A COMPARATIVE STUDY OF ONDANSETRON VERSUS GRANISETRON IN THE PREVENTION OF POST-OPERATIVE NAUSEA AND VOMITING (PONV) IN DAY CARE GYNAECOLOGICAL LAPAROSCOPIC SURGERIES

Kousalya Chakravarthy[1], Swathi Shankar[2]

[1]Associate Professor, Department of Anaesthesia, MGMH, Pitlaburj, Osmania Medical College, Hyderabad, India.
[2]Consultant, Swapna Health Care, Begumpet, Hyderabad, India.

ABSTRACT

BACKGROUND

The antiemetic action of 5-hydroxytryptamine receptor antagonists (5HT3 receptor blockers) has been well established. The present study compared the efficacy of the 5HT3 receptor blockers Ondansetron and Granisetron, in reducing the Post-Operative Nausea and Vomiting in day care gynaecological laparoscopic surgeries.

Aims and Objectives- To compare the efficacy of intravenous Ondansetron versus Granisetron in the prevention of post-operative nausea and vomiting in patients undergoing day care gynaecological laparoscopic surgeries.

MATERIALS AND METHODS

60 patients of ASA Grade 1 and II, between 18 - 55 years of age undergoing day care gynaecological surgeries were included in the present study. They were allocated into 2 groups of 30 each. The sample size was taken for convenience during the study. Group A received 4 mg (2 mL) of Ondansetron intravenously, Group B received 2 mg (2 mL) of Granisetron intravenously prior to induction of general anaesthesia. Each of these groups were assessed for the incidence of post-operative nausea, pain, emesis and adverse effects.

RESULTS

Incidence of nausea in the first 2 hrs. was the same in both the groups 16.6% (n= 5). The overall incidence of nausea in 0 to 24 hrs. in Group A and Group B was 23.3% (n= 7) and 20% (n= 6) respectively. The overall incidence of emesis in 0 – 24 hrs. after the surgery was found to be similar 6.6% (n= 2) in both the groups. No adverse effects were observed in both the groups. There was no statistically significant difference between Ondansetron and Granisetron with regards to their efficacy in minimising post-operative nausea and vomiting (p value > 0.05).

CONCLUSION

In conclusion, intravenous administration of 4 mg Ondansetron or 2 mg Granisetron prior to induction of general anaesthesia is equally effective in preventing the post-operative nausea and vomiting in day care gynaecological laparoscopic surgeries.

KEY WORDS

Day Care Gynaecological Laparoscopy, Nausea, Vomiting, PONV.

HOW TO CITE THIS ARTICLE: Chakravarthy K, Shankar S. A comparative study of ondansetron versus granisetron in the prevention of post-operative nausea and vomiting (PONV) in day care gynaecological laparoscopic surgeries. J. Evolution Med. Dent. Sci. 2018;7(23):2753-2756, DOI: 10.14260/jemds/2018/622

BACKGROUND

The incidence of post-operative nausea and vomiting (PONV) is important in determining the length of stay after ambulatory anaesthesia. 49% of patients regard it as a side effect of greatest concern.[1] It is the leading cause of delayed discharge and unanticipated admissions in ambulatory surgeries. It is not only distressing for the patient, but also adds to the hospital expenditures. The commonly identified risk factors of PONV are female gender, non-smokers, post-operative use of opioids, history of PONV/ motion sickness and laparoscopic surgeries.[2] The incidence of PONV after day care gynaecological surgeries has been found to be high (54% - 92%).[3,4] There are a number of drugs available to manage PONV, of which 5HT3 receptor antagonists have an important position. Ondansetron is a carbazalone derivative that is structurally similar to serotonin and possess specific 5HT3 receptor antagonistic properties.[5] Granisetron is an indazole derivative, which is a more selective 5HT3 antagonist than ondansetron.[6] The aim of this study was to compare the antiemetic efficacy of Ondansetron and Granisetron in the prevention of post-operative nausea and vomiting in day care gynaecological laparoscopic surgeries.

