A Comparative study on efficacy of Granisetron and Ondansetron in the Prevention of Post- Operative Nausea and Vomiting after Laparoscopic surgery

Sharma M[1], Sapkota S[2], Sharma S[1], Shakya S[1]
1. Department of Anesthesia and Critical Care, Nepalgunj Medical College
2. Department of Biochemistry, Nepalgunj Medical College

ABSTRACT

Introduction: Postoperative nausea and vomiting (PONV) are a common surgical complication. Risk factors include, type, and patient-specific factors like young females, duration of anaesthesia (>30 min), type of surgical procedure, history of motion sickness or a family past history of PONV. Effective management with 5-HT3 antagonists, such as ondansetron and granisetron, improves patient recovery, reduces discomfort and days of hospitalization. The current study's objective is to evaluate the efficacy of Granisetron and Ondansetron in preventing PONV in patients having laparoscopic procedures.

Methods: This is prospective interventional study at Nepalgunj Medical College involved 80 patients scheduled for laparoscopic surgery. Participants aged 15-55 with American society of anaesthesiologist (ASA) grades I and II received either ondansetron 4mg intravenous (group A) or granisetron 2 mg intravenous (Group B) before anaesthesia. Postoperatively, patients were monitored for nausea, vomiting, and need for rescue antiemetics. Adverse effects were recorded during a 24-hour observation period. Written informed consent was obtained from all participants.

Results: There were no statistical differences between the two groups in terms of gender, age, weight, or surgery type ($p > 0.05$). Group B experienced a significantly lower incidence of PONV (25%) compared to Group A (55%) with a p-value of 0.03. During the 0–6-hour period, 90% of Group B and 75% of Group A had no PONV ($p = 0.18$). No significant differences were observed between the 6-12- and 12-24-hour intervals.

Conclusion: The study concludes that Granisetron prevents PONV better than Ondansetron in patients undergoing laparoscopic surgery when given 2 mins just prior to induction of anaesthesia.

Keywords: Granisetron; Laparoscopic surgery; Ondansetron; Postoperative nausea and vomiting

INTRODUCTION

Postoperative nausea and vomiting (PONV) refer to the occurrence of nausea and vomiting after surgical intervention particularly involving general anesthesia, typically within 24 to 48 hours. The incidence of PONV is between 20% and 40%, and occurs up to 80% of high-risk patients.[1] The incidence of postoperative nausea and vomiting (PONV) varies depending on the type of laparoscopic procedure. Following several surgical procedures, PONV is primarily attributed to patient-related and anesthesia-related factors, factors of self-surgery.[2] Individual factors like young females, duration of anaesthesia (>30 min), type of surgical procedure, history of motion sickness or a family Past history of PONV might cause PONV.[3] Among them are risk scoring systems, Apfel and Eberhart, which utilize the length of the surgery, family history as well as other parameters to ascertain the levels of PONV amongst adult and pediatric patients.[4] PONV is a self-limiting complication but it can cause dehydration, electrolyte imbalance, increased pain and discomfort from surgical strain, aspiration

Corresponding author:
Dr. Mahesh Sharma
Assistant professor
Department of Anesthesia and Critical Care
Nepalgunj Medical College
Phone no: 9851233519
Email: mahesh.anesthesai@gmail.com

pneumonitis.[5] Studies confirmed that PONV increases hospitalization and delayed recovery of the patient. [6]

Due to the multifactorial etiology of PONV and the absence of a definitive preventive strategy, the administration of antiemetic agents such as ondansetron remains the primary method for preventing PONV in clinical settings.[5,6] The treatment of PONV has significantly improved with the development of certain 5-HT receptor antagonists. Their use has considerably decreased the incidence and severity of PONV in many patients, enhancing recovery and comfort after surgery.[7] It has been argued in various studies whether all surgical patients should be routinely given combination antiemetics to prevent PONV.[8]

A well-known antagonist of the 5-HT receptor, which is which is used to reduce nausea and vomiting is ondansetron.[7] Onset of action is less than 30 minutes and it lasts for about 12-24 hours.[9] Granisetron is an efficient, well-tolerated drugs with a half-life almost twice as long as that of ondansetron.[10] It is highly selective antagonist of the 5-HT receptor's then ondansetron at both central and peripheral sites and produces irreversible block of 5HT3 receptors, also acts on vagal afferent nerves of gut and produces blockade of 5HT3 receptors.[11,12] It has no interaction with other receptors assumed to be responsible for its safe and well-tolerated side effects.[11]

The present study was conducted with the specific aim of evaluating the effect of two widely used 5HT3 receptor antagonist antiemetic agents, intravenous ondansetron and granisetron in preventing PONV in patient undergoing laparoscopic surgery.

