A Comparative Study Of Ondansetron And Granisetron For Prevention Of Nausea And Vomiting Following Laparoscopic Surgeries

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Citation

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Abstract

Background and objectives Laparoscopic surgeries are associated with an appreciably high rate of post operative nausea and vomiting (PONV). This study was designed to compare the effectiveness of Ondansetron with that of Granisetron for prevention of PONV after laparoscopic surgery and their effect on clinical recovery and recovery time.Methods This is a randomized prospective study of 60 adult patients of both sexes received either Ondansetron 4mg or Granisetron 2mg intravenously at the end of surgery. Perioperative anaesthetic care was standardized in all patients. Patients were then observed 24 hours after administration of the study drug.Results A complete response (defined as no PONV and no need for another rescue antiemetic) was achieved in 75% of the patients given ondansetron and 86% of the patients given granisetron with (p<.05%). No significant difference observed in the recovery time from anesthesia between the two drugs and slight differences in the adverse events were observed between the two groups.Conclusion This study concludes that the prophylactic intravenous administration of Granisetron is more effective drug than ondansetron for controlling postoperative nausea and vomiting with fewer incidences of side effects.

INTRODUCTION

Despite continuing advances in anesthetic and surgical techniques, both the incidence and severity of post-operative nausea and vomiting have remained relatively unchanged. Post operative nausea and vomiting are the most common distressing symptoms occurring after surgery[1]. These factors prevent patients returning home at the end of the day, after surgery and necessitating readmission to the hospital. The etiology of postoperative nausea, vomiting is complex and depends upon a variety of factors, including patient characteristic, type of surgery, anaesthetic technique and postoperative care.

Postoperative nausea and vomiting are more common in female patients[1]. Women undergoing Laparoscopic surgeries are particularly at risk of experiencing these problems. It leads to dehydration and electrolyte imbalance. These factors reduce the quality of life of the patients and interfering with continuation of curative therapy[2]. So an effective antiemetic therapy is needed. In the absence of any antiemetic treatment following laparoscopic surgery the incidence of nausea and vomiting is considerably high[3].

The introduction of 5-HT_3 receptor antagonist was a major advancement in the treatment of post operative nausea and vomiting because of less adverse effects that were observed than commonly used traditional antiemetic[4].

Certain procedure such as middle ear surgeries, strabismus surgeries, laparoscopies, gynecological surgeries are associated with higher incidence of PONV[5]. Ondansetron is selective 5-hydroxy tryptamine receptor antagonist possess property of superior antiemetic prophylaxis[6]. This has been now used widely for the treatment of postoperative nausea and vomiting[7,8]. Granisetron is recently introduced, 5-hydroxy tryptamine receptor antagonist, with stronger $5HT_3$ binding. It is more potent and longer acting antemetic agent compared to Ondansetron against emesis associated with chemotherapy, and have been found to be very effective for preventing PONV after laparoscopic surgery[9]. Granisetron has less incidence of side effects[10].

The aim of this clinical trial is to compare, the efficacy of

prophylactic administration of 4mg Ondansetron i.v. with that of 2mg Granisetron i.v. administered at the end of the surgery in preventing PONV in patients undergoing laparoscopic surgeries, their effect on clinical recovery and recovery time and the side effects of Inj Ondansetron and Inj Granisetron.

MATERIAL AND METHODS

A randomized prospective study was conducted in 60 adult patients of class ASA I and ASA II, of either sex in age group of 18-50yrs, weighing 45 to 70kgs, posted for Laparoscopic surgery. The patients were randomly divided into two groups of 30 each: Group 'A' – Ondansetron group (n = 30), Group 'B' – Granisetron group (n = 30). Patients belonging to ASA III and ASA IV, history of drug allergy, extremes of ages, obesity, history of motion sickness, emergency surgeries, full stomach, respiratory diseases, uraemia and Diabetes Mellitus where excluded .

Ethical clearance and written informed consent was taken from patients in both groups. The patients were premedicated with 0.2mgkg $^{-1}$ diazepam orally 12 hr before giving general anaesthesia. Patients were kept NPO for 12 hours before surgery. In the preoperative room, iv line was secured. In the operation theatre routine monitoring devices, like pulse oximetry, NIBP, ECG monitors were attached; and baseline blood pressure, heart rate and O_2 saturation values were recorded. Later capnography was attached after the intubation. The anaesthetic regimen and surgical procedures were standardized for all patients.

