Original Research Article

A comparative study between ondansetron, metoclopramide and placebo as a prophylactic medication to reduce postoperative nausea and vomiting

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Abstract

Background: Nausea and Vomiting are commonly faced post operative health illnesses among the patients undergoing surgery under general anesthesia. This study was planned to compare the effect of ondansetron, metoclopramide and placebo as a prophylactic medication in order to avoid nausea and vomiting among the adult patients undergoing surgery with general anesthesia. **Methods:** This prospective randomized study was conducted among adults admitted in various departments of Meenakshi Medical College Hospital and Research Institute, Kanchipuram during month of September 2017 to December 2017. Sixty patients between age 19-65 years, who belongs to ASA grade I and II were included Patients who were allergic to the study drugs, pregnant and lactating mothers and patients who were already on antiemetic drugs were excluded. Patients were randomized and divided into three groups and group I- Placebo (Normal saline-10ml, intravenous), group II– Metoclopramide (10mg, intravenous) and group III- Ondansetron (4mg, intravenous). The results were analyzed using SPSS 16. **Results:** Overall, 38.3% of patients developed postoperative nausea and vomiting. The occurrence of nausea and vomiting was found to be 60%, 35% and 5% in placebo group, Metoclopramide group and Ondansetron group, respectively. Nausea alone was reported in 5%, 10% and 10% of participants in placebo group, metoclopramide group and ondansetron group, respectively. The difference between placebo and metoclopramide was found to be significant (p 0.02) and the difference between placebo and ondansetron was also found to be significant (p 0.01) and the difference between the metoclopramideand ondansetron was found to be statistically significant (p 0.04). This shows that ondansetron is comparatively better than metoclopramide. **Conclusion:** Ondansetron was more effective than metoclopramide in decreasing the occurrence of postoperative nausea and vomiting. Thus a single intravenous injection of ondansetron of 4mg significantly controls nausea and vomiting and helps to eliminate the distressing postoperative nausea vomiting which continues to be a problem for the patients.

Key Words: Ondansetron, Metoclopramide, Nausea, Vomiting.

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INTRODUCTION

Postoperative nausea and vomiting is a distressing complication[1] and unpleasant experience for patients undergoing anesthesia and surgery. Despite significant advances in the delivery of anesthesia postoperative nausea and vomiting continues to be“ The big little problem”[2] with the incidence varying between 20 -30%,[3] especially during the first 24 hours following surgery. Nausea is a very aversive stimulus and if induced by operative experience, may cause life-long aversion to surgery. Whereas retching and vomiting are fairly violent

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acts and may place considerable stress upon certain structures leading to esophageal tears, resulting in hemorrhage (Mallory – Weiss syndrome) and rupture of the esophagus (Boerhaave syndrome) rib fracture, gastric herniation, muscular strain and fatigue. Vomiting may cause wound dehiscence, intraocular bleeding and bleeding of skin flaps in the upper body after plastic surgery. The major problem associated with vomiting in the postoperative period is aspiration of vomitus, respiratory observation and aspiration pneumonia. Once of the first extensive descriptions of the phenomenon was by John Snow, published in 1848 within 18 months of the introduction of anesthesia into Britain. He observed that vomiting was more likely to occur if the patient had eaten recently. For which, over the years, numerous approaches have been used in the management of post operative nausea and vomiting (PONV). Various techniques including olive oil and insulin-glucose infusions were reported to be effective. The effect of atropine was appreciated by Brown- Sequard as early as 1883 when he wrote "in the very great majority of cases, the addition of a certain amount of atropine to morphine prevents the nausea and vomiting occurring with morphine alone[3]. Robert Ferguson described the use of olive oil in 1912 and he postulated that oil in the stomach "absorbed any ether that may be present there". In the late 1930s, promethazine was found to have antiemetic property.Charpentier synthesized chlorpromazine in 1949, but sedation and hypotension were limiting side-effects. Following which there were several drugs used as antiemetic agents including scopolamine, promethazine, metoclopramide and droperidol. Also, non-traditional antiemetics like ephedrine, propofol and corticosteroids were used. The newest class of antiemetics used for prevention and treatment of PONV are serotonin (5-HT3) receptor antagonists-ondansetron, granisetron, tropisetron and palonosetron. These antiemetics do not have adverse effects of older traditional antiemetics. Available antiemetics like 5-HT3 antagonists are effective in very low doses. Thus, costs can be lowered and drug side-effects prevented when given as prophylaxis, lowering the economic burden imposed due to complications and increased medical care resulting from PONV. Thus this study was planned to compare the effect of placebo (Normal saline 10 ml, intravenous) Ondansetron (4mg, intravenous) andMetoclopramide (10mg,intravenous) among postoperative adult patients to prevent nausea and vomiting.