METHODS

Study design

This prospective interventional study was conducted at Nepalgunj Medical College after approval from Institutional review Committee. The study period was 6 months from date of approval from IRC. Total 80 patient posted for laparoscopic surgery were involved in the study.

Sample size calculation

The sample size was calculated using the following formula: n= [Z α √{(r+1)p(1-p)}+Z 1-β √{rp 1 (1-p 1)+p 2 (1-p 2)}] 2 /r(p 2 -p 1) 2 where, type 1 error (α)=0.05, type 2 error (1-β)=0.2, expected proportion of PONV in group 1 (p 1)=53.33%, from the previous study.[12] Expected proportion of PONV in group 2 (p 2)= 23.33%, and Taking sample size ratio (group2/group 1) as 1, the sample size was calculated to be 40 in each group.

Inclusion and exclusion criteria

Individuals ASA grade I and II , both sexes, age above 15 years and those patients scheduled for laparoscopic surgeries under general anesthesia were included in study. Patients were excluded if they were unable or unwilling to give informed consent, had documented hyper sensitivity to any of the study drugs, had a history of motion sickness or previous PONV, had taken antiemetic drugs within 24 hours before surgery, had a history of neurological or renal diseases, pregnant or lactating female, patients with cancer on chemotherapy/radiotherapy. Informed written consent was taken from all participants.

Preanesthetic evaluation was done on the previous day of surgery, detailed history and present complaints were noted. Patients were instructed to remain nil per oral 8 hours for solid and 2 hours for clear liquid. The anesthetic regimen was standardized for all patients. After shifting the patient to operation theatre, baseline pulse rate, blood pressure (systolic and diastolic) and peripheral oxygen saturation were recorded. Peripheral venous access was established using an 18 Gauge cannula and intravenous fluid normal saline was started. Two minutes prior to induction, participants in Groups A and B received intravenous doses of Ondansetron (4 mg) and Granisetron (2 mg), respectively. Simple random sampling was used to allocate participants into groups, ensuring unbiased distribution. Granisetron was selected for comparison due to its longer duration of antiemetic action and higher receptor binding affinity compared to other 5-HT3 antagonists, making it a clinically relevant alternative to Ondansetron in preventing postoperative nausea and vomiting (PONV). The drugs were injected slowly over thirty seconds in undiluted form. Patients were premedicated

with Midazolam 0.05 mg/kg, and Fentanyl 2 µg/kg. Patients were preoxygenated and then induced with Propofol 2mg/kg ,Rocuronium 50 mg was used as muscle relaxant for intubation. Anesthesia was maintained with Oxygen and sevoflurane (1.5-2%) using controlled ventilation and intermittent bolus dose of rocuronium. Patients were monitored using continuous electrocardiogram, heart rate, blood pressure, pulse oximetry and capnography. During surgery the abdomen was insufflated with carbon dioxide with an intraabdominal pressure of 12 to 15 mm of Hg. On completion of surgery the residual paralysis was reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg. Postoperative analgesia was maintained by using Nonsteroidal anti-inflammatory Like diclofenac thus avoiding opioids post-operatively. Postoperatively, patients were assessed for episodes of nausea, retching and vomiting and the need for rescue antiemetic at intervals of 0-2 hours, 2-12 hours, 12 - 24 hours. Episodes of PONV was identified by spontaneous complaints by the patients or by direct questioning and recorded. Rescue antiemetic Metoclopramide 10 mg IV was given in the event of one or more episodes of vomiting. Any adverse effects like headache, dizziness, constipation during the 24- hour postoperative observation period was noted. Complete Response were noted 24 hours postoperatively.