Anaesthesia was induced with glycopyrollate 5µgkg^{-1} and intravenous thiopentone 5mgkg^{-1}. For tracheal intubation suxamethonium 2mgkg^{-1} was used. Anaesthesia was maintained with N20 66%, O_2 33%, halothane 0.5-2%; neuromuscular blockade with intermittent doses of vecuronium bromide and analgesia with fentanyl 1.5µgkg^{-1}. Ventilation was controlled mechanically and adjusted so as to keep the end tidal carbon dioxide 35-40 mm of Hg.

Laparoscopic surgeries were performed under video guidance. During surgery the patients were placed in trendlenburg position wherever required and the abdomen was insufflated with carbon dioxide with an intra abdominal pressure of 12-15 mm of Hg. At the end of the surgery Group I patients received 4mg Inj ondansetron and Group II patients received 2mg Inj. granisetron administered slow iv over period of 30 seconds. At the cessation of surgery patients were made supine and residual neuromuscular block was reversed with inj glycopyrollate 0.005mgkg^{-1} and neostigmine 0.05mgkg^{-1} and patient was extubated.

The recovery time (in minutes) was measured from the time nitrous oxide was switched off until the patient respond to simple verbal commands. The patients were then assessed with the help of a clinical recovery score, to compare effects on clinical recovery. The score consisted of simple questions to evaluate vigilance, cognition and orientation (Kumar et al 1996).

Vigilance

Unconscious, not arousable — 0
Unconscious, arousable by nociceptive stimuli — 1
Unconscious, arousable by verbal stimuli — 2
Drowsy — 3
Awake, not attentive — 4
Awake, attentive — 5

Cognition

No understanding of simple orders — 0
Good understanding of simple orders — 1

Orientation

Confused — 0
Disturbed — 1
Well oriented — 2

Evaluation by patient of his/her condition

Uncomfortable — 1
Comfortable — 2
Excellent — 3

Clinical Recovery Score

11 : Excellent recovery
9-10 : Good Recovery
8 : Fair recovery
<8 : Poor recovery

The clinical recovery score was assessed at 0, 1, 2, 3 and 4 hours after patient's arrival in recovery room and assessments were made and appropriate recording was done.

In post anaesthesia care unit blood pressure and heart rate was recorded every 10 min for 30 min. Episodes of nausea and vomiting experienced by each patient were recorded by direct questioning. The number of patients who suffered

nausea/vomiting was noted during the period's 0-4hrs, 4-12hrs, 12-24hrs. Rescue Antiemetic (inj. metaclopramide 10mg) was used if patient had vomiting.

Any adverse reactions of the drug like headache, dizziness, hypersensitivity, constipation if any was noted in the 24 hr study period. Statistical analysis was done using student't' test. A 'P' value of less then 0.05 will be considered to be significant

RESULTS AND ANALYSIS

Total 60 patients were included in this study. Patient populations were comparable across the two groups with respect to Age, Weight, Systolic BP, Diastolic BP, Heart rate. Statistical analysis was done by using student 't'test and rest of the study data have been categorically analyzed.

In our study most of the patients in both groups belonged to age group 18-30. In both the groups females predominated males : in Ondasetron group male were 7 (23%) and females 23 (77%) and in Granisetron group male were 5 (17%) and females 25 (83%).

There was no significant weight difference between the two groups: in Ondasetron group 45-60 kg - 20 (67%), 61-70kg - 10 (33%); in Granisetron group 45-60 kg - 23 (77%), 61-70 kg 7(23%). Mean weight ±SD of Group A was 56.93±10.62 and in Group B 50.86±10.85. Both groups had almost similar numbers of ASAI and ASAII as shown in (table: 1).

In our study Laparoscopic tubal occlusion (LTO) predominated in both groups than any other surgery as shown in (table: 2). Systolic, Diastolic BP , Heart rate and oxygen saturation showed no statistically significant difference recorded in PACU between the study groups as shown in (table:3)

Occurrence of nausea in Ondanstron group and Granisetron group showed that incidence of nausea in 0-4 hours were 4 cases (14%)in Ondansetron group as compared to 2 cases (7%) in Granisetron group(P<0.01). Incidence of nausea in 4-12 hours were 2 cases (7%)in Ondansetron group as compared to 1 cases (4%) in Granisetron group(P<0.05). Incidence of nausea in 12-24, hours was only 1 case (4%) in Ondansetron group as compared to 0 cases (0%) in Granisetron group. The incidence of nausea was greatest during the first four hours and it was more in the Ondansetron group. (Table: 4)

Incidence of vomiting episodes in Ondansetron group were 4 cases (14%) as compared to 2 cases (7%) in granisetron group in 0-4 hours(P<0.01). In 4-12 hours ondansetron group had 3 cases(10%) of incidence of vomiting as compared to 1 case (4%) in granisetron group(P<0.05). Again the incidence of vomiting was maximum during first four hours and no patient in any group vomited from 12 hours onwards. (table: 5).