MATERIALS AND METHODS

This prospective randomized, double blinded study was conducted among adults admitted in various surgical departments like General Surgery, Gynecology, Orthopedicsand ENT in Meenakshi Medical College Hospital and Research Institute, Kanchipuram during month of September 2017 to December2017. Sixty patients between age 19-65years, who belongs to American Society of Anesthesiologists (ASA) grade I and II, undergoing elective surgical procedures were included in the study. Patients who were allergic to the study drugs, pregnant and lactating mothers and patients who were already on antiemetic drugs were excluded from the study. During the pre anesthetic fitness, complete history and physical examined was done to all the participants. Investigations including complete blood counts, fasting and postprandial blood sugars, serum liver function test and renal parameters and urine routine were carried out in all to rule out any laboratory evidence of hepatic and renal disorder. Also other investigations like including ECG and chest X-ray were done. The study was approved by the ethical committee of this institution. Informed consent was obtained from the patients, before starting the study. The study patients were randomized and divided into three groups with twenty participants in each group. Patients of group I received normal saline (placebo) 10 ml through intravenous route, group II received Metoclopramide 10 mg through intravenous route and group III received Ondansetron 4 mg through intravenous route. Just after intravenous cannulation, based on the randomization, drugunder study was injected slowly, to the respective participant through intravenous route, prior to the induction. Following the surgical procedure, the assessment of nausea and vomiting started soon after the patient shifted into the recovery room. The first half hour was designated as immediate postoperative period and subsequently patients were observed for 24 hours. Patient's vital signs like ECG, blood pressure and respiratory rate were recovered. The number of nausea and vomiting (emetic) episodes was observed in the first 24 hours and time of occurrence of each episode was also recorded. Patients were also observed for any side effects such as headache, sedation, flushing, extrapyramidal symptoms, itching, urticaria etc. During the postoperative period all patients received non-narcotic analgesics for postoperative pain relief. All the observations were recorded in the proforma especially prepared for this study. The results were analyzed using Statistical Package for Social Sciences (SPSS) version 16 and chi square test was used to compare the different groups.

OBSERVATION AND RESULTS

The study was carried out among sixty patients, whose age ranged from 19 to 65 years. The mean age in group I, group II and group III was 37.5, 33.1 and 36.95 respectively. Majority of the participants were belongs to age group 36-45 years. The study group included both

male and female patients. Out of the 60 patients in the study, 33 (55%) patients were female and 27 (45%) were male. Also there were 9 males and 11 females in all the three groups. The weight of the patients ranged between 41-80 kilograms (kgs). The mean weight of the patients in the group I, II and III were 54.9 kgs, 58.6 kgs and 56 kgs respectively. Majority of the participants were between the weights of 41-50 kgs, in this study.

Table 1: Characteristics of participants in each group

Variables	Group I (n=20) Frequency (%)	Group II (n=20) Frequency (%)	Group III (n=20) Frequency (%)
Age			
19-25 years	3 (15%)	6 (30%)	3 (15%)
26-35 years	6 (30%)	6 (30%)	5 (25%)
36-45 years	8 (40%)	5 (25%)	9 (45%)
46-55 years	0 (0%)	2 (10%)	3 (15%)
56-65 years	3 (15%)	1 (5%)	0 (0%)
Age (Mean ± SD)	37.50±12.58	33.10±12.29	36.95±10.15
Sex			
Male	9 (45.0%)	9 (45%)	9 (45%)
Female	11 (55%)	11 (55%)	11 (55%)
Weight			
41-50 kgs	10 (50%)	8 (40%)	10 (50%)
51-60 kgs	6 (30%)	4 (20%)	4 (20%)
61-70 kgs	3 (15%)	6 (30%)	2 (10%)
71-80 kgs	1 (5%)	2 (10%)	4 (20%)
Weight (Mean±SD)	54.9±9.9	58.65±11.61	56.00±12.03