In this study, statistical analysis of both descriptive and inferential was done. Mean ± SD (standard deviation(Min-Max) was used to display results for continuous measurements, and Number (%) was used to display findings for categorical measurements. The five percent significance level was used to evaluate significance. The relevance of the research parameters using a continuous scale based on metric characteristics across two groups (relationships analysis) was evaluated using the student t test. When comparing the two groups, the significance of the study Fisher/Chi-square analysis was used to assess the variables on a categorical scale. Notable numbers: + Significance suggestion (P value: 0.05<P).

RESULTS

Group A and Group B's baseline demographic characteristics were compared in Table 1. Group A's average age was 44.0 ± 11.00 years, while Group B's average age was somewhat lower at 42.14 ± 11.67 years in which there was no discernible change (p=0.36). The distribution of genders in the two groups does not differ much which is shown in table 1. Likewise, there are no notable distinctions between the groupings with the average weight in Group A being 62.67 ± 11.78 kg and that in Group B being 58.34 ± 9.34 kg(p=0.37). Both Group A and Group B's demographics were not significantly different from one another.

Table 2 presents the incidence of postoperative nausea and vomiting (PONV) in both groups. In Group A (Ondansetron), 45% of patients experienced no PONV, while 55% had PONV. In contrast, Group B (Granisetron) showed a significantly lower incidence, with 75% of patients experiencing no PONV and only 25% reporting symptoms. The difference between the groups was statistically significant, with a p-value of 0.03, indicating that granisetron was more effective than ondansetron in preventing PONV in this study.

Table 3 reports the frequency of nausea and vomiting during three postoperative periods: 0-6 hours, 6-12 hours, and 12-24 hours. During the first 0-6 hours, 90% of Group B and 75% of Group A had no PONV, with no significant difference between the groups. Regarding nausea, 10% of Group B and 25% of Group A experienced nausea, but the difference was not statistically significant. In the 6–12-hour period, 70% of Group A and 90% of Group B did not experience nausea, with no significant difference (p = 0.30). However, 10% of Group A experienced retching or vomiting, while none in Group B did (p = 0.09). In the 12–24-hour period, 82.5% of Group A and 97.5% of Group B had no PONV (p = 0.09), with Group A reporting higher levels of nausea (12.5%) compared to Group B (2.5%), although this difference was not statistically significant (p = 0.17).

Overall, while statistical significance was not achieved for all time periods, Group B consistently showed a lower incidence of nausea and vomiting across all intervals.

The requirement of antiemetics in each group is

displayed in Table 4. Compared to just 5% Group B included two patients, whereas Group A had five patients, or 12.5% who required rescue antiemetic medication. The p-value of 0.16, obtained using the Chi-square test, indicates that the difference between the number of patients in Group B and Group A who required rescue antiemetic medications is not statistically significant.

Table 1: Comparison of demographic data and types of surgery in both groups

Demographic characteristic	Group A (ondansetron)	Group B (granisetron)	p-value
Age (years)	44.0 ± 11.00	42.14 ± 11.67	0.36
Gender (M/F)	12/28	15/25	0.42
Weight (kg)	62.67 ± 11.78	58.34 ± 9.34	0.37
Types of surgeries			
Laparoscopic Cholecystectomy	15	18	0.069
Laparoscopic Appendectomy	10	7	0.077
Laparoscopic Hernia Repair	5	5	0.085

Table 2: Incidence of PONV in both groups

Group	PONV		P-value
	Absent	Present	
Group A (ondansetron)	18 (45%)	22 (55%)	0.03
Group B (granisetron)	30 (75%)	10 (25%)	

Table 3: PONV prevalence in two groups at different intervals of time

Nausea and vomitingat different periods of time	Group A	Group B	p-value
0-6 hours			
No nausea vomiting	30 (75%)	36 (90%)	0.18
Nausea	10 (25%)	4 (10%)	0.18
Retching or vomiting	0	0	
6-12 hours			
No nausea vomiting	28 (70%)	36 (90%)	0.07
Nausea	8 (20%)	4 (10%)	0.30
Retching or vomiting	4 (10%)	0	0.09
12-24 hours			
No nausea vomiting	33 (82.5%)	39 (97.5%)	0.09
Nausea	5 (12.5%)	1 (2.5%)	0.17
Retching or vomiting	2 (5%)	0	

