MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.59218/makrjms.2024.2.148.154

Comparison of Ramosetron with Ondansetron for Prevention of Nausea and Vomiting in Women Undergoing Hysterectomy

[1]Bhavesh B. Zinzala, [2]Hardul V. Modi, [3]Dhara Joshi and [4]Jagdishbhai G. Mer

[1-4]*Department of Anaesthesiology, Shantaba Medical College and General Hospital, Amreli, Gujarat, India*

ABSTRACT

Postoperative nausea and vomiting (PONV) remain a significant concern following surgical procedures, particularly in gynecological interventions such as hysterectomy. This study aims to compare the efficacy oftwo 5-HT3 receptor antagonists, Ramosetron and Ondansetron, in preventing PONV in women undergoing hysterectomy. Both drugs have distinct pharmacokinetic profiles and this investigation seeks to evaluate their comparative effectiveness in reducing the incidence of nausea and vomiting during the postoperative period. A prospective single-blinded randomized study was conducted on 60 healthy women aged 18-65, undergoing abdominal hysterectomy under spinal anesthesia. Patients were randomly assigned to receive either Ramosetron (0.3 mg) or Ondansetron (4 mg). The evaluation of nausea and vomiting was performed using the PONV SCORE system at different time intervals (0-6 hrs, 6-12 hrs and 12-24 hrs). The scoring system included categories for Complete Response, Nausea, Vomiting and the need for Rescue antiemetic. Statistical analyses were employed to compare the outcomes between the two groups. In the 0-6 hrs. time interval, Ramosetron exhibited comparable efficacy to Ondansetron in reducing the PONV score, with statistically nonsignificant differences. However, during the 6-12 hrs and 12-24 hrs. intervals, Ramosetron demonstrated superior efficacy, significantly lowering the PONV score compared to Ondansetron. The incidence of nausea and vomiting was consistently lower with Ramosetron, especially during the later postoperative intervals. While both Ramosetron and Ondansetron were effective in preventing postoperative emesis, Ramosetron emerged as a more potent antiemetic, particularly in the 6-12 hrs. and 12-24 hrs. postoperative periods. The extended half-life and higher receptor affinity of Ramosetron may contribute to its prolonged duration of action. These findings suggest that Ramosetron could be considered a favorable choice over Ondansetron for preventing PONV in women undergoing hysterectomy. The study contributes valuable insights into optimizing postoperative care strategies in gynecological surgeries.

OPEN ACCESS

Key Words
Ramosetron, ondansetron, hysterectomy, gynaecology

Corresponding Author
Jagdish G. Mer,
Department of Anaesthesiology, Shantaba Medical College and General Hospital, Amreli, Gujarat, India
jagdish.mer32@gmail.com

Author Designation
[1,3,4]Assistant Professor
[2]Associate Professor

Received: 18 November 2023
Accepted: 22 December 2023
Published: 23 December 2023

Citation: Bhavesh B. Zinzala, Hardul V. Modi Dhara Joshi and Jagdishbhai G. Mer, 2023. Comparison of Ramosetron with Ondansetron for Prevention of Nausea and Vomiting in Women Undergoing Hysterectomy. Res. J. Med. Sci., 18: 148-154, doi: 10.59218/makrjms. 2024.2.148.154

INTRODUCTION

Postoperative nausea and vomiting (PONV) represent prevalent and distressing complications following anesthesia and surgical procedures, with the potential to give rise to significant postoperative challenges. The reported incidence of PONV ranges from 20-30%, escalating to as much as 80% in individuals deemed high-risk, notably in the context of gynecological surgery[1,2]. The heightened intra-abdominal pressure accompanying forceful vomiting poses a threat to abdominal suture lines and increases the likelihood of esophageal rupture. Elevated central venous pressures, a consequence of PONV, are recognized as contributors to heightened morbidity, particularly following ocular, tympanic, and intracranial procedures. Furthermore, the propensity for aspirating gastric contents is heightened in the presence of PONV, presenting an increased risk, especially when airway reflexes are compromised[1].

