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Anti-emetic Prophylaxis in Major Gynecological Surgery with Intravenous Granisetron Versus Metoclopramide: A Randomized Double Blind Comparative Study

B Sunitha[1], B Keshavanarayana[2]

[1]Assistant Professor, Department of Anesthesiology, Government Medical College, Mahabubnagar, Telangana 509001, India.
[2]Assistant Professor, Department of Anesthesiology, Dr. VRK. Women's College, Teaching Hospital and Research, Aziz Nagar, R.R. District, Telangana 500075, India.

Abstract

Introduction: Post-operative nausea and vomiting is one of the most common and distressing side effect encountered by patients following anesthetic and surgical procedures. *Aims:* The aim of the present study is to compare the effectiveness of intravenously administered Granisetron with Metoclopramide in the prevention of post-operative nausea and vomiting in patients undergoing major gynecological surgery under general anesthesia. *Materials and Methods:* This study was carried out for a period a total number of 50 cases were taken into study 25 of them received Granisetron (40 µg/kg) and the other 25 patients received Metoclopramide (0.2 mg/kg) for preventing post-operative nausea and vomiting through a period of 24 hours. *Results:* There were no statistically significant differences between the groups with respect to patient's characteristics, type of surgery and duration of anesthesia. There was statistically significant increase in pulse rate and systolic blood pressure in metoclopramide group while the diastolic blood pressure remained relatively constant. Granisetron group did not show significant variation in either pulse rate or blood pressure. The incidence of post-operative nausea and vomiting in 24 hours period was 12% and 48% in granisetron and metoclopramide respectively. The incidence of nausea in first 24 hours of post-operative period was 12% and 48% in granisetron and metoclopramide groups respectively. The incidence of retching/vomiting in first 24 hours post-operative period was 32% in metoclopramide group and no such episodes occurred with granisetron. *Conclusion:* The administration of granisetron before induction of anesthesia is superior to metoclopramide in long-term prevention of post-operative nausea and vomiting following major gynecological surgery.

Keywords: Granisetron; Metoclopramide; Gynecological surgery.

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Introduction

Post-operative nausea and vomiting is one of the most common and distressing side effect encountered by patients following anesthetic and surgical procedures. In the present scenario, it is estimated that 22 to 30% of adult patients will develop post-operative emesis which is consistently lower when compared to 75 to 80% incidence reported during the "Ether Era".[1,2] As per the literature, incidence of post-operative nausea and vomiting ranges from 25 to 55% following inpatient

Corresponding Author: B Keshavanarayana, Assistant Professor, Department of Anesthesiology, Dr. VRK. Women's College, Teaching Hospital and Research, Aziz Nagar, R.R. District, Telangana 500075, India.

E-mail: drkeshava10@gmail.com

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surgery and 8 to 47% for outpatient surgery. When questioned before surgery, it was observed that patients are concerned. about post-operative nausea and vomiting apart from pain.[3] Severe and persistent post-operative nausea and vomiting can cause tension on suture lines, bleeding at operative sites and wound dehiscence, venous hypertension, oesophageal tears and rupture, rib fractures, gastric herniation and muscular fatigue: In neurosurgical cases, post-operative nausea and vomiting can cause increased intracranial tension. It can also increase the risk of pulmonary aspiration. It may result in dehydration and electrolyte imbalance in pediatric population.

Post-operative nausea and vomiting is a major contributor to burgeoning healthcare costs for both the hospital and the patient. These costs may result from longer recovery, extended stay in the hospital, added attention required from nurses and physicians, additional drug supplies as well as unanticipated admissions following outpatient procedures. Over 49% of patients accounted post-operative nausea and vomiting as the post-operative side effect of greatest concern, during their pre-anasthetic checkup.[4] Over 70% of patients considered avoidance of post-operative nausea and vomiting to be very important for a relatively comfortable and symptom free post-operative recovery.[5] Most of the currently used anti-emetic drugs like antihistamines, anticholinergics and dopamine receptor antagonists possess clinically significant side effects.[4] In this study, metoclopramide which is the most commonly used anti-emetic which prevents vomiting by increasing the resting tone of gastro esophageal sphincter[5] and blocking central dopaminergic receptors is compared with Granisetron which acts by selective antagonism of sub-type 3, 5-HT_3 receptors.[6]

Materials and Methods

This study was carried out in the Department of anesthesiology, Government Medical College and General Hospital, Mahabubnagar, Telangana from *Dec 2012–August 2014*. The study was approved by the institutional ethical committee. A total number of 50 patients, 25 in each group with inclusion and exclusion criteria were selected for study, patients were allocated randomly to each group by drawing lots.