'Financial or Other Competing Interest': None.
Submission 06-04-2018, Peer Review 20-05-2018,
Acceptance 26-05-2018, Published 04-06-2018.
Corresponding Author:
Kousalya Chakravarthy,
Associate Professor,
Department of Anaesthesia,
MGMH, Pitlaburj,
Osmania Medical College,
Hyderabad, India.
E-mail: dr.kausi.c@gmail.com
DOI: 10.14260/jemds/2018/622

MATERIALS AND METHODS

The present study was a single centre prospective study conducted in Modern Government Maternity Hospital, Petlaburz, Osmania Medical College, Hyderabad between October 2017 and March 2018. We selected 60 patients allocated to two groups of 30 each based on our inclusion exclusion criteria. Randomisation and allocation to the groups was done by computer generated simple random sample strategy and the sample size was taken for convenience during the study.

The study included the patients of ASA grade I and II, aged between 18 - 55 years, undergoing elective daycare gynaecological laparoscopic surgeries under general anaesthesia. Patients with ASA grade ≥ III, major systemic illness, those taking medications with anti-emetic effects were excluded from the study. Preoperative data included age, weight, history of previous postoperative nausea and vomiting, history of motion sickness and history of any drug intake. The patients were admitted for day care surgery following confirmation of an NPO (nil per oral) status. During the pre-anaesthetic check-up, the demographic data was noted, and assessment of the cardiovascular and respiratory system was done. Airway was assessed. Baseline investigations like complete blood picture, serum creatinine, blood glucose, ECG and blood grouping Rh typing were done. At the pre-anaesthetic interview, the patients were familiarised with a post-operative questionnaire and a scale (0 to 10) for recording the visual analogue score for pain and nausea. Standard anaesthetic techniques were used in all patients. On arrival into the operation theatre, heart rate, blood pressure, room air saturations and temperature were noted. An 18-G intravenous cannula was secured, and hydration was maintained with Lactated Ringer's solution. The patients were pre-medicated with intravenous Glycopyrrolate 0.2 mg and Fentanyl at dose of 2 mcg/kg. The patients of Group A (n= 30) received injection Ondansetron 4mg intravenously 2 minutes prior to induction of anaesthesia and Group B (n= 30) received injection Granisetron 2 mg intravenously 2 minutes before induction of anaesthesia. No other anti-emetic was given. Anaesthesia technique was standardised in all the patients. Induction was done with injection Propofol 2 mg/kg intravenously. Atracurium 0.5 mg/kg intravenous was the muscle relaxant used for intubation. The patients were intubated with a cuffed endotracheal tube of an appropriate size. Bilateral air entry was confirmed, cuff was inflated, and the tube was secured. The initial reading of end tidal CO_2 was noted. Mechanical ventilation with intermittent positive pressure was initiated with nitrous oxide, oxygen, sevoflurane with intermittent doses of Atracurium. Intraoperatively, the heart rate, blood pressure, SPO_2, ECG and End tidal carbon dioxide were assessed and recorded at 10-minute intervals. The patients were positioned in reverse Trendelenburg position, abdomen was insufflated with carbon dioxide to an intra-abdominal pressure of 12 - 15 mmHg. $EtCO_2$ was maintained around 34 – 38 mmHg throughout the surgery. Any allergic reactions were noted. At the completion of surgery, the position was made supine and the neuromuscular blockade reversed with injection glycopyrrolate and neostigmine. Patients were extubated on table. The duration of surgery and anaesthesia were recorded for each patient. The patients were shifted to post-operative ward after complete recovery. Post-operatively the pulse rate, respiratory rate, blood pressure, nausea, retching and vomiting, VAS scores for pain, level of consciousness and sedation score; any adverse effects like headache, extrapyramidal symptoms, allergic reactions, urinary retention were observed at intervals of 30 minutes, 1 hr., 2 hrs., 4 hrs. and 6 hrs. The patients were discharged 6 hrs. after surgery and were followed up for 24 hrs. by phone. Nausea was defined as the desire to vomit without indulging in expulsive movements. A single vomitus or retching or combination of the two occurring within one minute of each other was considered as a single Emetic episode. When no stomach contents are expelled, the expulsive efforts were classified as Retching. Vomiting was defined as the production of even small amounts of stomach contents due to the expulsive efforts.[7,8,9] Nausea was interpreted as Grade 0= No Nausea, Grade 1= Mild Nausea, Grade 2= Moderate Nausea and Grade 3= Severe Nausea. The intensity of post-operative pain and nausea was assessed by the patients using a verbal 10-point scale that ranged from Scale 0= No pain at all to Scale 10= Worst pain imaginable. Emesis was graded as Grade 0= Emesis free, Grade 1= Mild nausea with 1 vomiting, Grade 2= Nausea with > 1 episode of vomiting, Grade 3= multiple and > 2 episodes of vomiting. A Complete Response was defined as the absence of any nausea or vomiting during the study period (24 hours). Sedation was assessed by Modified Ramsay Sedation Score.[10] Sedation score 0=paralyzed, 1= awake, 2= lightly sedated and 3= moderately sedated follows simple commands, 4= deeply sedated responds to non-painful stimulus, 5= deeply sedated responding to painful stimuli, 6= deeply sedated unresponsive to painful stimuli. Student 't' test and chi-square tests were used for statistical analysis and to infer the data presented in descriptive tables. P value < 0.05 was taken as statistically significant. SPSS software version 17 was used for statistical analysis.

