A Comparative Clinical Study Of Prevention Of Post-Operative Nausea And Vomiting Using Granisetron And Ondansetron In Laparoscopic Surgeries.

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Citation

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Abstract

Despite the advances made in anesthesia, postoperative nausea and vomiting is one of the most common postoperative complications. The efficacy of granisetron with that of ondansetron as prophylactic antiemetic is compared in 90 patients undergoing laparoscopic surgeries. The patients were divided into three groups of 30 patients each. In group- G, patients received 40 mcg/kg intravenously 3 min before induction. Group-O patients received 80 mcg/kg intravenously 3 min prior to induction while group–C patients received 3 ml of 0.9% normal saline as control. All the patients were selected for general anesthesia and observations were made for pulse rate, blood pressure, nausea, vomiting and side effects of the drugs under study up to 12 hours postoperatively. The frequency of nausea was 10%, 30% and 40% in group-G, group-O and group-C respectively .The statistical analysis shows that granisetron is significantly efficient for prevention of post-operative nausea and vomiting (PONV) ($p<0.05$) in comparison to ondansetron and is highly significant ($p<0.01$) in comparison to control group. As far as the side effects of the drugs are concerned, postoperative headache, dizziness, diplopia and shivering was significantly higher in ondansetron groups.Thus from the present study, it is concluded that intravenous granisetron 40 mcg/kg intravenously is superior to ondansetron 80 mcg/kg as a prophylactic antiemetic in laparoscopic surgeries in controlling PONV.

INTRODUCTION

Nausea, retching and vomiting are among the most common postoperative complications and can occur after general, regional or local anesthesia. Laparoscopic surgery is one condition, where risk of PONV is particularly pronounced due to pneumo-peritoneum causing stimulation of mechanoreceptors in the gut [1] Now, there has been a general trend towards a decrease in the incidence and intensity of the problem because of the use of less emetic anesthetic agents, improved pre and post operative medication (e.g. analgesics), refinement of operative techniques and identification of patient predictive factors. However, in spite of these advances, nausea and vomiting still occur with unacceptable frequency in association with surgery and anesthesia and the description of it as “the big little problem” [2]. Encapsulates much of general perception. Experience of postoperative nausea and vomiting can also alter the attitude of the patient. PONV can also lead to delay in recovery and prolongs hospitalization [3] In spite of plenty of antiemetic drugs available, no single drug is 100% effective in prevention of PONV and combination of have got a lot of side effects. [4].

Prophylactic antiemetic therapy in patients at higher risks for PONV may not only be beneficial but also admission for PONV and extra cost associated with nursing care can be avoided. Granisetron is relatively new antiemetic which is selective 5-HT_3 antagonist agent. So the present study was undertaking to compare the antiemetic effects of IV granisetron and ondansetron for prophylaxis of PONV in patients undergoing laparoscopic gynecological surgeries.

MATERIALS AND METHODS

After approval from the institutional ethical committee and informed written consent from the patients, ninety patients of ASA gr I or II aged between 12-58 yrs weighing between 31-65 kgs are selected for the study from the routine list of Laparoscopic Surgeries,. All of them were studied into three groups of thirty each as group- G, Group- O, Group- C. Patients with positive history of nausea and vomiting in past were excluded from the study All the patients of three groups were premeditated with Glycopyrrolate 4 mcg/kg intramuscularly and Midazolam 20 mcg/kg intravenously 1

hr before the induction of anesthesia. Antiemetic drugs were given 3 minutes before the induction of anesthesia. Intravenous line was maintained with Ringer lactate solution 4 ml/kg.

Group-G: Granisetron 40 mcg/kg I/V.

Group-O: Ondansetron 80 mcg/kg I/V.

Group-C: 3 ml of 0.9% normal saline.

