Original Research Article

Indian Journal of Anesthesia and Analgesia
January – February 2020; 7(1) (Part -II): 341-346
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.7120.46

Comparative Study of Granisetron and Ondansetron for the Prevention of Post Operative Nausea and Vomiting in Patients Undergoing Total Abdominal Hysterectomy Under General Anaesthesia

Saurabh Kapoor[1], Bhavini Bhushan Shah[2], Soumya Garlapati[3], Dipanjali Mahanta[4]

[1]Third Year PG Resident [2]Professor [3]Third Year PG Resident [4]First Year PG Resident, Department of Anaesthesiology, Dr. D.Y. Patil Medical College, Hospital & Research Centre, Dr. D.Y. Patil Vidyapeeth, Pimpri, Pune, Maharashtra 411018, India.

Abstract

The aim of this study was to compare the efficacy of intravenous granisetron and intravenous ondansetron for prevention of postoperative nausea and vomiting in patients undergoing total abdominal hysterectomy under general anesthesia. In this prospective double-blind randomized controlled clinical trial, 60 American Society of ASA Grade I and II patients aged between 18 and 60 years scheduled for elective total abdominal hysterectomy under general anesthesia were selected. The patients were divided in the following Groups of 30 patients each: *Group 1 (Granisetron):* 30 patients were given 1 mg of Granisetron was diluted in NS to make upto 10 ml; *Group 2 (Ondansetron):* 30 patients were given 4 mg of Ondansetron was diluted in NS to make upto 10 ml. Postoperative Nausea and Vomiting (PONV), hemodynamic and side effects were observed at scheduled intervals. The incidence of PONV was significantly lower in Group 1 (Granisetron) than in Group 2 (Ondansetron). Requirement of rescue antiemetic was significantly lower in Group 1 (Granisetron) 6.7% as compared to Group 2 (Ondansetron) 33.3%. At all times the changes in the vital parameters like pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and SpO_2 were within the normal physiological limits. There was no statistical significant difference between the groups. It was observed that there was no significant difference in adverse effects amongst the groups as well. We conclude that granisetron is more effective, potent and longer acting antiemetic as compared to ondansetron for reducing PONV in patients undergoing Total Abdominal Hysterectomy under general anesthesia.

Keywords: Granisetron; Ondansetron; PONV; Total Abdominal Hysterectomy.

How to cite this article:
Saurabh Kapoor, Bhavini Bhushan Shah, Soumya Garlapati. Comparative Study of Granisetron and Ondansetron for the Prevention of Post Operative Nausea and Vomiting in Patients Undergoing Total Abdominal Hysterectomy Under General Anaesthesia. Indian J Anesth Analg. 2020;7(1 Part -II):341-346.

Introduction

Postoperative Nausea and Vomiting (PONV) constitutes a most common anesthesia related undesirable event. Its incidence in the available literature is reported to vary between 20 and 80%[1] PONV has significant adverse effects. It can cause profound distress to the patients. Oral administration of drugs, fluids and nutrients can be delayed and can lead to dehydration and alkalemia. It is an important cause of delayed discharge. It may be associated with poor surgical outcome.

Corresponding Author: Bhavini Bhushan Shah, Professor,Department of Anaesthesiology, Dr. D.Y. Patil Medical College, Hospital & Research Centre, Dr. D.Y. Patil Vidyapeeth, Pimpri, Pune, Maharashtra 411018, India.

E-mail: saurabhkapoors2@gmail.com

Received on 30.11.2019, **Accepted on** 29.01.2020

Vomiting can disrupt neck, abdominal and eye sutures. PONV is often severe on movement and may delay postoperative mobilization.[2]

The aetiology of PONV is multifactorial[3] with increased incidence in pediatric patients, adult females, obese and in patients with a history of motion sickness. The surgery related factors are after strabismus surgery, orchidopexy, middle ear surgery, intraabdominal and orthopedic surgeries. Anesthesia related factors like Intravenous anesthetic agents are associated with differing degrees of emesis. Perioperative use of opioids is associated with an increased incidence of PONV. It is generally accepted that nitrous oxide is responsible for a significant degree of emesis. Inhalational agents like halothane and isoflurane also cause PONV, though to a lesser extent.[4]

