European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 09, Issue 04, 2022

Title page

Type of the Manuscript: Research article

Title of the Manuscript-

Comparative Study of Ondansetron and Granisetron for Postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy under general anaesthesia – Randomized double blind study

Name of the Corresponding author & Co-authors:

Dr. Rajini Sathanish Corresponding Author junior resident department of Anesthesiology, Government Medical College And Hospital, Aurangabad,Maharashtra, India.

Dr. Rashmi V Bengali Professor Anesthesiology Department, Government Medical College And Hospital, Aurangabad,Maharashtra, India.

Dr. Kalidass junior resident department of Anesthesiology, Government Medical College And Hospital, Aurangabad,Maharashtra, India.

Dr. S Amuthan junior resident department of Anesthesiology, Government Medical College And Hospital, Aurangabad,Maharashtra, India.

Objective: Postoperative nausea and vomiting is (PONV) a very distressing complication and preventive measures are justified when the risk of PONV is very high. Ondansetron is the first 5-HT3 antagonist used alone or in combination for prophylaxis of PONV due to its lower cost. Granisetron is recently introduced 5-HT3 antagonists with greater affinity for 5-HT3 receptor and having longer half-life. Aim of the present study is to compare the antiemetic efficacy of ondansetron, granisetron in high-risk patients undergoing laparoscopic cholecystectomy under general anaesthesia. **Method:** This study was prospective and randomized one. Written informed consent will be taken from patients in both groups. Patients will be kept NPO for 12 hours before surgery. In the preoperative room, iv line will secured. In the operation theatre ASA Standard monitoring devices pulse oximetry, NIBP, ECG will be attached and baseline blood pressure, heart rate and O2 saturation values will be recorded. Later capnograpy will be attached after the intubation.

The anaesthetic regimen and surgical procedures will standard for all patients. Patient will be preoxygenated with 100% oxygen for 3 min. Patient will be premedicated with Inj Glycopyrrolate 5µgkg-1,inj midazolam 0.2mg/kg ,inj fentanyl 2mcg/kg.

Result: The incidence of nausea between 0 to 4 hours was 27% in the Ondansetron group and 20% in the Granisetron group. The incidence of nausea was maximum during the first four hours and it was more in the Ondansetron group.The incidence of vomiting between 0 to 4 hours was 20% in the Ondansetron group and 10% in the Granisetron group.The rescue anti emetic was used for 20% in the Ondansetron and 10% in the Granisetron group. Need for rescue antiemetic was more in Ondansetron group compared to Granisetron group.

Conclusion: This study found that newly introduced 5-HT3 antagonist, Granisetron, given prophylactically intravenously, is a more effective medicine than Ondansetron for reducing postoperative nausea and vomiting, with fewer adverse effects.

Key words : post operative nausea, vomiting, Granisetron, Ondansetron.

INTRODUCTION

Laparoscopic operations are quickly becoming popular surgical techniques these days. These have considerably decreased the surgical mortality and morbidity. For symptomatic cholelithiasis, laparoscopic cholecystectomy is rapidly emerging as an alternative to open cholecystectomy. It is the preferred procedure for symptomatic cholelithiasis because it has a lower risk of morbidity and mortality.

Postoperative nausea and vomiting (PONV) are common (overall incidence, 25%-30%)[2] and possibly distressing adverse events related to surgery and anesthesia.

In patients undergoing laparoscopic cholecystectomy without antiemetic prophylaxis, the incidence of PONV can be as high as 60%.

However, the high incidence of PONV in patients not receiving antiemetic prophylaxis decreases the level of postoperative comfort that might be achieved with this minimally invasive surgery and makes antiemetic prophylaxis necessary.

General Anaesthesia is defined as reversible, intentional, temporary, controlled, drug induced loss of consciousness3. There are a variety of problems associated with general anaesthesia, with post-operative nausea and vomiting (PONV) being one of the most distressing and common.

There are various complications of general anaesthesia like aspiration pneumonia, hypoxia, respiratory obstruction, post-operative nausea and vomiting (PONV), hypoventilation, hypotension, hypertension, Out of these post-operative nausea and vomiting (PONV) is one of the most distressing and frequent adverse event occurring after general anaesthesia.

There has been a general trend towards decrease in the incidence because to the use of less emetogenic anaesthetic agents, improved pre-operative and postoperative drugs, refinement of operating technique, and identification of patient predicting characteristics, the problem of post-operative nausea and vomiting has been reduced.

