Original Article

Comparison of Ondansetron and Metoclopramide in the Prevention of Nausea and Vomiting after Laparoscopic Cholecystectomy Under General Anaesthesia

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ABSTRACT

Objective: To evaluate and compare the antiemetic efficiency of ondansetron with metoclopramide when administered prophylactically for the prevention of post operative nausea and vomiting after laparoscopic cholecystectomy.

Study Design: Prospective, Randomised, Comparative study.

Place and duration of study: The study was conducted at the department of Anaesthesia Fauji Foundation Hospital, Rawalpindi from Sep 2010 to may 2011.

Patients and Methods: Total 90 ASA grade-I and ASA grade-II patients, sex female, and age 35 – 70 years undergoing elective laparoscopic cholecystectomy were included in the study. Patients were randomly divided into three groups, 30 in each group. Group-I received 4 mg intravenous ondansetron, group-II received 10 mg, Intravenous metoclopramide and group-III received intravenous 0.9% normal saline 2 minutes prior to induction of anaesthesia. They received standard General Anaesthesia for surgery. Post operative analgesia was provided with intravenous ketorelac 30 mg. There was no difference among the groups in patient charactertics and risk factors for PONV. Patients were observed for 24 hours after operation for occurrence of nausea and vomiting and requirement of rescue antiemetic. Efficiency of the drug was evaluated as (a) complete response- no nausea and no vomiting. (b) Mild response – Nausea with no vomiting (c) Moderate response – 1-2 vomiting episodes / moderate nausea (d) Severe response - > 3 vomiting episodes /severe nausea.

Results: During 1st 24 hours after operation incidence of nausea and vomiting was 77% in patients in placebo group, was 33% in patients in the ondansetron group and 53% in patients in the metoclopramide group. The incidence of PONV was significantly lower in patients who received ondansetron ($P < 0.05$) as compared to metoclopramide or placebo. Complete response with no nausea and vomiting was higher in patients who received ondansetron (66 %) than in patients who received metoclopramide (46 %) or placebo (23 %). The incidence of nausea with vomiting (moderate to severe response) was significantly lower with ondansetron (20 %) as compared to metoclopramide (34 %) and placebo (60 %). There was no need for another rescue antiemetic in (80 %) patients, with ondansetron (67%) with metoclopramide, (40 %) with placebo.

Conclusion: Single intravenous dose of 4 mg ondansetron when administered prophylactically is more effective than 10 mg intravenous metoclopramide in the prevention of PONV after laparoscopic cholecystectomy. Single 4 mg IV dose of ondansetron reduces the incidence and severity of PONV and also requirement of rescue antiemetic in the Post operative period.

Key Words: Ondansetron, Metoclopramide, Laparoscopic Cholecystectomy.

INTRODUCTION

Post operative nausea and vomiting (PONV) are distressing and frequent adverse events after general anaesthesia & surgery ([1,2]). A number of factors which include age, sex, obesity, history of motion sickness, operative procedures, anaesthesic techniques and post operative pain are considered to increase the incidence of these symptoms post operatively ([3]). laparoscopic cholecystectomy is associated with shorter post operative hospital stays, overall less expensive, less morbidity, less post operative pain and has become a widely used surgical technique ([4]). It has been reported that the incidence of nausea & vomiting is as high as 60 -70% following laparoscopic cholecystecomy ([5,6,7,8]). Antiemetic prophylaxis is justified in patients undergoing laparoscopic cholecystectomy. There are several classes of drugs that constitute the mainstay of antiemetic therapy. These drugs range from older drugs like droperidol, metoclopramide to 5 HT antagonists. Ondansetron, a 5 hydroxytryptamine antagonist with selectively for type 3 (5-HT) receptors has been

introduced as a new class of antiemetics. It acts probably on both peripheral and central sites with little or no clinically relevant effects on dopamine or other receptors [9]. Recent studies suggest that ondansetrn is effective in the prevention of PONV in patients undergoing anaesthesia ([10,11]). Metoclopramide is a procainamide derivative and a benzamide prokinetic agent with dual site of action, blocking D2 receptor in the periphery (GI tract) and centrally (CTZ and area postrema, vomiting centre). It is effective for the treatment of post operative nausea and vomiting ([12]).