Prophylaxis for PONV in recent times include decreasing baseline risk for PONV,[5] use of non pharmacological measures,[6] change of anesthetic techniques and use of new antiemetic drugs. Drugs used to treat PONV are usually antihistaminic, anticholinergic, phenothiazine derivatives and dopamine receptor antagonist with side effects like extrapyramidal symptoms, sedation, tachycardia, dysphoria and restlessness.[7]

The treatment of nausea and vomiting has improved greatly in today's world with use of 5-hydroxytryptamine (5-HT_3, serotonin) receptor antagonist. Ondansetron is commonly used drug to prevent PONV. These drugs act by binding to the serotonin 5-HT_3 receptor in the chemoreceptor trigger zone (CTZ) and at vagal afferent supply in the gastrointestinal tract.[8]

Another 5-HT_3 receptor antagonist Granisetron is more effective and longer acting against Cisplatin induced emesis than Ondansetron. Granisetron is highly selective for 5-HT_3 receptors (1000:1) compared to Ondansetron which has a selectivity of 250–400:[9] Elimination half life of granisetron is 9 hrs which is 2.5 hrs longer than ondansetron[7] and its duration of action is more than 24 hrs.[7] This study was done to compare the antiemetic effect of Granisetron and Ondansetron in prevention of PONV in patients undergoing Total Abdominal Hysterectomy under General Anesthesia (GA).

Materials and Methods

A prospective, randomized, double blind study was conducted with 60 patients to compare the effects of granisetron and ondansetron for the prevention of Postoperative Nausea and Vomiting (PONV) in patients undergoing hysterectomy under general anesthesia. The patients were divided in the following Groups of 30 patients each:

Group 1 (Granisetron): 30 patients were given 1 mg of Granisetron was diluted in NS to make upto 10 ml;

Group 2 (Ondansetron): 30 patients were given 4 mg of Ondansetron was diluted in NS to make upto 10 ml.

Study design: Hospital based prospective, randomized, double blind study.

Study duration: 1 year.

Study area: The study was done at DY Patil Medical College, Hospital and Research Center, in the Department of Anesthesiology.

Study population: 60 ASA-I and ASA-II fit patients (30 in each Group) scheduled for elective total abdominal hysterectomy under general anesthesia that fulfilled the inclusion criteria.

Sample size: By keeping the significance level of 5%, power of study at 95% the sample size was calculated by WinEpi Statistical Package. The minimum sample size required was 25 in each Group. Keeping in mind dropouts or exclusions, we conducted the study in 60 patients after dividing 30 patients in each Group.

Inclusion criteria:

1. ASA Grade I and ASA Grade II patients;
2. Age between 18 and 60 years;
3. Hemodynamicaly stable patients with all routine investigations within normal limits and without any other comorbidity;
4. Availability of informed consent and willingness of the patient to be a part of the study.

Exclusion criteria:

1. Patients with ASA physical status III or more;
2. Patients below 18 years and above 60 years of age;
3. Patients with history of motion sickness or previous PONV;
4. Patient who have taken antiemetic drugs within 24 hours before surgery;
5. Patients with history of neurological or renal disease.

Methodology: After approval from the Institutional Ethics Committee, valid informed written consent was taken from patients and patient's attendant.

Once the patients were enrolled for the study, a thorough history and physical examination was done as per proforma.

Sixty patients of ASA-I and ASA-II in age group of 18 to 60 yrs. undergoing elective total abdominal hysterectomy were selected randomly after applying already mentioned stringent inclusion and exclusion criteria. The patients were divided into Two Groups of 30 each. The patients were allocated to respective groups by application of lottery method to ensure removal of selection bias and proper randomization:

Group 1 (Granisetron): 30 cases received 1 mg Granisetron diluted in NS to make up to 10 ml;

Group 2 (Ondansetron): 30 cases received 4 mg Ondansetron diluted in NS to make up to 10 ml.