The present study was done to compare the antiemetic effects of optimal dose of intravenous ondansetron (0.1mg/kg) and granisetron(30mcg/kg) to prevent PONV following laparoscopic cholecystectomy

The goal of this study was to assess the antiemetic efficacy of ondansetron and granisetron in avoiding nausea and vomiting after general anaesthesia.

MATERIAL & METHODS:

This study was conducted at Government medical college Aurangabad, on patients admitted for elective Laparoscopic surgeries under general Anaesthesia.

STUDY DESIGN :

Prospective, randomized, double blind comparative study.

INCLUSION CRITERIA:

Patients categorized as American society of Anaesthesiology (ASA) class I and II.

Age 18 to 60 years of either sex. Patients coming for elective laparoscopic cholecystectomy surgical procedure.

METHOD OF COLLECTION OF DATA:

Sixty adult patients of class ASA I and ASA II either of sex in age group of 18yrs to 60yrs, weighing 45 to 70kgs, posted for Laparoscopic surgeries were selected for the study.

Patients were randomly divided into two groups of 30 each.

Group – ‘O’ – Ondansetron group (n = 30)

Group – ‘G’ – Granisetron group (n = 30)

Ethical committee clearance was taken from our college for this study. Written informed consent will be taken from patients in both groups. Patients will be kept NPO for 12 hours before surgery. In the preoperative room, iv line will secured. In the operation theatre ASA Standard monitoring devices pulse oximetry, NIBP, ECG will be attached and baseline blood pressure, heart rate and O2 saturation values will be recorded. Later capnograpy will be attached after the intubation.

The anaesthetic regimen and surgical procedures were standard for all patients. Patient will be preoxygenated with 100% oxygen for 3 min. Patient will be premedicated with Inj Glycopyrrolate 5µg/kg,inj midazolam 0.2mg/kg ,inj fentanyl 2mcg/kg.

RESULTS AND ANALYSIS

The study was conducted among the patients undergoing laparoscopic cholecystectomy under general anaesthesia. In total the study was conducted among 60 participants.

More than half of the study population in both the groups belong to the age group of 18 to 30 years. In the ondansetron group, 10% of the population were in the age group of 31 to 40 years and 41 to 50 years. There was no statistically significant difference in the two groups ($P > 0.05$).The mean (SD) weight of the study participants were 58.4±12.6 and 55.9±11.5 in the Ondansetron and Granisetron group.The weight category of the study population were between 61 to 70 kg in 50% group O and 47% in group G. There was no significant weight difference between the two groups ($P > 0.05$).

On the basis of ASA grading, 76% of participants were in ondansetron group and 73% were in granisteron group. The rest were in the ASA II garding.

The mean HR of the study population was 77.9±5.1 in the Ondansetron and 78.4±5.7 in the Granisetron group. The mean SBP of the Ondansetron group was 129.5±6.3 and in the Granisetron group was 130.5±7. The mean DBP was 80.3±5.2 and 79.8±5 in the Ondansetron group and the Granisetron group. The Mean SPO_2% was in both the group 99.4±0.6.

Systolic, Diastolic BP, Heart rate and oxygen saturation showed no statistically significant difference recorded in PACU between the study groups .

The incidence of nausea between 0 to 4 hours was 27% in the Ondansetron group and 20% in the Granisetron group. The incidence of nausea was 6.7% in both the groups at the end of 4 to 12 hours. At the end of 12 hours , none of the participants had nausea . The incidence of nausea was maximum during the first four hours and it was more in the Ondansetron group.

The incidence of vomiting between 0 to 4 hours was 20% in the Ondansetron group and 10% in the Granisetron group. The incidence of nausea was 6.7% in ondansetron group and 3.3% in the granisteron at the end of 4 to 12 hours. At the end of 12hours, none of the participants had nausea. Again the incidence of vomiting was maximum during first four hours and no patient in any group vomited from 12 hours onwards.

The side effects seem to be in high proportion in the granisteron group with 17% of headcahe, 13% of constipation and 6.7% of dizziness in the odansetron and granisteron group. Occurrence of side effects like headache, constipation and dizziness in Ondansetron group are 7(23.3%),7(23.3%),5(16.7%) respectively compared to 5 (16.7%), 4(13.3%),2 (6.7 %) in Granisetron group. The number of patients who suffered side effects were more in Ondansetron group.