RESULTS

The two groups were comparable with regard to age, weight of the patients, surgical duration and awakening time (Table-1). Both the drugs Ondansetron and Granisetron had no significant effect on pulse rate and blood pressure. Saturations by pulse oximetry (SPO_2) was maintained throughout the procedure in both the groups. There were no episodes of hypoxia or ECG changes. $EtCO_2$ was maintained at almost equal level in both the groups (Table 2).

Demographic Feature	Group A (OND) (n= 30)	Group B (GRA) (n= 30)	P value
Age (years)	27.25 ± 3.44	28.35 ± 4.96	0.053
Weight (kgs)	52.85 ± 5.60	53.5 ± 3.5	0.013
Duration of Surgery (mins)	30.5 ± 8.25	30.25 ± 8.5	0.873
Awakening (mins)	39.5 ± 7.41	40 ± 7.4	0.99

Table 1. Demographic Features

Parameter	Group A (n=30)	Group B (n=30)	P value
Heart rate (mean)	84.2 ± 10.6	85.5 ± 10.1	0.796
NIBP (mean)	88.85 ± 6.5	87.45 ± 6.5	1
EtCO2 (mean)	34.55 ± 1.06	33.98 ± 1.57	0.038
SPO_2 (mean)	98.8 ± 4.4	98.65 ± 4.9	0.565
ECG	WNL	WNL	

Table 2. Intraoperative Monitoring

VAS Score	Group A (OND) n=30	Group B (GRA) n=30
≥ 3(3-10)	2 (6.6%)	3 (10%)
≤ 3(0 -3)	28 (93.3%)	27 (90%)

Table 3. VAS Score for Pain (0 - 24 hrs. Post-Operatively)

Chi-square= 0.21, df= 1, P value= 0.64.

		Group A (OND) (n=30)	Group B (GRA) (n=30)	P-value
0-2 hrs.	Nausea	5(16.6%)	5(16.6%)	>0.05
	Nausea free	25(83.33%)	25(83.33%)	
0-24 hrs.	Nausea	7(23.3%)	6(20%)	>0.05
	Nausea free	23(76.6%)	24(80%)	
0-24 hrs.	Overall episodes of emesis	2(6.6%)	2(6.6%)	>0.05
	Emesis free	28(93.3%)	28(93.3%)	

Table 4. Incidence of Nausea and Emesis in 0 – 24 hrs.

VAS score for pain was comparable in both the groups. The VAS score was ≤ 3 (0 - 3) in majority of cases, that is 93.3% in Group A and 90% in Group B (Table 3). None of the patients required additional pain killers. In the post-operative two-hour observation period, there was no statistically significant difference in the occurrence of nausea between the two groups, Ondansetron (Group-A 16.6%) and Granisetron (Group-B 16.6%). P value was > 0.05 (Table 4). In the 24 hrs. observation period, the overall incidence of nausea in Ondansetron group (Group A) was 23.3% and in Granisetron group was 20% which was also not statistically significant (p value > 0.05). Two patients in Ondansetron Group (Group A) and 2 patients in Granisetron group (Group B) had single episode of emesis, classified a Grade 1 (Mild nausea with 1 vomiting). Hence, the overall incidence of emesis in 0 - 24 hours in the Ondansetron group was 6.6% (n= 2) and in the Granisetron group was 6.6% (n= 2). Complete response was found to be 93.3% in both the groups with 93.3% of patients being emesis free in the post-operative period. None of the patients required additional or rescue anti-emetics. There was no statistically significant difference in the efficacy of Ondansetron and Granisetron in reducing both early and delayed post-operative nausea and vomiting. P value was > 0.05. Significant adverse effects like drowsiness, sedation, dizziness, headache or extrapyramidal effects were not observed in both the groups.