In the present study we have compared in our population the efficacy of 4 mg IV ondansetron with that of 10 mg IV metoclopramide for prevention of PONV in Female patients undergoing laparoscopic cholecystecomy. Both drugs were administered prophylactically two minutes prior to induction of anaesthesia. For this the study was designed to evaluate and compare the antiemetic efficiency of ondansetron and metoclopramide by observing incidence and severity of nausea and vomiting and requirement of rescue antiemetic in the 1st 24 hours after operation.

PATIENTS & METHODS

This randomized, prospective comparative clinical study was carried out at the department of Anaesthesia, Fauji Foundation Hospital Rawalpindi from Sep 2010 to May 2011. 90 ASA grade-I and ASA grade-II patients, Sex female age 35 – 70 years (Table-1) undergoing elective laparoscopic cholecystectomy under general anaesthesia were included in the study. Patients with gastro enteritis, intestinal disease, history of motion sickness, previous PNOV, pregnancy, or those who had taken antiemetics within 24 hours before operation were excluded from the study. After pre-anaesthesia check up, all the patients were kept NPO after mid night.

On arrival in operation theatre intravenous line was established on the dorsum of hand. Routine monitoring devices were attached and continuous monitoring of ECG, NIBP, Heart rate, SPO2 and End tidal CO2 was done during the surgical procedure.

Patients were randomly divided into three groups, thirty patients in each group.

Group-I received inj. Ondansteron (4 mg) intravenously, group-II received inj metoclopramade (10 mg) intravenously and group –III (placebo) received. 0.9 % normal saline. All drugs were administered prophylactically two minutes prior to induction of Anaesthesia. The Anaesthetists, nurses and surgeons caring the patients were blinded to the studied drugs.

The standard Anaesthetic technique was used for all patients. Inj Midazolam 3 mg IV and nalbuphine 0.1mg/kg was given intravenously to all patients immediately before induction of Anaesthesia. Anaesthesia was induced with propofol 1.5 to 2 mg/kg and tracheal intubation was facilitated with atracurium 0.5 mg/kg intravenously. Anaesthesia was maintained with Isoflurane 0.7 % to 1 % (inspired concentration), nitrous oxide 50 % in oxygen. Ventilation was controlled mechanically with tidal volume and respiratory rate adjusted to maintain End tidal CO2 between 30 – 35 mm Hg. Neuromuscular blockade was maintained with incremental dose of IV atracurium. After tracheal intubation a nasogastric tube was placed and suction was applied to empty the stomach of air and other contents.

Patients were placed in supine position on operating table. Abdominal insufflation for the laparoscopic procedure was achieved with CO2 and intra- abdominal pressure was maintained between 10 -15 mm Hg. Reverse trendelenburg positon 15 to 20 degree tilt was made in the beginning of laparoscopic procedure. At the end of surgery residual neuromuscular block was reversed with IV inj atropine 0.02/kg and IV inj neostigmine 0.05 mg/kg. The nasogastric tube was removed at the end of procedure and the trachea was extubated. IV Ringer's lactate was given as maintenance fluid to each patient during the laparoscopic surgery. After operation all the patients were transferred to recovery room. During their one hour stay in the recovery room oxygen was given via face mask. All the vital signs, oxygen saturation, ECG and Blood pressure were monitored. After one hour in recovery the patients were transferred to post operative ward for observation.

Inj Ketorolac 30 mg IV was given for postoperative analgesia.

Collection of Data

Patients were observed for 24 hours after operation for incidence and severity of nausea and vomiting and also requirement of rescue antiemetic. The anaesthesiologist or ward sister registered whether vomiting had occurred and asked the patients whether they felt nauseated. The number of vomiting episodes were counted. Rescue antiemetic was given if vomiting occurred. Efficacy of the drug was evaluated as (a) complete response no nausea, no vomiting and no rescue antiemetic. (b) Mild response, nausea, no vomiting, no rescue antiemetic (c) Moderate Response – 1-2 vomiting episodes / moderate nausea, rescue antiemetic received. (d) Severe Response (Failure) vomiting episodes >3/ severe, nausea, rescue antiemetic received.