Need for rescue antiemetic is more in Ondansetron group that is 7 (23 %) compared to Granisetron group 3 (10 %). There was no significant difference in CRS and RT between the two groups as shown in (table: 6). Occurrence of side effects like headache, constipation and dizziness in Ondansetron group are 6(20%),4(13%),4(13%) respectively compared to 4 (13%), 2(7%),2 (7 %) in Granisetron group. The number of patients who suffered side effects was more in Ondansetron group. As shown in (table: 7).

Figure 1

Table: 1 asa grade wise

Grade	Ondasetron	Granisetron
I	25 (83%)	23 (77%)
II	5 (17%)	7 (23%)

Figure 3

Table: 3, comparision of systolic bp, diastolic bp, hr and spo%

Type of Procedure	Ondansetron	Granisetron
Laparoscopic tubal occlusion (LTO)	18 (60%)	15 (50%)
Laparoscopic Appendicectomy (LAPP)	2 (7%)	6 (20%)
Laparoscopic Cholecystectomy (LCHO)	7 (23%)	5 (17%)
Diagnostic Laparoscopy	3 (10%)	3 (10 %)
Laparoscopic Hernioplasty	0 (0%)	1 (3%)

Figure 4

Table: 4, incidence of nausea

Duration	Ondansetron (n=30)	Granisetron (n=30)
0-4hr	**4 (14%)	**2 (7%)
4-12hr	*2(7%)	*1 (4%)
12-24hr	1(4%)	0 (0%)

* (P<0.05) * * (P<0.01)

Figure 5

Table:5, incidence of vomiting

Duration	Ondansetron (n =30)	Granisetron (n=30)
0-4hr	**4 (14%)	**2 (7%)
4-12hr	*3 (10%)	*1 (4%)
12-24hr	0 (0%)	0

* (P<0.05) **(P<0.01)

Figure 6

Table: 6, clinical recovery score (CRS) and recovery time (RT)

Time Interval	Ondansetron	Granisetron
0 hour	5.16	5.46
1 Hour	7.03	7.33
2 hour	8.33	8.46
3 Hour	8.83	9.03
4 Hour	10.33	10.66
Recovery time (Minutes)	MEAN±SD 5.67±0.23	5.75± 0.25

Figure 7

Table: 7 , comparison of side effects

Side effects	Ondansetron (n =30)	Granisetron (n =30)
Headache	*6(20%)	*4 (13 %)
Constipation	*4(13%)	*2 (7 %)
Dizzness	*4 (13%)	*2 (7 %)

* (P<0.05)

{image:7}

DISCUSSION

Postoperative nausea and vomiting (PONV) is of multifactorial origin. The incidence of PONV after anaesthesia, despite the advances in antiemetic therapy in the last decades is still found to be relatively high. The three most common causes for admission following day care surgery are pain, bleeding and intractable vomiting[1]. Factors affecting PONV include patient related factors (age, sex, phase of the menstrual cycle), anaesthesia related factors (use of volatile anesthetic agents, N_2O, Opioid) and surgery related factors[1]. Female gender has been associated with higher incidence of PONV compared to male patients.[1, 2] On an average, female patients suffer three times more often from PONV than men[2].

Our study was aimed at comparing the antiemetic efficacy of Ondansetron and Granisetron in preventing PONV in laparoscopic surgery. In our study the factors that would have contributed to nausea and vomiting may be laparoscopic surgery, use of Halothane, use of Fentanyl etc. Use of facemask, use of Nitrous Oxide may or may not have contributed to nausea and vomiting. Avoidance of Pethidine towards the end of surgery must have helped in preventing PONV[3].

Laparoscopic surgery was chosen because of high incidence of PONV associated with it. Naguib et al demonstrated that the incidence of PONV after laparoscopic surgeries in their placebo group was remarkably high (72%).[11]

We have conducted studies on 60 patients of ASA I and II

with demographic data in terms of age, weight, which were similar in the two groups. There was no significant difference in Ondansetron and Granisetron (P< 0.05) in terms of Age and Weight. Study done by Pearman[12] shows that postoperative nausea and vomiting is more common in young age group and obese patients.