DISCUSSION

Post-operative nausea and vomiting are among the most common complications that occur after surgery was performed under general anaesthesia. Post-operative nausea and vomiting is also a leading cause of delayed discharge and unanticipated readmission after ambulatory surgical procedures.[11] Age, menstrual cycle and laparoscopic surgeries influence the incidence of post-operative nausea and vomiting (PONV). Increased incidence of PONV in ambulatory gynaecological surgeries has led to the use of prophylactic anti-emetic drug before induction. Except for headache, the serotonin antagonists have negligible side effects. They produced no sedation, drowsiness and extrapyramidal symptoms. Figueredo and Canosa[12] reported a 7.05% incidence of headache with Ondansetron and Fujii et al[13] documented a 2% to 5% incidence of headache with Granisetron. The 5HT3 antagonist drugs Ondansetron and Granisetron have been extensively studied and compared in terms of efficacy to prevent and control post-operative nausea and vomiting. Ondansetron has shown to prevent post-operative nausea and vomiting in ambulatory gynaecological surgeries at a dose of 4 mg.[14] A single oral dose of Granisetron 2 mg was shown to have equivalent levels of antiemetic protection in ambulatory surgeries.[15]

We studied the effects of Ondansetron 4 mg IV versus Granisetron 2 mg IV, administered at induction of anaesthesia in patients undergoing day care laparoscopic gynaecological surgeries. Sufficient care has been taken to standardise the anaesthesia technique, age, phase of menstrual cycle and duration of surgery in both the groups. In the present study, the incidence of nausea in the first 0 – 2 hours was similar in both the groups (16.6%). A trivial increased incidence of nausea was noted in Ondansetron Group as compared to Granisetron group in the 2 – 24 hrs. period (23.3% in Ondansetron Group A vs. 20% in Granisetron Group B), which was neither clinically nor statistically significant (P value > 0.05). Similarly, there was no statistically significant difference in the antiemetic properties of both the drugs. The overall incidence of emesis in 0 - 24 hours was similar in both the groups (6.6% in both Group A and Group B), p value > 0.05. Our findings were comparable to the studies by Gigilo[16] and Bestas et al.[17] Gigilo in their study to prevent post-operative nausea and vomiting following cancer chemotherapy concluded that both Ondansetron and Granisetron have similar antiemetic efficacy.[16] Bestas et al compared the effects of Ondansetron and Granisetron on PONV in adult patients undergoing laparoscopic cholecystectomy and observed no significant differences in PONV between both the groups.[17] In the present study, complete response was found to be 93.3% in both the groups which was comparable to the study by Bhattacharya and Banerjee P[18] when they compared the efficacy of intravenous Granisetron and Ondansetron in preventing post-operative nausea and vomiting in laparoscopic gynaecological surgeries. (Complete response 80% in Ondansetron group and 93% in Granisetron group). But they concluded that Granisetron is much more effective than Ondansetron to prevent post-operative nausea and vomiting following day care gynaecological laparoscopic surgeries, which differs from our study. Incidence of emetic episodes were also high in the study by Bhattacharya and Banerjee P (20% in Ondansetron group, 7% in Granisetron group and 50% in placebo), whereas the incidence of emetic episodes was less in the present study (6.6% in both groups). The lower incidence of emesis in the present study may be due to change in the anaesthesia technique. The drugs like Thiopentone sodium, halothane and pethidine which were used in Bhattacharya and Banerjee P study can aggravate the PONV and were avoided in the present study. In the present study, it was observed that 4 mg intravenous Ondansetron or 2 mg intravenous Granisetron prior to induction of general anaesthesia in laparoscopic surgeries could prevent post-operative nausea and vomiting with equal efficacy. Both drugs were well tolerated, and no adverse effects were noticed in both the groups.