Statistical Analysis

Data was analyzed using SPSS version 10.0. Mean, standard deviation, standard error of mean (SEM) and percentages were calculated. The statistical analysis was done by student's t-test and P- value less than 0.05 was considered significant.

RESULTS

The data collected from 90 patients were analyzed. The patients characteristics, Age, weight, sex, duration of Anaesthesia, surgery, and CO_2 insufflation were similar among the groups (Table No.1). During 24 hours post operative observation period, arterial blood pressure, heart rate and respiration were stable and were not significantly different among groups.

In 1st 24 hours, PONV was seen in 23 (77 %) of 30 women in the placebo group (Figure No.I).

10 (33 %) 30 women in the ondansteron group (P-0.04) and 16 (53 %) 30 women in the metocolopramide group (P- 0.529). The incidence of PONV was significantly decreased in the ondansteron group as compared to metoclopramide and placebo group.

Table No.1:Patient Demographics and Operative Characteristics (n=90)

Variable	Group 1 Ondansteron 4 mg IV	Group II Metoclopra-mide 10 mg IV	Group III Saline Placebo
No of patients (n)	30	30	30
Age (yrs)	44 ± 13	51 ± 12	47 ± 13
Weight (kg)	65 ± 12	68 ± 12	66 ± 12
Sex , F	30	30	30
ASA grade1: 2	26 : 4	22: 8	24: 6
Duration of Anaesthesia (min)	77 ± 21	92 ± 28	82 ± 21
Duration of Surgery (min)	63 ± 20	76 ± 27	66 ± 21
Duration of CO2 Insufflation	51 ± 18	60 ± 24	55 ± 20

All values are expressed as mean ± SD.

The efficacy of study drug was assessed in each group 24 hours after operation. Complete response with no PONV was observed in 20 patients (66 %) in group-1, in 14 patients (46 %) in group-II, and in 7 patients (23 %) in group - III, placebo (Table No.2 Figure No.2). Patients experiencing only mild nausea (mild response) was noted in 4 (13 %) patients in group - I, in 6 (20 %) patients in group -II, in 5 (17 %) patients in group III, Moderate response, nausea with vomiting episodes 1-2 was noted in 4 (13 %) patients in group-I, 5 (17 %) patients in group -II in 10 patients (33 %) in group -III. Severe response, nausea with vomiting. Episodes > 3 was seen in 2 patients (7 %) , in group I, 5 patients (17 %) , in group II and 8 patients (27 %) , in group III, (Table-2, Figure-1). The rescue antiemetic was given to 6 (20 %) patients in group-I (P value 0.032) to (33 %) patients in group-II (P- 0.445) and to 18 (60 %) patients in group-III (Figure No.3, Table No.2).

Table No.2. The evaluation of post operative nausea and vomiting (PONV) 0 - 24 hours after laparoscopic cholecystectomy (n=90).

Variable	Group 1 Ondansetron 4 mg	Group II Metoclopr-amide 10 mg	Group III Saline
1. No of patients	30	30	30
2. No (%) of patients experiencing no PONV (complete Response).	20 (66 %)	14 (46%)	7 (23 %)
3. No of (%) of patients experiencing nausea only (mild Response).	4 (13 %)	6 (20%)	5 (17%)
4. No of (%)of patients experiencing nausea with vomiting episodes < 3 (moderate Response).	4 (13 %)	5 (17%)	10 (33%)
5. No of (%) of patients experiencing nausea with vomiting episodes > 3 (severe Response).	2 (7%)	5 (17%)	8 (27%)
6. No of (%) of patients experiencing (PONV).	10 (33 %)	16 (53 %)	23 (77 %)
7. Rescue Antiemetic	6 (20 %)	10 (33%)	18 (60 %)

DISCUSSION

PONV is the most common complication following anaesthesia and surgery with a selectively high incidence after laparoscopic cholecystectomy. Better anaesthetic technique, identification of precipitating factors, use of new generation of antiemetics and improvement in operative techniques reduce the incidence and severity of PONV. Despite these changes, there is still unacceptable frequency of PONV with incidences up to 85 % reported in some studies ([13]).