Materials Required:

1. Standard anesthesia machine (Boyle's apparatus);.
2. Intravenous cannula 20G;
3. Intravenous fluids – Crystalloids and colloids;
4. Bain's circuit with face mask of appropriate size;
5. Monitoring equipments such as pulse oximeter, ECG monitor noninvasive blood pressure apparatus;
6. Anesthetic drugs – Inj. Glycopyrrolate, Inj. Midazolam, Inj. Pentazocine, Inj. Propofol, Oxygen, Nitrous oxide, Isoflurane;
7. Equipments of endotracheal intubation;
8. Disposable syringe;
9. Drugs and instruments necessary for resuscitation;
10. Injection Granisetron ampoule;
11. Injection Ondansetron ampoule.

All preparations that are drugs and equipment's necessary for resuscitation for general anesthesia were kept ready.

Procedure:

Patients enrolled in the study were visited a day prior to surgery. Detailed history, general and systemic examination of cardiovascular, respiratory and central nervous system was done. Routine laboratory investigations such as hemogram, Liver Function Tests (LFTs), Renal Function Tests (RFTs), serum electrolytes, urine routine, Bleeding Time and Clotting Time (BT-CT), were done. Patients were nil by mouth from midnight prior to surgery.

Preoperative pulse, noninvasive blood pressure, ECG and oxygen saturation were noted. Peripheral venous access with 20 gauge intravenous cannula was established and Intravenous (IV) fluids were given.

Three readings of systolic, diastolic blood pressure and heart rate were obtained at three minutes of interval with patient in supine position. Lowest reading of blood pressure and highest reading of heart rate were taken as baseline values to minimize influence of anxiety in patients with high initial values. Highest Nausea and Vomiting Score value was taken as baseline.

Drugs were given

Group 1 (Granisetron): 1 mg diluted in NS to make up to 10 ml;

Group 2 (Ondansetron): 4 mg diluted in NS to make up to 10 ml.

These drugs are given by double blinding method. Patients were preoxygenated for 3 minutes. Then patients were premedicated with Inj. Glycopyrolate 0.2 mg, Inj. Midazolam 1 mg and Inj. Pentazocine .03 mg/kg then patients were induced with propofol 2 mg/kg body weight, Inj. succinylcholine 2 mg/kg body weight. Patient was intubated with appropriate ET tube, bilateral air entry was confirmed by auscultation, tube was fixed. Maintenance of anesthesia was done with nitrous oxide (60%) and oxygen (40%) and isoflurane as required using Intermittent Positive Pressure Ventilation (IPPV) with Bain's circuit. On completion of surgery patients pts. were given reversal and were shifted to recovery room after regaining satisfactory tone and then to the respective wards after confirming as adequate level of consciousness and intact reflexes. The incidence of PONV was recorded within first forty eight hours after surgery at an interval of 30 mins, 1 hour, 6 hours, 12 hours and 48 hours. Postoperative nausea and vomiting were recorded by spontaneous complaints by the patient. Pulse, blood pressure and oxygen saturation were recorded preoperatively, intraoperatively and postoperative period.

Score table to assess postoperative nausea and vomiting is as follows:

Score Table:

0 = No symptom;
1 = Mild sausea;
2 = Severe nausea but no vomiting;
3 = Vomiting.

Statistical Analysis:

All the cases were completed in the stipulated time. Data was collected, compiled and tabulated. The statistical analysis was done using parametric test and the final interpretation was based on *Z*-test (standard normal variant) with 95% level of significance.

Quantitative data was analyzed by *Student 't'-test.*

Qualitative data was analyzed by *Chi-square test.*

Results

A total of 60 patients were enrolled in the present study and were randomized into two groups of 30 each, both the groups were comparable with respect to age, sex, BMI, duration of surgery, and the duration of anesthesia. The mean age of the patients in Group 1 (Granisetron) was 44.27 ± 12.54 years; and patients in Group 2 (Ondansetron) was 45.03 ± 8.64 years (p =.785), (p =.785) (Table 1).

Table 1: Comparison of demographic data between Groups

		Group 1 (Granisetron)	Group N (Ondansetron)	p - Value
1	Age (yrs)	44.27 ± 12.54	45.03 ± 8.64	> 0.05
2	BMI (kg/m^2)	25.03 ± 3.50	25.73 ± 3.41	> 0.05
4	ASA I/II	22/8	24/6	> 0.05

The incidence and severity of PONV was significantly lower in Group 1 (Granisetron) as compared to Group 2 (Ondansetron) at all time intervals (Table 2).

