finding is consistent with previous research. Jamil et al. (2014) reported a nearly identical mean age of 41.2 ± 10.4 years among patients at Bahawal Victoria Hospital, Bahawalpur [15]. Faizi et al. (2013) similarly documented a mean age of 40.2 ± 3.3 years at Nishtar Hospital, Multan [16]. Comparable results were observed by Chhajed et al. (2018) in an Indian cohort, with a mean age of 41.8 ± 11.6 years [17]. Arafa et al. (2019) noted a mean age of 41.1 ± 6.9 years in Egyptian patients [18], and Kirkil et al. (2015) reported a mean age of 42.4 ± 14.7 years in a Turkish population [19]. Similarly, Jee et al. (2016) recorded a mean age of 42.5 ± 11.6 years in Malaysian patients undergoing the same procedure [20]. These findings collectively affirm that our study's age distribution aligns well with both local and international research.

A notable female predominance was observed in our study, with a male-to-female ratio of 1:2.1 among patients undergoing laparoscopic cholecystectomy. This trend is similar to that of Bhurt et al. (2020) at Services Polyclinic Hospital, Islamabad, who had a very similar gender representation of 1:1.9 [21]. Faizi et al. (2013) in the study of Nishtar Hospital, Multan observed an identical distribution with a ration of 1:1.9 [16]. Correspondingly, at Aga Khan University Hospital, Karachi, the researchers recorded comparable results, whereby the proportion of males was decreased relative to women (male/female 1:1.8) [22]. Studies carried out in other countries have produced similar results. Among the Turkish patients, Ozkardes et al. and Kirkil et al. observed a female-to-male ratio of 1:2 and 1:2.1 [23], respectively, compared with a ratio of 1:2 in an Indian cohort [17], and a ratio of 1:1.8 in a Malaysian population [20]. The regularity in all these widely spread geographic settings is a sign of larger trends of increased prevalence of laparoscopic cholecystectomy in women worldwide. So, the given procedure is often performed among females of middle age.

Among the current patients, 19.6 % of the patients subjected to laparoscopic cholecystectomy fell into obese category. The proportion is comparable with the one found by Ghazanfar et al. at the Holy Family Hospital, Rawalpindi (17.0 %) [24] and with the level of obesity estimated by Maitra et al. (19.8 %) in Bangladesh patients [25].

The current study described a randomized clinical trial that tested the frequency of postoperative shivering following the administration of either of the drugs tramadol or ondansetron in patients. Results showed that shivering was experienced in 8.7 percent of the patients who were administered with tramadol and 34.8 percent of the patients who were administered with ondansetron ($p = 0.002$). The gap remained even after age, gender, BMI, and ASA classification were controlled, showing evidence of persistence among all controller groups.

The research results reported here are consistent with those reported recently in an article by Hasanat et al. (2018) in Bangladesh, which demonstrated that postoperative shivering was statistically significantly reduced among patients who received intravenous tramadol compared with those who received ondansetron (10.0 % vs. 33.3%; $p = 0.034$) [26]. A similar benefit of tramadol over ondansetron was observed in the study by Chowdhury et al. (2018) with the Indian cohort, where the prevalence of shivering was also lower in the tramadol group (8.1 % vs. 16.6 %; $p < 0.05$) [13]. Similarly, in Nepal, Lakhe et al. (2017) demonstrated that prophylactic tramadol countered shivering more effectively than ondansetron (10.0 % vs. 16.7 %; $p < 0.001$) [12]. All these findings clearly show that tramadol is better than ondansetron in the prevention of postoperative shivering in various cultural settings.

The current study is the first study of this type among the resident population and hence enriches the discourse on the topic that already exists internationally. Intra-venous tramadol was proved to have a better efficacy in comparison of standard intra-venous Ondansetron in pre-operative shivering patients who underwent surgery under general anesthetic condition. This is a benefit sustained between various demographic and clinical groups age, gender, BMI, and ASA level and should hence be given the serious attentions as a promising treatment drug in future anesthetic care practices.

As revealed in the current research, there are various methodological strengths that help make the research valid. First, the sample size was 92 people, a reasonably large group that allows conducting sound statistical measures. Second, confounding age, gender, BMI or ASA status was ruled out because of strict exclusion criteria. Moreover, group-to-group randomization and stratification of the continuous variables also eliminated the bias in study results due to known effect modifiers. Despite these strong points, the non-existence of the comparative study of adverse reactions (sedation, nausea, and vomiting) undermines the safety of the tramadol. This should be followed up by further clinical studies to overcome this limitation.

CONCLUSION

In this study involving patients undergoing surgery under general anesthesia, intravenous tramadol was found to be more effective than the conventional use of intravenous ondansetron in preventing postoperative shivering. This superiority was consistent across all subgroups, irrespective of age, gender, body mass index, and ASA classification, thereby supporting its potential role as a preferred agent in future anesthetic practice.

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