Patients in all the three groups were selected for general anesthesia. Pre-induction measurement of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and peripheral oxygen saturation from the anesthesia monitor was taken as the baseline measurement. All the patients were induced with Thiopentone sodium 5 mg/kg and succinylcholine 1.5 mg/kg IV, after preoxygenation for 3 minutes and endotracheal intubation was done. Orogastric tube was introduced and suction was applied to empty the stomach from air and other contents. Maintenance of anesthesia was done with 33% oxygen and 66% nitrous oxide and traces of isoflurane. Vecuranium muscle relaxation and controlled ventilation was maintained manually through closed circuits. All patient received Tramadol (1 mg/kg) for intraoperative analgesia. At the end of the surgery patients were reversed with neostigmine 0.05 mg/kg and Glycopyrrolate 8 mcg/kg as a mixture from the same syringe intravenously. The nasogastric tube was suctioned and then removed prior to tracheal extubation. IM diclofenac was given for postoperative analgesia. Nausea, vomiting, pulse and blood pressures –both systolic and diastolic were recorded before premedication, after premedication, 5 minutes after induction, 15 minutes after induction and thereafter every 15 minutes interval up to 1 hour and thereafter every 2 hours up to 12 hours of induction of anesthesia.

Nausea, vomiting incidences with side effects of the drugs like headache, drowsiness, dizziness, shivering, pain at the site of injection, malaise, fatigue, anxiety or agitation, diplopia, pruritus and urticaria was also recorded, perioperatively and postoperatively up to 12 hours. Frequency and severity of nausea and vomiting were also included in the observation.

RESULTS

Demographic data (Table 1) like age, sex, weight, were comparable in both the groups.

Figure 1

Table no. 1

		Group G	Group O	Group C
Age (years)	Mean	26.77	27.57	25.37
	S.D.	±5.60	±10.63	±7.68
Weight (Kgs)	Mean	50.83	48.83	47.83
	S.D.	±6.29	±7.58	±6.26

DEMOGRAPHIC DATA

All the results for the changes in mean arterial pressure and pulse in group in Group-G and Group-O were very linear with the patients in group-C (TABLE 2). So it is evident that there is no significant changes mean arterial pressure and pulse in all the three groups. Thus in all the three groups cardiovascular changes are insignificant and suggest that study drugs are not having any effects on cardiovascular system.

Figure 2

Table – 2 Showing Changes observed in cardiovascular system in all three groups

Time	Group – G	Group – O	Group – C
Preoperative	84.46 89.33	81.00 90.44	81.23 93.33
After Premeditations pulse MAP	84.66 91.99	82.26 89.97	83.60 92.88
After Anesthesia 5min pulse MAP	85.20 92.10	84.56 86.77	85.06 91.10
After Anesthesia 15min pulse MAP	84.93 91.62	84.26 86.21	85.20 90.77
After Anesthesia 30 min pulse MAP	84.33 89.99	85.80 85.21	84.30 85.42
After Anesthesia 45 min pulse MAP	86.73 87.32	86.73 85.33	84.13 86.21
After Anesthesia 60 min pulse MAP	87.20 86.43	85.13 84.45	82.66 85.55
After Anesthesia 2 Hours pulse MAP	87.66 87.43	82.26 84.44	83.06 85.21
After Anesthesia 4 Hours pulse MAP	87.66 87.55	82.26 85.21	83.46 86.88
After Anesthesia 6 Hours pulse MAP	87.60 87.66	82.46 86.19	83.73 86.99
After Anesthesia 8 Hours pulse MAP	87.20 87.98	82.66 86.21	84.53 88.10
After Anesthesia 10 Hours pulse MAP	86.93 88.39	82.66 85.97	85.26 87.55
After Anesthesia 12 Hours pulse MAP	86.00 86.98	83.20 85.86	84.66 88.77

In Group-G, only 3 (10%) patients experienced nausea as compared to Group-O in which 9 (30%) patients experienced nausea and in Group-C 12 (40%) experienced nausea.So, in Group-G patients' incidence of nausea was comparatively less than Group-O patients. In Group-G, only 3(10%) patients experienced vomiting in comparison to Group-O in while 10 (33.33%) experienced vomiting and in Group-C 15 (50%) patients experienced vomiting. So, in Group-G patients, incidence of vomiting was quiet less than Group-O patients.