Table 4: Requirement of rescue antiemetic

Group	Rescue antiemetic use	p-value
Group A	5 (12.5%)	0.16
Group B	2 (5%)	

DISCUSSION

Post operative nausea and vomiting remains significant concerns following laparoscopic surgery, despite advancement in antiemetic medication. PONV is frequent, significant, and upsetting adverse events that is experienced following various surgical procedure particularly

involving general anesthesia. Often patient express more concern about PONV than postoperative pain.[13] Naguib et al demonstrated that the incidence of PONV after laparoscopic surgeries in their placebo group was remarkably high 72%.[14] Pneumoperitoneum is believed to cause PONV due to stretching of mechano receptor in the peritoneum as well as stimulation of nociceptors by absorbed carbon dioxide.[15] The incidence of PONV is subjected to various factor including patient characteristics, duration of surgery and anesthesia technique used. Treating PONV is challenging, and requires a variety of medications in combination. The main pharmacological classes of drugs used in the treatment are anti-cholinergic, anti-histaminic, butyrophenones, benzamide, Neurokinin receptor antagonists and glucocorticoids. Each drug used has its own merits and demerits like dry mouth, extrapyramidal signs, hallucinations, excessive sedation, headache and hypotension.[16,17]

The usage of 5-HT receptor antagonists has been significant antiemetics for a variety of illnesses, including radiation-induced emesis, nausea and vomiting brought on by chemotherapy, in addition to nausea and vomiting after surgery (PONV). They bind to the 5-Hydroxytryptamine subtype-3 (5HT3) receptors, selectively blocking the emetogenic stimuli during anesthesia and surgery. They have proven efficacy and is recommended as a prophylactic antiemetic at the time of induction of anesthesia.[18]

In our study the incidence of PONV was significantly lower in group B (25%) compared to group A (55%) withstatically significant p values of 0.03.Over various time interval(0-6,6-12,12-24 hrs.) post-surgery group B generally experienced fewer case of nausea and vomiting, though this difference was not statically significant for individual time period. The need for rescue antiemetic medication was also low in group B (5%) then in group A (12.5%) though this difference was not statically significant (p=0.16). Overall group B showed better outcomes in term of PONV. A Study done by Bhattrai R et al have shown similar finding as ours where there was prevalence of nausea and vomiting of 26.3% in granisetron and 54% in ondansetron however they have studied only in laparoscopic Cholecystectomy and study drugs were given 30 mins before end of surgery.[19] Study done by Pradhan S et al also showed similar finding as ours where PONV was 53% in ondansetron group and 23.3% in granisetron group, although our finding was not statically significant across the specific time interval (0-6,6-12,12-24,) group B constantly reported fewer case of nausea and vomiting which is similar to their studies.[20] However they have done only in laparoscopic cholecystectomy and study drugs were given at the end of surgery just before giving reversal. It is in contrast to our study where we gave study drugs at beginning of surgery.

The timing of preventive administration of antiemetic has been found to significantly affect the efficacy of the medication in avoiding severe PONV. Both the drugs reached the peak plasma concentration with in 30 mins of intravenous administration.[21] Therefore we decided to administer study drugs just 2 mins prior to induction, which was at the beginning of surgery considering for adequate time for peak plasma concentration of both drugs. Various study done by different authors, Honkavaara, Bhattacharya and Banerjee, Nethra het et al, Kirat savant had also given both drugs just before induction which was towards the beginning of surgery.[22-25]

Although ondansetron is reportedly associated with a higher frequency and severity of CNS side effect compared to others serotonin receptor antagonist.[26,27] Our study didn't reveal any significant adverse events in either group. This suggest that both drugs are well tolerated in our patient population. The significantly reduced PONV incidence in the Granisetron group supports its preferential use, as also recommended by prior meta-analyses, for better patient outcomes and reduced need for additional interventions.