Surgical Characteristics of participants in each group: Majority of the participants in this study were from department of general surgery, in all three groups. In group I, there were 35% of participants from department of general surgery and gynecology, each and 15% of participants from department of orthopedic and ENT, each. The rest 5% of participants were from dental surgery. In group II, there were 50% of participants from department of general surgery and 15% of participants from department of gynecology and orthopedics, each. 10% of the participants were from department of ENT and dental surgery, each. In group III, 40%, 35%, 15% and 10% of the participants were from department of general surgery, gynecology, ENT and dental surgery, respectively**.** In this study, the duration of surgery ranged from 30 to 240 minutes. The mean duration of surgery in each group I, II and III was 104.5, 103.75 and 117 respectively. Majority of cases 48.3% had duration of surgery ranging from 61 to 120 minutes.

Table 2: Surgical Characteristics of participants in each group

Variables	Group I (n=20) Frequency (%)	Group II (n=20) Frequency (%)	Group III (n=20) Frequency (%)
Surgery			
General surgery	7 (35%)	10 (50%)	8 (40%)
Gynecology	6 (35%)	3 (15%)	7 (35%)
ENT	3 (15%)	2 (10%)	3 (15%)
Orthopedics	3 (15%)	3 (15%)	-
Dental	1 (5%)	2 (10%)	2 (10%)
Duration of surgery			
30-60 minutes	2 (10%)	4 (20%)	3 (15%)
61-120 minutes	12 (60%)	10 (50%)	7 (35%)
121-180 minutes	5 (25%)	5 (25%)	9 (45%)
181-240 minutes	1 (5%)	1 (5%)	1 (5%)
Duration (Mean±SD)	104.5±36.09	103.75±50.73	117±41.75

Comparison of participants with nausea and vomiting in each group: In this study, overall, 38.3% of patients developed postoperative nausea and vomiting. Nausea preceded all the cases that had vomiting. The occurrence of nausea and vomiting was found to be high in the group I (placebo) 60%, group II (Metoclopramide) 35% and less in group III (Ondansetron) 5% of participants. Nausea alone was reported in 5%, 10% and 10% of participants in placebo group, metoclopramide group and ondansetron group, respectively. The difference between placebo group and metoclopramide group was found to be significant (x^2:1.56, p 0.02) and the difference between placebo group and ondansetron group was also found to be significant (x^2:5.57, p 0.01) and the difference between the metoclopramide group and ondansetron group was found to be statistically significant (x^2:3.34, p 0.04). This shows that ondansetron is comparatively better than metoclopramide.

Table 3: Proportion of participants with nausea and vomiting in each group

Variables	Group I (n=20) Frequency (%)	Group II (n=20) Frequency (%)	Group III (n=20) Frequency (%)
Nausea and Vomiting	12 (60%)	5 (25%)	1 (5%)
Nausea alone	1 (5%)	2 (10%)	3 (10%)
Total	**13 (65%)**	**7 (35%)**	**3 (15%)**

Frequency of emetic episodes in each group: One episode of nausea and vomiting was reported by 41.7%, 71.4% and 100% of participants who had nausea and vomiting in placebo group, metoclopramide group and ondansetron group, respectively. Two episodes of nausea and vomiting were reported by 41.7% and 28.6% of

participants who had nausea and vomiting in placebo group, metoclopramide group and ondansetron group, respectively and three episodes of nausea and vomiting was reported only in the place group. Among 16.7% of participants who had nausea and vomiting.

Table 4: Proportion of emetic episodes in each group

Variables	Group I (n=20) Frequency (%)	Group II (n=20) Frequency (%)	Group III (n=20) Frequency (%)
No. of emetic episodes			
One Episode	5 (41.7%)	5 (71.4%)	4 (100%)
Two Episodes	5 (41.7%)	2 (28.6%)	-
Three Episodes	2 (16.7%)	-	-

DISCUSSION

Postoperative nausea and vomiting is the major concern of patients undergoing surgery. In Orkin FK *et al* study[1], among the patients questioned "what do patients want", 72% of patients wanted freedom from nausea and vomiting as their most important postoperative requirement. In this study, there were 38.3% of patients developed postoperative nausea and vomiting. In the study done by, Toner GC *et al*, 1996[3] on prediction of postoperative nausea and vomiting they reported that 20-30% of patients were developing postoperative emetic episodes.