Figure 3

Table – 4 Showing Statistical Analysis of Nausea and Vomiting: Comparison of Group – G, Group – O, Group – C

Operative Procedure	Technique of Anaesthesia	Group–G N V	Group–O N V	Group –C N V
Diagnostic Laparoscopy for Gynecological Surgery	G / A	3 3	4 4	7 7
Laparoscopic Appendicectomy	G /A	- -	5 6	5 8
Total		**10% (3/30)**	**30% (9/30)**	**40% (12/30)**

Figure 4

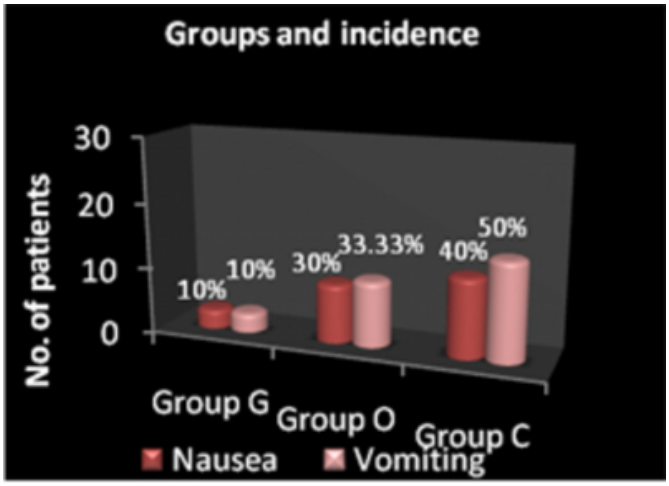
Table – 3 Showing Postoperative Observations in all three groups

No.	Criteria	Group – G	Group – O	S.E.P.	Z value	P value	Inference
1	Nausea	3(10.00%)	9(30.00%)	0.094	1.40	P<0.05	S
2	Vomiting	3(10.00%)	10(33.33%)	0.102	2.28	P<0.05	S
No.	Criteria	Group – O	Group – C	S.E.P.	Z value	P value	Inference
1	Nausea	9(30.00%)	12(40.00%)	0.115	1.73	P<0.05	S
2	Vomiting	10(33.33%)	15(50.00%)	0.119	2.23	P<0.05	S
No.	Criteria	Group – G	Group – C	S.E.P.	Z value	P value	Inference
1	Nausea	3(20.00%)	12(40.00%)	0.105	2.86	P<0.01	H.S.
2	Vomiting	3(20.00%)	15(50.00%)	0.106	3.75	P<0.01	H.S.

All these incidence of postoperative nausea and vomiting are plotted on Bar chart

Figure 5

FIGURE 1



No patients experienced headache in comparison to 2 (6.66%) patients in Group-O. So incidence of headache is higher in Group-O patients than in patients in Group-G. Similarly incidence of dizziness is significantly higher in

Group-O patients (2 patients, 6.66%) as compared to Group-G in which no patients experienced drowsiness. In Group-G no patients experienced shivering and diplopia while in Group-O 3(10.00%) patients developed shivering and 2(06.66%) patients experienced diplopia. Thus incidence of shivering and diplopia is also higher in Group-O patients receiving ondansetron as premedication. In Group-C, one patient experienced shivering and diplopia. Other side effects of the drugs like pain at the site of injection, malaise, fatigue, anxiety, agitation, pruritus, urticaria, hypotension or respiratory obstruction were also monitored and observed but these were not seen in any patients taking either granisetron or Ondansetron.

Figure 6

Table – 5 Showing Incidence of Postoperative Nausea and Vomiting (PONV) in Relation to the Operative Procedure

Event	*Group–G*	*Group – O*	*Group – C*
Nausea	3(10.00%)	9(30.00%)	12 (40.00%)
Vomiting	3(10.00%)	10(33.33%)	15(50.00%)
Headache	-	2(06.66%)	-
Drowsiness	-	-	-
Dizziness	-	2(06.66%)	-
Shivering	-	3(10.00%)	1(03.33%)
Pain at site of Injection	-	-	-
Malaise / Fatigue	-	-	-
Anxiety / Agitation	-	-	-
Diplopia	-	2(06.66%)	1(03.33%)
Pruritus	-	-	-
Urticaria	-	-	-
Hypotension	-	-	-
Respiratory Obstruction	-	-	-

DISCUSSION

As post-operative nausea and vomiting is a “big little problem”, which is very much distressing to the patient and is very frequently associated with anesthesia. In 1848, John described in detail for post operative nausea and vomiting. Thereafter many person studied incidence of nausea and vomiting with different anesthesia, technique and agents and other factors. Inhalational anesthetic agents such as nitrous oxide [5], ether and cyclopropane are liable for higher incidence of PONV [6]. Many of intravenous anesthetic agents like Thiopentone, ketamine, etomidate are likely to cause PONV [7]. There was also increased incidence of PONV when opioids like morphine, mepridine, fentanyl or sufentanyl were used for analgesia during anesthesia; it is also not uncommon for PONV to be due to regional anesthetic technique[8]. It is believed that hypoxemia at the vomiting centre was the stimulus for post operative nausea and vomiting[9]. For various type of surgery, there are different incidences for PONV especially gynecological surgery is associated with higher incidence of PONV. As females because of higher levels of gonadotropin and progesterone plasma concentration are more prone. PONV is also common in gynecological surgery where vagina is packed and insufflations during laparoscopic procedures may add to the higher incidence of PONV due to unpleasant sensations [10].