The clinical recovery score was found to be increased from 5.47 and 5.66 at 0 hour to 10.3 and 10.5 at the end of 4 hours in the ondansteron and granisetron group.

The mean recovery time was 5.7 and 5.9 in the odensteron and granisteron group.

There was no significant difference in CRS and RT between the two groups($P>0.05$).

The rescue anti emetic was used for 20% in the Ondansetron and 10% in the Granisetron group. Need for rescue antiemetic was more in Ondansetron group compared to Granisetron group.

Table no.1 General charecteristics

General charecteristics	Group O	Group G
Age (Years, Mean±SD)	31.5± 7.8	30.4±8.7
Weight (Kg, Mean±SD)	58.4±12.6	55.9±11.5
Height (Cm, Mean±SD)	149.10±6.74	151.20±7.43
ASA Grade Number I/II	23/7	22/8
Vital parameters		
Mean HR(bpm, Mean±SD)	77.9±5.1	78.4±5.7
Mean SBP(mmhg,Mean±SD	129.5±6.3	130.5±7
Mean DBP(mmhg,Mean±SD	80.3±5.2	79.8±5
Mean SPO_2%(Mean±SD)	98.2±1.0	98.3±0.9

Table no.2 Incidence of nausea and vomiting:

Nausea/ vomiting Over time	Group O	Group G
Up to 4 hours Nausea vomiting	 8 (26.7%) 6(20%)	 6 (20%) 3(10%)
Between 4 hrs to 12 hrs Nausea Vomiting	 2(6.7%) 2(6.7%)	 2(6.7%) 1(3.3%)
Between 12hrs.- 24hrs. Nausea Vomiting	 1(3.3%) 0	 0 0

Table no. 3 Comparison of side effects:

Side effects	Group O	Group G
Headache	*7(23.3%)	*5 (16.7 %)
Constipation	*7(23.3%)	*4 (13.3 %)
Dizziness	*5 (16.7%)	*2 (6.7 %)

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

Table no.4 Clinical recovery score and recovery time:

Time Interval	Group O	Group G	P VALUE
0 hour	5.47	5.66	**0.73**
1 Hour	7.23	7.38	**0.63**
2 hour	8.1	8.5	**0.71**
3 Hour	8.8	9.3	**0.70**
4 Hour	10.3	10.5	**0.76**
Recovery time (Minutes)	5.7±0.26	5.9± 0.3	**0.722**

Table 5. Comparison of rescue antiemetic:

Anesthetic Sequalae	**Group O (n=30)**	**Group G (n=30)**
Rescue antiemetic	6 (20 %)	3 (10 %)

DISCUSSION

In a double blinded randomised control trial, we compared the antiemetic efficacy of ondansetron with recently introduced 5-HT3 antagonist, granisetron. The incidence of PONV were significantly higher in patients receiving ondansetron for prophylaxis of PONV (Group O). Incidence of PONV was found to be 63%. Our findings are consistent with findings of Kumkum Gupta [6], who found high incidence of PONV despite prophylactic use of ondansetron.

High incidence of PONV in group O may be due to the fact that ondansetron was metabolised via CYP2D6 such that select genetic polymorphism of P450 enzyme can lead to ultrarapid metabolism. Due to this ultra-rapid metabolism ondansetron is found to be most effective when given at the end of surgery rather than just before induction as in this study. The half-lives of recently introduced 5-HT3 antagonistare very high; $t^{1/2}$ of granisetron was 10 hours.

There was no discernible difference in nauseous episodes after 12-24 hours. Study done by **SK PARK** [12]observed that **nausea and vomiting** is more common in first 6 hours post operatively.

There was no statistically significant difference in baseline values of **haemodynamic variables** between the two groups before, during, or after administration of the study medication, according to our findings. Ondansertron and Granisetron, which were used in the study, were given around half an hour before the procedure. In PACU, we took regular readings of SBP, DBP, and HR over a 30-minute period. There was no difference in haemodynamics between these results, according to our research. The same findings were found in a study conducted by **Dev[11].** During the study period, no changes in PR, SBP, or DBP were observed.

In our study groups, there was a considerable increase in **the incidence of side effects**. The incidence of headache was 7% in the Ondansetron group and 5% in the Granisetron group,

indicating a statistically significant difference (P 0.05). **According to Abhishek Kumar's[3]** research, the incidence of headache and constipation was higher in the Ondansetron group than in the Granisetron group, which was consistent with our findings. Constipation and dizziness rates varied significantly between the Ondansetron and Granisetron groups (P0.05).