Figure No.1: Incidence of PONV in different Study Group

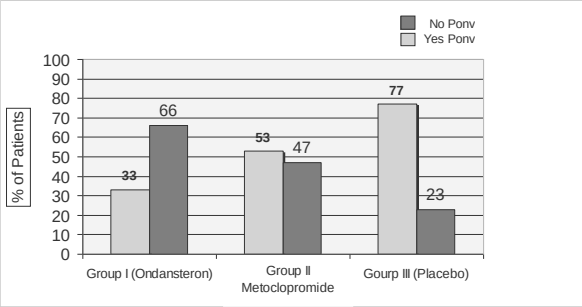


Figure No.2: Post operative response of nausea vomiting in different study group value expressed in %

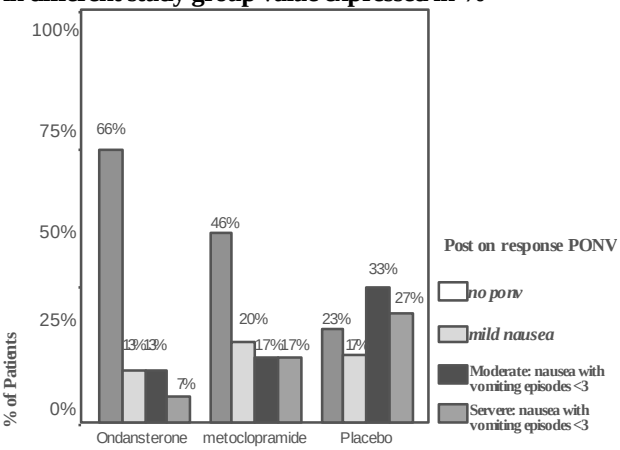
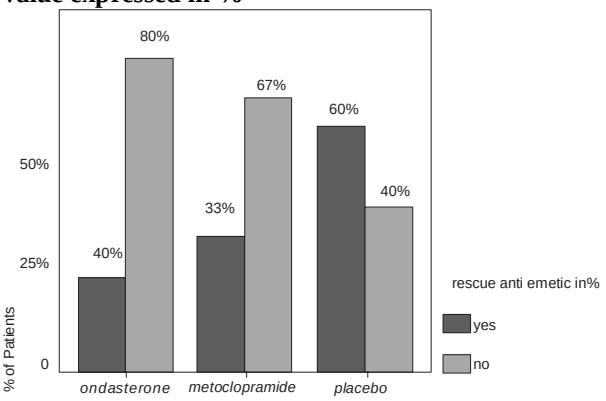


Figure No.3: Rescue anti emetic in different group value expressed in %



This problem is multifactorial in origin, including the patient demographics, the nature of underlying disease, the duration of surgery, anaesthetic technique and post operative care [14]. The main patient related factors are age, sex, obesity, history of motion sickness and / or previous PONV. Surgical factors also include the effects of intraperitoneal

CO2 insufflation on residual stretching and irritation of the peritoneum[15]. In this study, however the treatment groups were similar with respect to patient characteristics, surgical procedures, anaesthetics drugs administered and analgesia used post operatively (Table No. 1). Therefore, the difference in the incidence of PONV between the patients who had received ondensetron and those who had received metoclopramide or placebo can be attributed to the differences in these agents tested.

Both ondansetron and metoclopramide were given at the time of induction of anaesthesia to evaluate their antiemetic efficacy. In our study the incidence of PONV in group-I was 33 %, in group-II 53 % and in group-III 77 % during 1st 24 hours after operation (Table No.2,Figure No.1). The study demonstrated lower incidence of PONV (33 %) with ondansetron (P-0.04) compared with metoclopramide (53 %). The difference is statistically significant with ondansetron ($P < 0.05$). The incidence of PONV was very high (77 %) in patients, who did not receive antiemitic drugs prophylacticaly. (Figure No.1)

The treatment with metoclopramide (P- 0.529) did not significantly decrease the incidence of PONV. Recent studies have shown that although popular metoclopramide performs poorly in well controlled clinical trials and our findings confirm this for women undergoing laparoscopic cholecystectomy (16,17).