Ondansetron group: Ondansetron is a selective 5-HT3 receptor antagonist, which inhibits nausea and vomiting caused by cytotoxic agents and radiation. Its action is mediated via antagonism of 5-hydroxytryptamine receptors located centrally in chemoreceptor trigger zone (CTZ) in the area postrema of the brain and peripherally as vagal afferents in the upper gastrointestinal tract. Its actions start within 30 minutes of administration through intravenous route. In this study, among the patients administered with intravenous ondansetron, there were 15% of patients developed nausea and vomiting, postoperatively. In the placebo group, 65% of patients developed nausea and vomiting, postoperatively. Similarly, Sung YF *et al*[4], in double blinded, placebo controlled study examined the effectiveness of intravenous ondansetron in prevention of postoperative nausea and vomiting and reported that, in the ondansetron group 62% of patients and in the placebo group 40% of patients were free from emetic episodes. Its actions also start within 30 minutes of administration through intravenous route. In another double blinded randomized study conducted by Kenzie MC *et al*[5], to examine the use of intravenous ondansetron in the prevention of postoperative nausea and vomiting. After 24 hours period following surgery, 40% of patients who received ondansetron and 74% of the patient who received placebo, had nausea and vomiting.

Metoclopramide group: Mechanism of action of metoclopramide is complex. In general, it facilitates acetylcholine release from enteric neurons, an action that may be mediated indirectly by several different mechanisms including suppression of inhibitory interneurons by antagonism of 5-HT3 receptors and stimulation of excitatory neurons via activation of 5-HT4 receptors. In this study, 35% of patients developed nausea and vomiting, postoperatively in the group administered with intravenous metoclopramide. Similarly, Alexander *et al*[6] reported 43% reduction in post operative nausea and vomiting,among patients who were administered with metoclopramide 10 mg intravenously. In another study, Ucanda roy *et al*[7] reported administration of metoclopramide significantly reduced the incidence of postoperative nausea and vomiting from 70% to 15%, which was reported as statistically significant.

Comparison of Ondansetron and Metoclopramide: In this study, 65%, 35% and 15% of the patients developed nausea and vomiting among the patients administered with intravenous normal saline (placebo), metoclopramide and ondansetron, respectively. This is comparable with the study done by Mallins AF *et al*[8], compared the incidence of postoperative nausea and vomiting up to 48 hours after day care gynecological laparoscopy after oral pre-medication with ondansetron 4mg, metoclopramide 10mg or a placebo allocated randomly and assessed blindly. Emetic symptoms occurred in 26% of patients who received ondansetron, 42% of those who received metoclopramide and 50% in those who received placebo. Another study done by Austreberrto *et al*[9], in which they compared the effectiveness of ondansetron and metoclopramide in prevention of postoperative nausea and vomiting in elective surgery and reported incidence of vomiting was significantly smaller with ondansetron group (5%) than with metoclopramide group (15%). Nausea in ondansetron group was reported among 10% of patients and in metoclopramide group among 24%of patients and hence they concluded that ondansetron was more effective than metoclopramide to prevent postoperative nausea and vomiting. Similarly, Alon E *et al*[10] evaluated the prophylactic anti-emetic efficacy of ondansetron in a randomized, double blinded comparison with Droperidol and Metoclopramide in 66 patients undergoing general anesthesia and reported the incidence of vomiting was 13% in ondansetron group, 45% in Droperidol group and 45% in Metoclopramide group and concluded that pre-operative prophylactic administration of ondansetron is superior to Droperidol and Metoclopramide. Also, Raphasel JH *et al*[11] compared the prophylactic antiemetic efficacy of ondansetron with metoclopramide and reported that among 82% of patients who received

ondansetron and 47% of patients who received metoclopramide, were free of emetic episodes.

CONCLUSION

On the basic of observation made in the present study, it was found ondansetron was more effective than metoclopramide in decreasing the occurrence of postoperative nausea and vomiting. Also, it was found that there was decreasing the number of episodes in ondansetron group than the metoclopramide group during the postoperative period. Thus a single intravenous injection of ondansetron of 4mg significantly controls nausea and vomiting and helps to eliminate the distressing postoperative nausea vomiting which continues to be a problem for the patients, anesthesiologists and surgeons.

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