CONCLUSION

The study concludes that Granisetron prevents PONV better than Ondansetron in patients undergoing laparoscopic surgery when given 2 mins just prior to induction of anesthesia. The study supports Granisetron' s usage as a preferred treatment in clinical anesthetic practice by proving its greater efficacy, particularly in lowering the

need for emergency antiemetic medications and PONV management for a longer time.

LIMITATION

Some of the limitations of our study include the

1. Smaller sample size which is only 80 patients thus limiting generalizability of results.
2. Single-center study conducted at Nepalgunj Medical College creating the scope for institutional biases - results not being applicable to other
3. The study excluded patients with a history of motion sickness or previous PONV, and those on chemotherapy/radiotherapy. This exclusion means the findings may not be applicable to these high-risk populations, who are more prone to PONV health care settings.

REFERENCES

1. Luo D, Huang Z, Tang S, et al. Risk analysis of postoperative nausea and vomiting in patients after gynecologic laparoscopic surgery. BMC Anesthesiol. 2024;24(345).
2. Chatterjee S, Rudra A, Sengupta S. Current concepts in the management of postoperative nausea and vomiting. Anesthesiol Res Pract. 2011;2011:748031.https://doi.org/10.1155/2011/748031
3. Gan TJ, Diemunsch P, Habib AS, Kovac A, Kranke P, Meyer TA et al. Consensus guidelines for the management of postoperative nausea and vomiting. AnesthAnalg. 2014;118(1):85-113.
4. Apfel CC, Laara E, Koivuranta M, Greim CA, Roewer N. A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers. Anesthesiology. 1999;91(3):693-700. doi:10.1097/00000542-199909000-00022.
5. Rodgers A, Cox RG. Anesthetic management for pediatric strabismus surgery: Continuing professional developmnt. Can J Anaesth. 2010;57(6):602–17. doi:10.1007/s12630-010-9300-x. PMid:20393822.
6. Eberhart LH, Geldner G, Kranke P, Morin AM, Schäuffelen A, Treiber H, et al. The development and validation of a risk score to predict the probability of postoperative vomiting in pediatric patients. AnesthAnalg. 2004;99(6):1630–7. https://doi.org/10.1213/01.ANE.0000135639.57715.6C PMid:15562045.
7. Kovac AL, O'Connor TA, Pearman MH, Kekoler LJ, Edmondson D, Baughman VL, et al. Efficacy of repeat intravenous dosing of ondansetron in controlling postoperative nausea and vomiting: a randomized, double-blind, placebo-controlled multicenter trial. J ClinAnesth. 1999;11:453-9.https://doi.org/10.1016/S0952-8180(99)00067-7
8. Darkow T, Gora-Harper ML, Goulson DT, Record KE. Impact of antiemetic selection on postoperative nausea and vomiting and patient satisfaction. Pharmacotherapy. 2001;21(5):540-8.https://doi.org/10.1592/phco.21.6.540.34543
9. Roila F, Del Favero A. Ondansetron clinical pharmacokinetics. Clinical Pharmacokinetics. 1995;29(2):95-109. doi:10.2165/00003088-199529020-00004.
10. Salajegheh S, Kuhestani S, Kermani MS, Taheri O, Bafghi NN. Comparison of Ondansetron and Granisetron Effects for Prevention of Nausea and Vomiting Following Strabismus Surgery. Open access Macedonian journal of medical sciences. 2019 Oct 10;7(19):3195.
11. Muchatuta NA, Paech MJ. Management of postoperative nausea and vomiting: focus on palonosetron. TherClin Risk Manag. 2009;5:21-34.https://doi.org/10.2147/TCRM.S3437
12. Pradhan, S, Dhakal, S. Comparative Study of Ondansetron and Granisetron for Preventing Post-Operative Nausea and Vomiting in Laparoscopic Cholecystectomy under General Anaesthesia. Nepal Journal of Medical Sciences,6(2),4–11. https://doi.org/10.3126/njms.v6i2.42220
13. Kishore CP, Rao MS, Karoon SP, Arora RK, Roy AB.Comparative study of ondansetron,granisetron and granisetron with dexamethasone for prevention of postoperative nausea and vomiting in patients undergoing laproscopic cholecystectomy.Indian journal of clinical anesthesia,2021;8(2):236-42.
14. Naguib M, El Bakry AK, Khoshim MHB, et al. Prophylactic antiemetic therapy with ondansetron, tropisetron, granisetron, and metoclopramide in patients undergoing

laparoscopic cholecystectomy. Can J Anaesth. 1996;43:226-31.https://doi.org/10.1007/bf03011739