In our study complete response with no nausea and vomiting was significantly higher in patients who received ondansetron (66 %) than those who received metoclopramide (46 %) or placebo 23 % (Figure No.2 Table No.2). Mild response, nausea with no vomiting was observed in group-I (13 %), in group-II (20 %) and in group-III (17 %). There was no significant difference among the groups. Moderate response, nausea with vomiting episodes 1 -2 was (13 %) in group –I, 17 % in group-II and 33 % in group-III. Severe response (Treatment failure) nausea with vomiting episodes > 3 was observed in 7 % in group-I, 17 % in group-II and 27 % in group –III. Incidence of nausea with vomiting was significantly lower with ondansteron 20 % as compared to metoclopromide (34 %) or placebo (60 %). Study demonstrated very high incidence and severity of vomiting in patients who had not received antiemeitc drug prophylatically. In the present study 20 % patients in group-I, 33 % patients in group-II and 40 % patients in group-III required another rescue antiemetic medication (Figure No.-3). The requirement of another rescue antiemetic medication was significantly lower with ondanstanron (P-0.032) as compared with metoclopramide. The difference is statistically significant with ondansetron

($P < 0.05$). The antiemetics commonly used e.g droperidol and metoclopramide, have limited efficacy and are associated with a variety of side effects. Droperidol even at a low dose, has been described as being associated with excessive sedation and extrapyramidal reactions [18]. Also, adverse reactions involving the nervous system after small doses of

metoclopramide have been described in the literature 18. Ondansetron lacks the sedative, dysphoric and extrapyramidal symptoms associated with other antiemetics.

Several recent studies [9, 19, 20] have shown that a single intravenous dose of ondansetron

4 mg, the dose chosen in this study, is an optimal dose and is effective at preventing PONV after a variety of surgical procedures. The majority of studies comparing the antiemetic efficacy and safety of ondansetron with other currently used antiemetics have been performed in patients undergoing gynaecolgical procedures under general anaesthesia. None has been performed in female patients in our population undergoing laparoscopic cholcystectomy under general anaesthesia. The findings in this study are in agreement with Raphael and Norton who showed that preoperative prophylactic intravenous ondansetron 4 mg was superior to metoclopramide 10 mg in preventing PONV after general anaesthesia for day case gynaecological laparaoscopic surgery [21]. In another study of patients undergoing therapeutic abortion, ondansetron 8 mg resulted in a significantly lower incidence of postoperative vomiting (13%) compared with metoclopramide 10 mg (54 %) ([22]).

Scuderi and coll. domonstrated that there is a difference in outcomes when routine antiemetic medication with ondansetron is administrated versus simply treating PONV when the symptoms occur. Moreover, Scholz and coll demonstrated that the ondansetron reduces the incidence of PONV in patients undergoing laparoscopic cholecystectomy as well as major gynaecological surgery ([23]). Our data support the prophylactic use of intravenous 4 mg Ondansetron for PONV.

CONCLUSION

From the results of study it is obvious that prophylactic intravenous 4 mg ondansetron reduces the incidence & severity of PONV and also the requirement of rescue antiemetic in the post operative period. The ondansetron is more effective than metoclopramide in preventing post operative nausea & vomiting in patients undergoing laparoscopic cholecystectomy.

It is concluded that pre-anaesthesia intravenous 4 mg ondansetron is superior to intravenous 10 mg metoclopramide as a prophylactic antiemetic in patients undergoing laparoscopic cholecystectomy under general anaesthesia.

The prophylactic use of intravenous 4 mg ondansetron is recommended for preventing post operative nausea & vomiting in patients undergoing laparoscopic cholecystectomy under general anaesthesia.

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