Inclusion Criteria

Patients with ASA Grade I and II, Age between *26* to *55 yrs* of female patients

Exclusion Criteria

Recent (within *24 hrs*) or chronic ingestion of any other medicine with potential anti-emetic property, Hypersensitivity to Granisetron or metoclopramide, H/o motion sickness. Clinically significant cardiovascular, pulmonary, renal, hepatic, neurological or endocrine abnormalities.

All patients were explained in detail about the study and written informed consent was obtained from patients. Every effort was made to standardize the anesthetic technique. Intra-operative hydration with solute was set at 10 ml/kg plus replacement of 3 ml for each ml of blood lost. Patients were asked to tell us as soon as they become uncomfortable so that pain-relieving medicine could be administered to them.

They were also asked to inform about any nausea, retching or vomiting during the first *24 hours* after anesthesia.

Pre-operative data collected included age, height, heart rate, blood pressure, respiration rate, history of motion sickness, previous surgery and post-operative nausea and vomiting. The patients were allocated randomly to one of the two groups. As it was a double blind randomized study, medication was prepared in two identical *10 ml* syringes to ensure blinding. Before induction of anesthesia, patients were randomized in a double-blind fashion to receive either intravenous granisetron at the dose of *40* µg*/kg* (Group A), or intravenous metoclopramide at the dose of *0.15 mg/kg* unto a maximum of *10 mg* (Group B) in a *10 ml* coded syringe containing the diluted drug. Patient's pulse rate and blood pressure were recorded before and after surgery.

Patients and investigator who collected the post-operative data were blind to randomization. The anesthetic technique and the drugs are standardized. The patients are pre-medicated with glycopyrrolate *0.2 mg*, Buprenorphine *4* µg*/kg*, and Midazolam *0.03 mg/kg* body weight all through intravenous route. Patients were induced with Thiopentone sodium (*5 mg/kg*); tracheal intubation was facilitated with vecuronium bromide (*0.1 mg/kg*) Anesthesia was maintained with N_20 & 0_2 (5:3) and muscle relaxation with vecuronium bromide with one fifth of loading dose. Ventilation was controlled manually. At the end of surgery Neostigmine *0.05 mg/kg* and atropine *0.02 mg/kg* I.V. was administered for reversal of neuromuscular blockade and after complete recovery patients were extubated.

After surgery patients were observed for

24 hrs post-operatively for nausea, retching and vomiting. Rescue anti-emetics were given if vomiting occurred more than once, for nausea lasting for more than *10 minutes* or at the patient's request. Inj. Ketorolac *0.1 mg/kg* were administered for patients who complain of pain. Incidence of nausea and vomiting occurring in first four hours post-operatively is considered as early nausea and vomiting and incidence of PONV after *four hours* was considered as late emetic episode. We made no distinction between vomiting and retching (*i.e.*, retching event was considered a vomiting event). Nausea and Vomiting were evaluated on three point ordinal scale.

0 = None; 1 = Nausea; 2 = Retching/vomiting.

The incidence of nausea and vomiting in the two different groups was analyzed using Chi-square test, $p < 0.05$ was considered significant. Statistical formulae used for analysis of the results of Student '*t*' test value Probability Value (*p*) was estimated by reusing '*t*' Test value in corresponding '*t*' Test.

Results

A total number of 50 cases were taken into study 25 of them received Granisetron (*40 µg/kg*) and the other 25 patients received Metoclopramide (*0.2 mg/kg*) for preventing post-operative nausea and vomiting through a period of *24 hours*, shows in Table 1.

There was no statistically significant difference between the two groups in respect of demographic and anesthetic characteristics, shows in Table 2.

Both the groups were observed for differences in pulse rate and blood pressure (systolic and diastolic) *5 minutes* after giving the anti-emetic medication. There was statistically significant increase in pulse rate and systolic blood pressure in metoclopramide group while the diastolic blood pressure remained relatively constant. Granisetron group did not show significant variation in either pulse rate or blood pressure, shows in Table 3.