15. Kishore CP, Rao MS, Kooran SP, Arora RK, Roy AB. Comparative study of ondansetron, granisetron, and granisetron with dexamethasone for prevention of postoperative nausea and vomiting (PONV) in patients undergoing laparoscopic cholecystectomy. Indian J ClinAnaesth. 2021;8(2):236-42. http://dx.doi.org/10.18231/j.ijca.2021.046
16. Gan TJ, Meyer T, Apfel CC, Chung F, Davis PJ, Eubanks S, et al. Consensus guidelines for managing postoperative nausea and vomiting. AnesthAnalg. 2003;97:62-71.https://doi.org/10.1213/01.ane.0000068580.00245.95
17. Morgan GE, Mikhail MS, Murray MJ. Clinical anesthesiology. 4th ed. New York: McGraw-Hill; 2008.
18. Toth B, Lantos T, Hegyi P, Viola R, Vasas A, Benkg R, Gyongyi Z, Vincze Á, Csécsei P, Mikó A, Hegyi D. Ginger (Zingiberofficinale): an alternative for the prevention of postoperative nausea and vomiting. A meta-analysis. Phytomedicine. 2018;50:8-18.
19. Bhattarai R, Vaidya PR, Chand MB. Birat Journal of Health Sciences. 2017;2(2):175-78.
20. Pradhan, S, Dhakal S.Comparative Study of Ondansetron and Granisetron for Preventing Post-Operative Nausea and Vomiting in Laparoscopic Cholecystectomy under General Anaesthesia.Nepal Journal of Medical Sciences.2021;6(2):4-11.
21. Beattie WS, Lindblad T, Buckley DN, Forrest JB. Menstruation increases the risk of nausea and vomiting after laparoscopy. A prospective randomized study. Anesthesiology. 1993;78(2):272-6. doi: 10.1097/00000542-199302000-00010. PMID: 8439022.
22. Honkavaara, P, Lehtinen, AM., Hovorka. Nausea and vomiting after gynaecological laparoscopy depends upon the phase of the menstrual cycle. Can J Anaesth 38, 876–9 (1991). https://doi.org/10.1007/BF03036963
23. Bhattacharya D, Banerjee Arnab. Comparison of ondansetron and granisetron for prevention of nausea and vomiting following day care gynaecological Laparoscopy. Indian Journal of Anaesthesia 2003;47(4):279-82.
24. Nanjundaswamy NH, Sridhara RB.A comparative study of ondansetron and granisetron in combination with dexamethasone-in prophylaxis for postoperative nausea and vomiting (PONV) in laproscopiccholecystectomies.Int J Res Med Sci2018;6:503-8.
25. Savant K, Khandeparker RV, Berwal V, Khandeparker PV, Jain H. Comparison of ondansetron and granisetron for antiemetic prophylaxis in maxillofacial surgery patients receiving general anesthesia: a prospective, randomised, and double blind study. J Korean Assoc Oral Maxillofac Surg. 2016;42(2):84-9. doi: 10.5125/jkaoms.2016.42.2.84. Epub 2016 Apr 27. PMID: 27162748; PMCID: PMC4860384.
26. Kovac, Anthony L. "Management of postoperative nausea and vomiting in children." Paediatric drugs vol. 2007;9(1):47-69. doi:10.2165/0;0148581-200709010-0000
27. Prasai A, Prasai A. Combination of Granisetron and Dexamethasone for prevention of postoperative nausea and vomiting following laparoscopic cholecystectomy. Nep. Med. Coll. J. [Internet]. 2023 Jul. 7 [cited 2024 Nov. 28];25(2):131-6. Available from: https://nepjol.info/index.php/nmcj/article/view/56050