Incidence of nausea in our study group was 25% in Ondansetron group, 11% in Granisetron group. Present study shows highly significant difference in first 0-4hr (P < 0.05). While in 4-12hrs incidence of nausea shows marginally significant difference. After 12-24hrs, there was no significant difference in nauseating episodes. Study done by Pueyo[13] observed that nausea and vomiting is more common in first 6 hours post operatively. Same results are seen in the study done by Fujii [14.]

According to Raphael[15], optimal dose of Ondansetron for preventing post operative nausea vomiting is 4 mg and half life is 3 hours. While optimal dose of Granisetron is 2 mg and half life is 8-9 hours. So it is observed that after 6 hours Granisetron is more effective than Ondansetron for preventing PONV. Vomiting in the present study group was 24% in Ondansetron and 11% in the Granisetron group. In our study group incidence of vomiting was highly significant in first 4hrs (P<0.01). Present study showed that Granisetron is better than Ondansetron for preventing PONV. Bhattacharya[16] in his study observed same results.

During 0-4hr and 4-12hrs postoperatively results are significant in nature (P< 0.05). After 12hrs, result of vomiting was insignificant (P>0.05). Janknegt studied that if Ondansetron is given at the induction time, it is ineffective in preventing PONV[17], so we administered study drug half an hour before end of the surgery. This makes the drugs to be effective postoperatively for longer time. Sinha[18] concluded the same results in his study.

Our study shows no statistically significant difference in the baseline values of haemodynamic variables between the two groups before, during or after giving study drug. Study drugs Ondansertron and Granisetron was given approximately half an hour before the end of the surgery. In PACU we have recorded the SBP, DBP and HR over a period of 30min at regular interval. According to our study there was no haemodynamic alteration between these results. Study conducted by Dev[19] also shows the same results. There is no haemodynamic alteration seen in PR, SBP and DBP during study period.

According to Gigilla[20] it shows that some haemodynamic variation in SBP, DBP and HR. Ondansetron mediated bradycardia and hypotension was reported in that study group. Kumar et al[21] in their clinical trial on recovery score and recovery time showed slightly lower clinical recovery scores with metoclopramide group compared to ondansetron which may be attributed to its established unpleasant sedative pharmacological activity. They did not notice any significant difference in the overall incidence of drowsiness or sedation in both the groups. They further stated that ondansetron does not affect patients vigilance, cognition or orientation and concluded that ondansetron (4 mg) and metoclopramide (10 mg) do not affect the cognitive aspects following major gynaecological surgery.

In our study on the clinical recovery score and the recovery time we observed slightly lower clinical recovery score in the Ondansetron group compared to Granisetron and there was not much of significant difference in the recovery time. Incidence of side effects was significant in our study groups. Incidence of headache was 20% in Ondansetron group while it was 12% in Granisetron group shows statistically significant difference (P < 0.05).

According to study by Mitra [22], incidence of headache and constipation is more in Ondansetron group as compared to Granisetron group which matches with our results. Incidence of constipation and dizziness also shows significant difference in Ondansetron and Granisetron groups (P <0.05).

The use of rescue antiemetic in ondansetron group which was about 7(23%) whereas in Granisetron group about 3(10%) of the patients received rescue antiemetic. Stewart[23] in his study also has same result. Updated guidelines for managing postoperative nausea and vomiting were recently announced at the 2006 Annual Meeting of American Society of Anaesthesiologists in Chicago, Illinois, USA. Evaluating the current medical literature, they recommended the use of antiemetics, with an emphasis on the use of the $5HT_3$ receptor antagonists.

The guidelines also suggest a potential benefit of combination prophylaxis. Overall the panel recommended, “prophylactic therapy with combination, three or more interventions, in patients at high risk for PONV.[24] So we have studied the effect of Granisetron 2mg i.v. versus Ondansetron 4mg i.v, administered to the patients, who had undergone laparoscopic surgery under general anaesthesia.

CONCLUSION

Our study concludes that the prophylactic intravenous administration of Granisetron is more effective drug than Ondansetron for controlling postoperative nausea and vomiting with fewer incidences of side effects.

Safety profile is more with Granisetron and it is more potent than Ondansetron. So we observed minimal emetic and nausea episodes in postoperative period in patients who had received i.v. Granisetron in comparison to i.v. Ondansetron, undergoing laparoscopic surgery under general anaesthesia.

Even though there was slightly higher clinical recovery score in the patients who had received intravenous Granisetron compared to patients who had received intravenous Ondansetron, there was no significant difference in the recovery time from anaesthesia between the two drugs.

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