CONCLUSION

In conclusion, the present study suggests that both Ondansetron and Granisetron have similar antiemetic efficacy for minimising the post-operative nausea and vomiting (PONV) in day care Gynaecological Laparoscopic surgeries. Routine prophylactic administration of either Ondansetron 4 mg or Granisetron 2 mg given 2 minutes prior to induction of general anaesthesia could equally prevent

post-operative nausea and vomiting in day care gynaecological laparoscopic surgeries.

REFERENCES

[1] Eberhart LH, Morin AM, Wulf H, et al. Patient preferences for immediate postoperative recovery. Br J Anaesth 2002;89(5):760-1.

[2] Gan TJ. Risk factors for postoperative nausea and vomiting. Anesth Analg 2006;102(6):1884-98.

[3] Yuksek MS, Alici HA, Erdem AF, et al. Comparison of prophylactic anti-emetic effects of ondansetron and dexamethasone in women undergoing day-case gynaecological laparoscopic surgery. Journal of International Medical Research 2003;31(6):481-8.

[4] Wang JJ, Ho ST, Liu SH, et al. Prophylactic anti emetic effect of Dexamethasone in women undergoing ambulatory laparoscopic surgery. Br J Anaesth 2000;84(4):459-62.

[5] Mckenzie R, Kovac A, O'Connor T, et al. Comparison of ondansetron versus placebo to prevent postoperative nausea and vomiting in women undergoing ambulatory gynaecological surgery. Anesthesiology 1993;78(1):21-8.

[6] Fujii Y, Tanaka H, Toyooka H. Effective dose of granisetron for preventing postoperative emesis in children. Can J Anaesth 1994;43:35-8.

[7] Knapp MR, Beecher HK. Postanesthetic nausea, vomiting and retching: evaluation of the antiemetic drugs Dimenhydrinate (Dramamine), chlorpromazine and pentobarbital sodium. JAMA 1956;160(5):376-85.

[8] Apfel CC, Laara E, Koivuranta M, et al. Simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers. Anesthesiology 1999;91(3):693-700.

[9] Apfel CC, Kranke P, Eberhart LH, et al. Comparison of predictive models for postoperative nausea and vomiting. Br J Anaesth 2002;88(2):234-40.

[10] Ramsay MA, Savege TM, Simpson BR, et al. Controlled sedation with alphaxalone-alphadolone. Br Med J 1974;2(5920):656-9.

[11] Gold BS, Kitz DS, Lecky JH, et al. Unanticipated admission to the hospital following ambulatory surgery. JAMA 1989;262(21):3008-10.

[12] Figueredo ED, Canosa LG. Ondansetron in the prophylaxis of postoperative vomiting: a meta-analysis. J Clin Anesth 1998;10(3):211-21.

[13] Fujii Y, Saitoh Y, Tanaka H, et al. Comparison of ramosetron and granisetron for preventing postoperative nausea and vomiting after gynecologic surgery. Anesth Analg 1999;89(2):476-9.

[14] Raphael JH, Norton AC. Antiemetic efficacy of prophylactic ondansetron in laparoscopic surgery: randomized double-blind comparison with metoclopramide. Br J Anaesth 1993;71(6):845-8.

[15] Fujii Y, Tanaka H, Toyooka H. Optimal anti-emetic dose of granisetron for preventing PONV. Can J Anaesth 1994;41:794-7.

[16] De Gigilio A, Soares HP, Caparroz C, et al. Granisetron is equivalent to ondansetron for prophylaxis of chemotherapy-induced nausea and vomiting: results of a meta-analysis of randomized controlled trials. Cancer 2000;89(11):2301-8.

[17] Bestas A, Onal SA, Bayar MK, et al. Effects of ondansetron and granisetron on postoperative nausea and vomiting in adult patients undergoing laparoscopic cholecystectomy: a randomized, double-blind, placebo-controlled clinical trial. Curr Ther Res Clin Exp 2007;68(5):303-12.

[18] Bhattacharya D, Banerjee A. Comparison of ondansetron and granisetron for prevention of nausea and vomiting following day care gynaecological laparoscopy. Indian J Anaesth 2003;47(4):279-82.