Table 3: Incidence of post-operative nausea and vomiting in first *24 hours*

Post-operative nausea and vomiting	GroupA (Granisetron)	Group B (Metoclopramide)
Present	3 (12%)	12 (48%)
Absent	22 (88%)	13 (52%)
Total	25	25

The incidence of post-operative nausea and vomiting in *24 hours period* was 12% and 48% in Group A and Group B respectively ($p < 0.01$).

Chi-Square = 7.8095, Degrees of freedom = 1, p (0.01) = 6.63 (Table value of X^2 at 0.01 level of significance, shows in Table 4.)

Table 1: Demographic and anesthetic data

Patient Characteristics	Mean Group A	Mean Group B	*p* value
Age	40.52 + 8.7	39.8400 + 7.44	0.2968 NS
Weight	50.3 + 5.8	48.1 + 6.7	1.2379 NS
Duration of Anesthesia (min)	100.0 + 26.6	89.0 + 23.6	1.5454 NS
Duration of Surgery (min)	91.2 + 17.39	99.2 + 25.1	1.3079 NS

Table 2: Change in hemodynamic parameters

Group A	Mean (before)	Mean (after)	Paired T
Pulse rate	86.96 + 8.15	86.24 + 6.99	1.3407 NS
Systolic Blood Pressure	126.64 + 14.09	126.32 + 13.73	0.6094 NS
Diastolic Blood Pressure	83.84 + 7.07	82.88 + 7.73	1.7677 NS
Group B			
Pulse rate	92.28 + 10.22	104.4 + 14.36	8.4974 **
Systolic Blood Pressure	127.28 + 15.61	130.32 + 16.01	5.2528 **
Diastolic Blood Pressure	81.76 + 4.74	82 + 5.89	0.4856 NS
Group A and Group B After 5 min			
Pulse rate	89.62 + 9.53	95.32 + 14.46	4.8003 **
Systolic Blood Pressure	126.96 + 14.72	128.32 + 14.9	2.9881 **
Diastolic Blood Pressure	82.8 + 6.05	82.44 + 6.81	

** Significant at 1% level ($p < 0.01$).

Table 4: Incidence of nausea and vomiting in first *24 hours* of post-operative period

Nausea	Group A (Granisetron)	Group B (Metoclopramide)
Present	3	12
Absent	22	13
Vomiting		
Present	0	8
Absent	25	17

The incidence of nausea in first *24 hours* of post-operative period was significantly high in Group B compared to Group A. Chi-Square = 7.8095, Degrees of freedom = 1, *p* (0.01) = 6.63 (Table value of X^2 at 0.01 level of significance).

There were no emetic episodes in Group A, incidence of emetic episodes in Group B is 32%. Incidence of emetic episodes in *24 hrs*. of post-operative period is significantly high in Group B compared to Group A ($p < 0.01$). Chi-Square = 9.6726, Degrees of freedom = 1, *p* (0.01) = 6.63 (Table value of X^2 at 0.01 level of significance), shows in Table 5.

Table 5: Incidence of early nausea and vomiting (*0–4 hours*)

Early nausea	Granisetron	Metoclopramide
Present	1	5
Absent	24	20
Vomiting		
Present	0	2
Absent	25	23

Incidence of early nausea (*0–4 hours*) in granisetron and metoclopramide groups did not show any statistically significant difference. (*p* value > 0.05) Chi-Square = 3.219, degrees of freedom = 1, *p* value (0.05) = 3.84 (Table value of X^2 at 0.05 level of significance). Both granisetron and metoclopramide were equally efficacious in preventing vomiting during early post-operative period after recovering from anesthesia (*p* value > 0.05). Chi-Square = 2.602, Degrees of freedom = 1, *p* value (0.05) = 3.84 (Table value of X^2 at 0.05 level of significance), shows in Table 6.

Table 6: Incidence of late nausea and vomiting from *4–24 hours*

Late Nausea	Granisetron	Metoclopramide
Present	3	10
Absent	22	15
Late vomiting's		
Present	0	8
Absent	25	17

Incidence of late nausea was 12% and 40% in metoclopramide and granisetron groups respectively, which was statistically significant difference. Chi Square = 5.1975, Degrees of freedom = 1, *p* value (0.05) = 3.84 (Table value of X^2 at 0).

There were no emetic episodes during *4–24 hours* post-operative period in granisetron group where as 32% of patients in metoclopramide group developed emesis during this late post-operative period, which showed statistically significant difference. Chi-Square = 9.6726, Degrees of freedom = 1, *p* value (0.05) = 6.63 (Table value of X^2 at 0.05 level of significance), displays in (Fig. 1).