Postop 30 min: 20% pts. from Group 1 vomited (Score 3) *versus* 50% in Group 2; Postop 1 hr: 16.7% pts. from Group 1 vomited as compared to 46.7% in Group 2;

Postop 6 hrs: 10% pts. from Group 1 vomited as compared to 40% in Group 2;

Postop 12 hr: 3.3% pts. from Group 1 vomited as compared to 33.3% in Group 2;

Postop 48 hrs: No. pts. from Group 1 vomited as compared to 16.7% in Group 2;

There was statistical significant difference between the Groups as per Chi-square test (p < 0.05).

The requirement of rescue antiemetic was significantly lower in Group 1 (Granisetron) as compared to Group 2 (Ondansetron) as per Chi-square test (p < 0.05), shown in Table 3.

Table 2: Comparison of incidence of PONV between Groups

Incidence of PONV	N		Group 1 (Granisetron)		Group 2 (Ondansetron)		p - Value
			%	N	%		
Postop mins	30	Score 0	10	33.3%	2	6.7%	< 0.05
		Score 1	8	26.7%	3	10%	
		Score 2	6	20%	10	33.3%	
		Score 3	6	20%	15	50%	
		Total	30	100%	30	100%	
Postop hr	1	Score 0	18	60%	3	10%	< 0.05
		Score 1	3	10%	4	13.3%	
		Score 2	4	13.3%	9	30%	
		Score 3	5	16.7%	14	46.7%	
		Total	30	100%	30	100%	
Postop hrs	6	Score 0	24	80%	6	20%	< 0.05
		Score 1	1	3.3%	4	13.3%	
		Score 2	2	6.7%	8	26.7%	
		Score 3	3	10%	12	40%	
		Total	30	100%	30	100%	
Postop hrs	12	Score 0	26	86.7%	9	30%	< 0.05
		Score 1	2	6.7%	5	16.7%	
		Score 2	1	3.3%	6	20%	
		Score 3	1	3.3%	10	33.3%	
		Total	30	100%	30	100%	
Postop hrs	48	Score 0	29	96.7%	15	50%	< 0.05
		Score 1	1	3.3%	7	23.3%	
		Score 2	0	-	3	10%	
		Score 3	0	-	5	16.7%	
		Total	30	100%	30	100%	

Table 3: Comparison of Requirement of Rescue Antiemetic between Groups

Requirement of Rescue Antiemetic	Group 1 (Granisetron)		Group 2 (Ondansetron)		p - Value
	N	%	N	%	
Yes	2	6.7%	10	33.3%	
No	28	93.3%	20	66.7%	< 0.05
Total	30	100%	30	100%	

Discussion

Postoperative Nausea and Vomiting (PONV) is a frequently encountered problem and distressing symptom in surgical patients. General anesthesia using inhalational agents is associated with incidence of PONV in 20–30% surgical patients.[10] These incidents are largely dependent on

preoperative patient characteristics, anesthesia, operation, gender, intensity of pain and its postoperative management.

Postoperative vomiting harms skin flaps, abdominal wall sutures and vascular anastomoses. It causes increases in intraocular, intracranial pressure and may also lead to tachycardia, electrolyte imbalance, wound dehiscence, oesophageal tears and aspiration pneumonitis.[11] It may at times lead to serious complications like Mallory Weiss syndrome and oesophageal rupture.[3] PONV especially after minor and ambulatory surgery causes delay in hospital discharge.

Four neurotransmitter systems seem to play an important role in elicitation of an emetic response these are dopaminergic, histaminic, cholinergic, muscaranic and 5-HT_3. As there are 4 different types of receptors involved in emesis so there are at least 4 sites for antiemetic dugs to act.[7] The advent of $5HT_3$ (serotonin) receptor antagonists in 1991 ushered in a new era in the treatment of PONV because of lack of side effects that were commonly observed with the use of antiemetic drugs.[12] Every $5HT_3$ receptor antagonist has the same basic double nitrogen ring backbone in their chemical structure, this maybe the chemical site of action of $5HT_3$ receptor antagonist.[7] Commonly used antiemetic agent from $5HT_3$ receptor antagonist class is ondansetron. Other alternatives are dolasetron, tropisetron, ramosetron.[13] Recent addition to this group is granisetron, which is more potent and has a longer half life of 8–9 hrs as compared to ondansetron's 3 hrs thus, it is much more effective and longer acting antiemetic agent.[5] The $5HT_3$ receptor antagonists caused no extra pyramidal symptoms, no sedation or any adverse effects on vital parameters and do not have any drug interaction with other anesthetic agents.