Many antiemetic drugs like prochlorperazine, metoclopromide including other benzamides like cisapride, alizopride, domperidone, clebopzide etc. droperidol, antihistaminics like cyclizine,hydroxyzine, hyosine and atropine like drugs were recommended for prophylactic as well as treatment purpose for PONV. Now 5HT3 receptor antagonists such as granisetron, ondansetron etc. used for effective management of PONV for prophylactic as well as treatment purpose. So for present study 90 patients were selected from routine list of laparoscopic surgery. Then each group was studied for the occurrence of nausea, vomiting, cardiovascular changes, and side effects of the drugs up to 12 hours postoperatively. Observation shows that there is no bradycardia or tachycardia and hypotension or hypertension after granisetron or ondansetron premedication and it remains throughout stable in all three groups. Thus it is obvious that granisetron is a drug with good cardiovascular stability which implies its pharmacological property. In Group-G, all patients received granisetron 40 mcg/kg of and out of that 3 patients (10%) had PONV. Group-O with ondansetron, 9 patients (30%) out of 30 had PONV and in Group-C with no antiemetic, 12 patients (40%) out of 30 had PONV. Thus result shows that granisetron is highly effective in prevention of PONV in patients undergoing laparoscopic surgery under general anesthesia.

The most important postoperative observation in present study is nausea and vomiting. In gynecological procedures, incidence of PONV is higher in comparison to other procedures. These may be explained by higher incidence of PONV in females due to hormonal state[11]. Still higher incidence occurring in laparoscopic procedures is due to

insufflations of air or carbon dioxide into the peritoneal cavity leading to stretching of peritoneum. A selective 5HT3 antagonist granisetron is helpful in reducing incidence of PONV. It prevents nausea and vomiting by 5HT3 receptor antagonism at two specific sites (i) centrally, in the area postrema or nucleus tractus solitarius and (ii) peripherally on vagus nerve trerminals. Patients receiving granisetron were having less incidence of nausea than control group and ondansetron group. Incidence of nausea was lowest 3 (10%) in granisetron group compared with 9(30%) and 12(40%) in ondansetron and control groups respectively as shown in table no 2. Statistical analysis confirmed that granisetron is highly effective than ondansetron and control groups as p value is less than 0.05. Incidence of vomiting was also lowest 3(10%) in granisetron group compared to ondansetron 10(33.33%) and control group 15 (50%). Thus it is evident that this is effective control of PONV by granisetron. Statistical analysis confirmed the results and suggests that granisetron is highly significant liable drug than control group and ondansetron group. Thus it is obvious from the observation and results that granisetron is very effective in reducing severity of vomiting. There was no vomiting in first 2 hours after the injection of the drug[11] this is in agreement with our study, [12] thus the results suggest that however ondansetron is having good control over PONV but it is less than granisetron in controlling PONV in early postoperative period up to 12 hours. In the present study, side effects of the drugs like headache, dizziness, drowsiness, shivering, pain at the site of injection, urticaria, pruritus or extra pyramidal side effects were observed up to 12 hours after anesthesia. Incidence of headache was 6.66% with ondansetron but no incidence noticed in granisetron and control group. Incidence of dizziness was 6.66% with ondansetron group compared to no incidence in control and granisetron groups. Incidence of diplopia is 6.66% with ondansetron and 3.33% with control while incidence of shivering is 10% with ondansetron and 3.33% with control. In present study no other side effects of the drugs was observed.

CONCLUSION

Thus from the present study it is obvious that selective 5HT3 antagonist granisetron 40 mcg/kg intravenously used as premedication is very safe and highly significantly effective than ondansetron 80 mcg/kg for prevention of PONV. Granisetron is an antiemetic which appears to be safe as is not having any effect on the cardiovascular system and devoid of side effects like extra pyramidal reaction sedation.

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