Granisetron has a better safety profile and is more powerful than Ondansetron. In patients undergoing laparoscopic surgery under general anaesthesia, we found that patients who got i.v.Granisetron had less emetic and nauseous episodes in the postoperative period than those who received i.v.Ondansetron.

Despite the fact that individuals who got intravenous Granisetron had a somewhat higher clinical recovery score than those who received intravenous Ondansetron, there was no significant difference in anaesthetic recovery time between the two medications. **Stewart[9]** found the same thing in his research. The rate of occurrence of most of the outcomes increased with inceasing body mass index category.

LIMITATIONS: We did not include any control group in our study because placebo does not control PONV. Azize Bestas [2] suggested that if active drugs are available placebo controlled trial should not be practiced because PONV is very distressful and associated with poor outcome. We used the optimal dosages of the drug (commercially available strength) and not the equipotent doses for the control of PONV, Equipotent doses of recently introduced 5- HT3 antagonists is yet to be discovered.

CONCLUSION: Present study clearly shows that the newly introduced 5-HT3 antagonists, Granisetron was better in efficacy in the prophylaxis of nausea and vomiting. Granisetron was comparable in efficacy to control post-operative nausea andvomiting.

REFERENCES:

1) Kailash chandra sharma,Geetha Singh oct 22;Page:14880-14890,Comparative Evaluation of odansetron ,Granisetron and Ramosetron to prevent post operative nausea and vomiting.

2) Azize Bestas, MD1; Selami Ates Onal, MD1; Mustafa Kema Bayar, MD~; Ash Yddlnm, MD2; and Erhan Aygen, MD 3 doi:l 0.1016/j.cur theres.2007.10.003- Effects of Ondansetron and Granisetron on Postoperative Nausea and Vomiting in Adult Patients Undergoing Laparoscopic Cholecystectomy: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial .

3) Abhishek Kumar Barnwal1, Geeta Karki2, K. C. Sharma3, H. S. Nanda ; Page: 13857-13866, DOI: 10.14260/jemds/2014/3940 Efficacy of Granisetron compared to Ondansetron As Prophylactic antiemetic in general anaesthesia.

4) [Update on PONV-What is new in prophylaxis and treatment of postoperative nausea and vomiting? : Summary of recent consensus recommendations and Cochrane reviews on prophylaxis and treatment of postoperative nausea and vomiting]
Peter Kienbaum [1], Maximilian S Schaefer [2]

5) Kumar. A et al, Effect of ondansetron and metocloparmide on vigilance, cognition and recovery time following major gynacecological surgery. J Anaesth clin

Pharmacol.1996:12:35-38.

6) Kumkum Gupta, Ivesh Singh, Prashant K. Gupta1 , Himanshu Chauhan, Manish Jain: Palonosetron, Ondansetron, and Granisetron for antiemetic prophylaxis of postoperative nausea and vomiting - A comparative evaluation of palonosetron and granisetron in postoperative nausea vomiting: A randomized double-blind prospective study.

7) Janknegt R. Clinical efficacy of antiemetic following surgery. Anaesthesia 1999; 54: 1054-1068..

8) Yong seon choi 2018:14 601–606. Comparison of ramosetron and ondansetron for the treatment of established postoperative nausea and vomiting after laparoscopic surgery: a prospective, randomized, double-blinded multicenter trial Therapeutics and Clinical Risk Management .

9) Stewart L, Crawford S.M; The comparative effectiveness of ondansetron and granisetron on once daily dosage in prevention of nausea and vomiting caused by cisplatin. The pharmaceutical journal 200; 265(104):59-62.

10) Amrita 2016: 10:402-7 A. Gugale, Pradnya Milind Bhalerao Palonosetron and granisetron in postoperative nausea vomiting: A randomized double-blind prospective study.

11) Dev N, Mehrotra S, Tyagi S K; A comparative study of metoclopramide and ondansetron. Indian Journal of Anaesthesia 1998,(42):52-56.

12) SK PARK AND EJ CHO A Randomized, Double –blind Trial of Palonsetron compared with ondansetron in preventing postoperative nausea and vomiting after gynaecological laparoscopic surgery.2011:39,(399-407).