The present study was conducted with 60 patients belonging to ASA-I and ASA-II between the age of 18 and 60 years undergoing Total Abdominal Hysterectomy under general anesthesia to compare the effects of granisetron and ondansetron for the prevention of postoperative nausea and vomiting (PONV).

The incidence and severity of PONV was significantly lower in Group 1 (Granisetron) as compared to Group 2 (Ondansetron) at all time intervals. The requirement of rescue antiemetic was significantly lower in Group 1 (Granisetron) 6.7% as compared to Group 2 (Ondansetron) 33.3% as per Chi-square test ($p < 0.05$).

It was observed that there was no significant difference in adverse effects amongst the groups as per Chi-square test ($p > 0.05$).

Conclusion

Granisetron is more effective, potent and longer acting antiemetic as compared to ondansetron for reducing PONV in patients undergoing Total Abdominal Hysterectomy under general anesthesia.

Limitations

Following are the limitations of our study:

1. No placebo control group was included in the study as both Granisetron and Ondansetron are well-known drugs to prevent PONV;
2. Quality of oral intake couldn't be analyzed as this was TAH being an abdominal surgery patient needed to be nill per oral for a longer time till there was return of adequate intestinal motility postoperatively.

References

3. Kaufmann MA, Rosov C, Schnieper P, et al. Prophylactic antiemetic therapy with patient controlled analgesia: A double blind, placebo-controlled comparison of droperidol, metoclopromide and tropisetron. Anesth Analg 1994 May;78(5):988–94.
4. Aitkenhead AR, Rowbotham DJ, Smith G. Nausea, vomiting and their treatment. Textbook of Anesthesia 2001, 4th edition; 244–49.
5. Gan TJ, Hetreed MC. Double-blind comparison of ondansetron, droperidol and saline in the prevention of postoperative nausea and vomiting. Br Jr of Anesthesia 1994 May;72(5):544–47.
6. Miller RD, Fleisher LA, Macario A. Anesthesia, editors. The postanesthesia care unit, 6th edition. Pennsylvania: Elsevier; 2010.pp.2703–727.
7. Pierre S, Corno G, Benais H, Apfel CC. A risk score-dependent antiemetic approach effectively reduces postoperative nausea and vomiting--a continuous quality improvement initiative. Can J Anaesth. 2004;51(4):320–25.
8. Helmers JH, Briggs L, Abrahamsson J. A single IV dose of ondansetron 8 mg prior to induction of anesthesia reduces postoperative nausea and vomiting in gynecological patients. Can J Anesth 1993;40(12):1155–161.
9. Bhattacharya D, Banerjee A. Comparison of

ondansetron and granisetron for prevention of nausea and vomiting following day care gynecological laparoscopy. Indian J Anestg 2003;47(4);279–82.

10. McKenzie R, Kovac A, O'Connor T, et al. Comparison of ondansetron versus placebo to prevent postoperative nausea and vomiting in women undergoing ambulatory gynecologic surgery. Anesthesiology. 1993;78(1):21–28.
11. McNulty R. Are all 5-HT3 receptor antagonists the same?. J Natl Compr Canc Netw. 2007;5(1):35–43.
12. Gan TJ, Meyer T, Apfel CC. Consensus guidelines for managing postoperative nausea and vomiting. Anesthesia and Analgesia 2003; 97(1):62–71.
13. Andrew PLR. Physiology of nausea and vomiting. Br J Anaesth. 1992;69(7 Suppl 1):2S-19S.
14. Sneader W. Drug Discovery: A History (John Wiley and Sons, Ltd.: West Sussex, England; 2005. pp. 217–19.
15. Hahm TS, Hwang JW, Kim WH, et al. A prospective, randomized, double-blind, multicenter trial to evaluate the therapeutic efficacy and safety of palonosetron in the treatment of postoperative nausea and vomiting over a 72-h period. J Anesth. 2015;29(1):21–28.