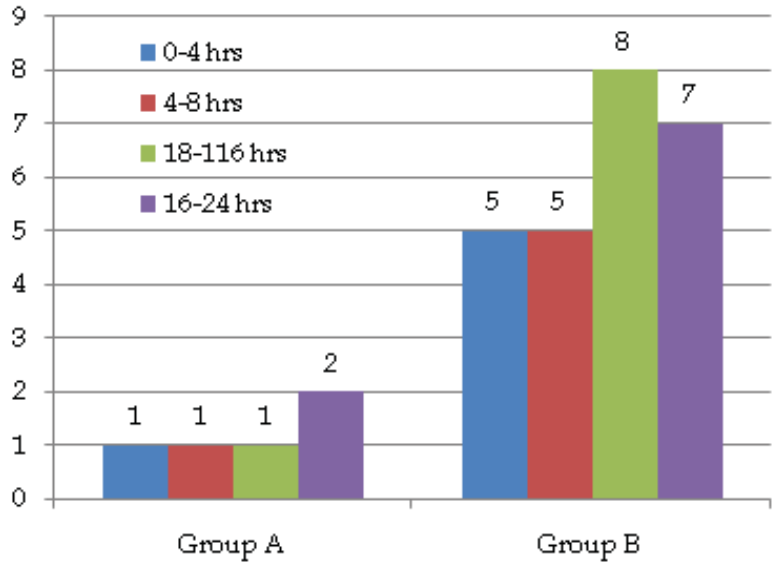

Fig. 1: Incidence of nausea from *0–4 hours*, *4–8 hours*, *8–16 hours* and *16–24 hours*.

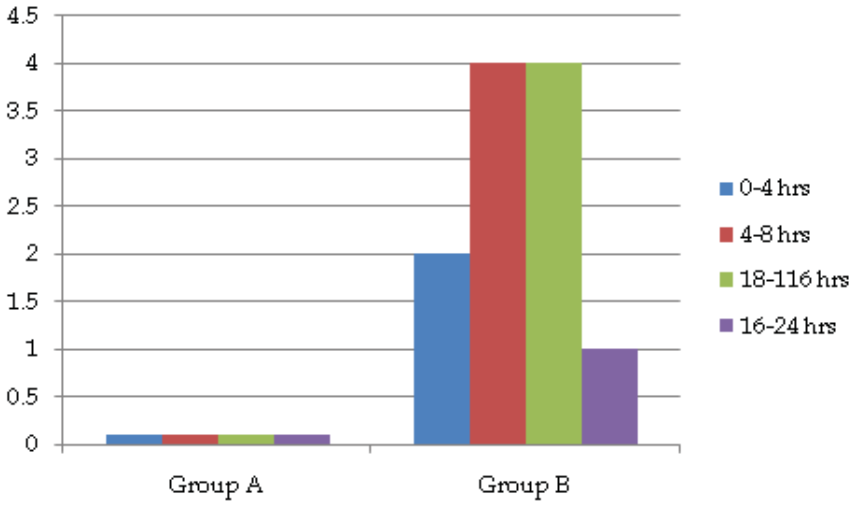

Fig. 2: Incidence of vomiting from *0–4 hours*, *4–8 hours*, *8–16 hours* and *16–24 hours*

Incidence of nausea from *0–4 hrs*, *4–8 hrs*, *8–16 hrs* and *16–24 hrs* assessment periods were 20%, 20%, 32% and 38% respectively in metoclopramide group but in contrary one patient (4%) had nausea during the first 3 assessment periods and 2 patients (8% 0 had nausea in *16–24 hrs* assessment period in granisetron group. Chi-Square = 34.1611, Degrees of freedom = 4, *p* value = (0.01) = 13.28 (Table value of X^2 at 0.01 level of significance), displays in (Fig. 2).

There were no episodes of vomiting in the group of granisetron, the patients in metoclopramide group of were observed to have 8%, 16%, 16% and 4% in *0–4 hours*, *4–8 hours*, *8–16 hours* and *16–24 hours* assessment periods respectively. Chi-Square = 16.1282, Degrees of freedom = 4, *p* value (0.01) = 13.28 (Table value of X^2 at 0.01 level of significance).

Discussion

Nausea and vomiting following general anesthesia has been a distressing problem for the patients and is frequently listed among the most important pre-operative concerns apart from pain. With the change in emphasis from inpatient to outpatient office based medical/surgical environment, there has been increasing interest in the "the big little problem" of post-operative nausea and vomiting following general anesthesia. Inspite of so much advancement in the management of post-operative nausea and vomiting with the invention of new drugs, multimodal approaches of management like administering multiple different anti-emetic medications, less emetogenic anesthetic techniques, adequate intravenous hydration, adequate pain control etc., the incidence of post-operative nausea and vomiting remains still high ranging from 25%–55% following inpatient surgery and 8%–47% following outpatient surgery.[3]

An effective anti-emetic that could be used to treat nausea and vomiting without extending recovery time and that remain effective for *24 hours* following treatment would be significant asset to the anesthesiologist's armamentarium, especially in settings like office-based anesthesia where the patient is admitted for daycare surgery and discharged on the same day. Drugs acting for longer duration also have an advantage in surgeries where the incidence of post-operative nausea and vomiting is very high like laparoscopic surgery, middle ear surgery, tonsillectomy, laparotomy, strabismus surgery, orchipexy etc. Unfortunately, commonly used anti-emetic medications like antihistamines, anticholinergics, gastroprokinetics, butyrophenones cause undesirable side effects like sedation, dysphoria, restlessness and extrapyramidal symptoms. To overcome this later serotonin antagonists like ondansetron, tropisetron, dolasetron, granisetron and ramosetron were introduced for treatment of nausea and vomiting. They were primarily used in treating chemotherapy induced vomiting with minimal and clinically acceptable side effects. The most distressing and intolerable emesis induced by antimalignant medication was better controlled with these 5-HT_3 antagonists and they proved to have a promising role in the field of oncology. Abundant research in oncology demonstrates the efficacy of these drugs. However, there were anecdotal reports in the literature about their role in prevention of post-operative nausea and vomiting. We compared most commonly used anti-emetic metoclopramide with 5-HT_3 antagonist; granisetron as there was no published data in Indian literature.[6]

In the present study, the anti-emetic efficacy of granisetron and metoclopramide was assessed in post-operative nausea and vomiting for a period of *24 hours*. The post-operative period was again subdivided into four groups of assessment periods (*0–4 hrs*, *4–8 hrs*, *8– 16 hrs* and *16–24 hrs*) to assess the efficacy of both the drugs during different time intervals. We have selected similar group of patients in respect of age, weight, duration of surgery and duration of anesthesia to compare the efficacy of the drugs. Analgesia for post-operative pain was standardized and patients of both groups were observed for a period of *24 hours* post-operatively. Hence, we believe that difference in the incidence of post-operative nausea and vomiting is attributed exclusively to the study drugs. Unlike Fujii Y *et al.* (2000), we have not included the placebo group in our study for want of approval from hospital ethical committee as the incidence of post-operative nausea and vomiting is very high in our set up without prophylactic anti-emetics.[7]

Like Fujii Y *et al.*, we did not find post-operative vomiting. during first *4 hours* of assessment period in both the groups in our study. The incidence of nausea and vomiting in *4–24 hours* post-operative period showed a significant difference with 48% for metoclopramide and 12% for granisetron (p value < 0.01). Fujii Y *et al.* (2000) also found significant difference in the incidence of nausea and vomiting in *3–24 hrs* post-operative period between both the groups with a p value of < 0.05. In our study, the sample size of each group was more *i.e.*, 25 when compared to 20 of Fuji's series, although we have not considered the placebo group for the reasons already mentioned.[8]

In our study, there were no episodes of vomiting in granisetron group, whereas 8 of 25 patients in metoclopramide group had vomiting. In Fuji's series, 6 of 20 patients in metoclopramide group had emetic episodes while none in granisetron reported vomiting. Fujii Y reported that 19 of 20 patients in the granisetron group had no emetic symptoms, with 12 of 20 patients receiving metoclopramide having emetic symptoms ($p < 0.05$).[8] In the present study, 22 of 25 patients receiving granisetron had not experienced emetic symptoms, while 12 of 25 patients in metoclopramide group had the symptoms. It was concluded that granisetron is superior to metoclopramide in the long-term prevention of post-operative nausea and vomiting after anesthesia in the present as well as Fujii's series.[7,8] Both the groups were observed for differences in pulse rate and blood pressure (systolic and diastolic) *5 minutes* after giving the anti-emetic medication. There was statistically significant increase in pulse rate and systolic blood pressure in metoclopramide group while the diastolic blood pressure remained relatively constant. Granisetron group did not show significant variation in either pulse rate or blood pressure (systolic and diastolic).

We have not observed any side effects with granisetron as well as metoclopramide contrary to Schellers's report, which describes toxic neurological reactions in patients who received metoclopramide.[9] In the present series, there are no side effects observed with granisetron where as Bilajham in his study on efficacy of granisetron in preventing vomiting with cytotoxic therapy over multiple cycles had observed headache in 6.6% and constipation in 3.5% of patients as frequent side effects.[10]

Yoshitaki Fujii *et al.* (1996) compared the frequency of retching and vomiting in children who had undergone strabismus repair by giving placebo, metoclopramide *0.25 mg/kg* and granisetron *40 μg/kg* in different groups.[11] During *0–3 hours* after anesthesia, the frequencies of retching and vomiting were: Placebo 62%, metoclopramide 22% and granisetron 13% ($p < 0.05$). Corresponding frequencies during *3–24 hours* were: placebo 50%, metoclopramide 39% and granisetron 13% ($p < 0.05$). Hence, granisetron was found to be more superior to metoclopramide or placebo in reducing vomiting.

In a study, conducted by Fujii *et al.* to assess the efficacy of granisetron, droperidol and metoclopramide for preventing PONV in female patients with a history of motion sickness undergoing major gynecological surgery.[12] The incidence of PONV was 70%, 50%, 57% and 23% in the placebo, droperidol, metoclopramide and granisetron groups respectively ($p < 0.05$). Granisetron is a better prophylactic anti-emetic than droperidol or metoclopramide in female patients with a history of motion sickness undergoing major gynecological surgery. In a study, conducted by Fujji *et al.* to assess the efficacy of granisetron, droperidol and metoclopramide for the prevention of post-operative nausea and vomiting in female patients undergoing middle ear surgery was compared.[13] In a randomised, double-blind study, 180 patients received granisetron *40 micrograms*, kg^{-1}, droperidol *20 micrograms*, kg^{-1} or metoclopramide *0.2 mg*, kg^{-1} given intravenously immediately before induction of anesthesia ($n = 60$ for each), prophylactic therapy with granisetron is superior to droperidol or metoclopramide in the prevention of post-operative nausea and vomiting after middle ear surgery.

Fujji *et al.* in a randomized, double-blind study, 120 patients received droperidol *25 micrograms*, *kg-1*, metoclopramide *0.2 mg*, *kg-1* or granisetron *40 micrograms*, *kg-1*, (*n* = 40 in each group) I.V. immediately before induction of anesthesia.[14] A standard general anesthetic technique and post-operative analgesia were used throughout. There was a complete response, defined as no PONV and no administration of rescue medication, during the *24-h* observation period in 45% of patients in the droperidol group, 38% in the metoclopramide group and 70% in the granisetron group ($p = 0.021$ vsdroperidol, $p = 0.003$ *vs* metoclopramide). There was no difference in the incidence of adverse events between groups. We conclude that the prophylactic anti-emetic efficacy of granisetron was superior to that of droperidol or metoclopramide for prevention of PONV in women during menstruation.

Fujji *et al.* evaluate the efficacy of granisetron, droperidol and metoclopramide for preventing PONV after breast surgery. In a randomized, double-blind, placebo-controlled trial, 120 female patients received granisetron *40 micrograms*, *kg-1*, droperidol *1.25 mg*, metoclopramide *10 mg* or placebo (saline) (*n* = 30 for each) intravenously immediately before the induction of anesthesia. The incidence of PONV was 17% with granisetron, 37% with droperidol, 43% with metoclopramide and 50% with placebo ($p < 0.05$; overall Fisher's exact probability test).[13] The incidence of adverse events was not different among the groups. Granisetron is highly effective for reducing the incidence of PONV in female patients undergoing breast surgery. Droperidol and metoclopramide are ineffective in this population.

Fujji Y *et al.* (1999) compared the efficacy and safety of granisetron, droperidol, and metoclopramide for preventing PONV after thyroidectomy and concluded that Prophylactic therapy with granisetron is superior to droperidol or metoclopramide for preventing PONV after thyroidectomy.[15] He incidence of a complete response, that is, no PONV and no need for another rescue anti-emetic during the first *3 hours* (*0* to *3 hours*) after anesthesia was 90% with granisetron, 55% with droperidol, and 50% with metoclopramide, respectively; the corresponding incidence during the next *21 hours* (*3* to *24 hours*) after anesthesia was 85%, 50%, and 45% ($p < 0.05$; overall Fisher's Exact probability test). No clinically important adverse events were observed in any of the groups. Prophylactic therapy with granisetron is superior to droperidol or metoclopramide for preventing PONV after thyroidectomy.

Fujii *et al.* evaluated 120 female patients undergoing major gynecological surgery in the treatment of established post-operative nausea and vomiting with in the first *3 hours* of anesthesia with granisetron (*40 µg/kg*), droperidol (*20* µg/kg) and metoclopramide (*0.2 mg/kg*).[16] Patients were then observed for *24 hours* and concluded that granisetron was more effective (88%) than droperidol (55%) or metoclopramide (50%) in the treatment of established post-operative nausea and vomting. Fujji Y *et al.* evaluated the efficacy of granisetron, droperidol and metoclopramide for the treatment of PONV after Laparoscopic Cholicystectomy.[16] Patients undergoing laparoscopic cholecystectomy (LC) may be especially at risk of experiencing post-operative nausea and vomiting (PONV). After experiencing PONV during the first *3 hr* after recovery from anesthesia, 120 patients (78 women) received, in a randomized double-blind manner, granisetron *40 µg/kg*, droperidol *20 µg/kg* or metoclopramide *0.2 mg/kg* (*n* = 40 per group) intravenously. Patients were then observed for *24 hr* after administration of the study drug. A high dose of granisetron (*40 µg/kg*) was more effective than droperidol *20 µg/kg* or metoclopramide *0.2 mg/kg* for the treatment of established PONV after laparoscopic cholecystectomy.

Fujji Y *et al.* in a prospective, randomized, double-blinded trial, 90 pediatric patients, aged *4* to *10 years*, received granisetron, *40 µg/kg*; droperidol, *50 µg/kg*; or metoclopramide, *0.25 mg/kg* (*n* = 30 of each) intravenously after an inhalation induction of anesthesia. Emetic episodes and safety assessments were performed during the first *24 hours* after anesthesia.[17] Prophylactic therapy with granisetron is superior to droperidol or metoclopramide for the prevention of PONV after tonsillectomy in children with a history of motion sickness. Oksuz H, Zencirci B, Ezberci M. *et al.*[18] to compare the anti-emetic activity of different 5-hydroxytryptamine-3 receptor antagonists with that of metoclopramide. In a randomised, double-blind study, 75 patients received the following: Group M, *10 mg* metoclopramide; Group K, *40 mcg*, *kg*(*-1*) granisetron; and Group Z, *15 mcg*, *kg*(*-1*) ondansetron intravenously (I.V.) diluted in 20 cc 0.9% NaCl (*n* = 25 of each) I.V. immediately before the induction of anesthesia. Granisetron, when given prophylactically, resulted in a significantly lower incidence of PONV than metoclopramide and ondansetron, whereas metoclopramide was ineffective. Garnisetron may be an effective treatment in the proflaxy of PONV.

Our study agrees with and confirms the various aspects of the above studies. We found that granisetron has a definite advantage over metoclopramide in the treatment of post-operative nausea and vomiting in female patients undergoing major gynecological surgery under general anesthesia. Post-operative nausea and vomiting was also assessed in four different time periods *i.e.*, *0–4 hours*, *4–8 hours*, *8–16 hours* and *16–24 hours* and our observation was that the incidence of nausea was 20%, 20%, 32% and 28% in the metoclopramide group during the four assessment periods respectively. In granisetron group the incidence of nausea during the four assessment periods were 4%, 4%, 4% and 8% respectively. Vomiting episodes were found to be 8%, 16%, 16% and 4% during *0–4 hrs*, 4–8 hrs, *8–16 hrs* and *16–24 hrs* in the metoclopramide group while none of the patients who received granisetron had vomiting throughout the assessment periods.

Conclusion

Administration of metoclopramide and granisetron before induction effectively controlled nausea and vomiting during early post-operative period *i.e.*, within *4 hours* after recovering from anesthesia. Post-operative nausea and vomiting during *4–24 hours* after recovering from anesthesia was significantly lower with granisetron when compared to metoclopramide (p value < 0.01). The administration of granisetron before induction of anesthesia is superior to metoclopramide in long-term prevention of post-operative nausea and vomiting following major gynecological surgery.

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