Several scoring systems have been devised to identify patients at risk of PONV, with Apfel's simplified score being among the notable ones[2]. This scoring system comprises four risk factors female sex, non-smoking status, a history of PONV or motion sickness, and post-operative opioid use[2,4-6]. The incidence of PONV is associated with the presence of none, one, two, three, or all four risk factors, corresponding to rates of 10-20%, 40-60% and 80%, respectively[2]. Having two or more risk factors increases the predisposition of the patient to a higher likelihood of experiencing PONV. According to current consensus guidelines, patients with two or more risk factors are recommended to receive prophylactic administration of an antiemetic[6].

Conventional antiemetic agents encompass anticholinergics (such as scopolamine), dopamine receptor antagonists represented by phenothiazines (e.g., promethazine), benzamides (e.g., metoclopramide) and butyrophenones (e.g., droperidol), as well as benzodiazepines like midazolam and lorazepam. Non-traditional antiemetic options encompass ephedrine, propofol and corticosteroids[1]. The most recent category of antiemetics employed for the prevention and management of postoperative nausea and vomiting (PONV) belongs to the serotonin (5-HT3) receptor antagonists, which include Ondansetron, Granisetron, Tropisetron, Dolasetron, and Ramosetron[7].

Ramosetron, a potent and selective 5-hydroxytryptamine (5-HT3) receptor antagonist, is indicated for preventing and treating nausea and vomiting associated with cytotoxic chemotherapy, radiotherapy and post-operative vomiting[8]. Similarly, Ondansetron, also a serotonin 5-HT3 receptor antagonist, operates by reducing vagus nerve activity, thereby deactivating the vomiting center in the medulla oblongata. Additionally, it blocks serotonin receptors in the chemoreceptor trigger zone[9]. Despite these known mechanisms, a comparative assessment of the intravenous antiemetic efficacy of Ramosetron in preventing postoperative nausea and vomiting (PONV) in comparison to intravenous Ondansetron or placebo in gynecological surgery patients has not been documented. The current investigation was undertaken to assess and compare the preventive effects of Ondansetron and Ramosetron on postoperative nausea and vomiting in women undergoing hysterectomy.

MATERIALS AND METHODS

Following approval from the Institutional Review Board of our hospital, written informed consent was procured for the execution of a prospective, single-blinded and randomized study involving 60 healthy women aged 18-65. These participants, classified with an American Society of Anaesthesiologists (ASA) physical status of I or II, were scheduled for abdominal hysterectomy under spinal anesthesia.

Exclusion criteria encompassed a history of allergies to any study medication, gastrointestinal disease, insulin-dependent diabetes mellitus, recent administration of antiemetics or steroids within 24 hrs before surgery, active pregnancy, major cardiac or neurological disorders, a medical history of motion sickness or migraine, and compromised hepatic or renal function. Patients were randomly assigned to two groups Group A, receiving ondansetron (4 mg) (n = 30), and Group B, receiving ramosetron (0.3 mg) (n = 30), utilizing a computerized randomization table. Intravenous access was established, and pre-loading with intravenous Ringer lactate (10 mL kg^{-1} body weight) occurred immediately before induction with spinal anesthesia. Ondansetron or ramosetron was administered based on the group assignment. Spinal anesthesia was administered aseptically and antiseptically, using a 23-gauge spinal needle in the L3-L4 or L4-L5 space after local anesthesia with 2% lignocaine (2 cc) in the sitting position. Injection of 0.5% hyperbaric bupivacaine (3.2 mL) followed in the same space (L3-L4 or L4-L5). At the conclusion of the surgery, intravenous diclofenac sodium (1.5 mg kg^{-1}) was administered as an analgesic. Intraoperative vital signs were monitored every 5 min for the first 15 minutes and then every 15 min until the end of the surgery. Patients were transferred to the post-anesthesia care unit for continued observation.

During the postoperative period, vital signs were monitored every 2 hrs and episodes of vomiting, severity of nausea, complete response, need for rescue antiemetic, and adverse drug reactions were assessed at 0-6, 6-12 and 12-24 hrs. No distinction was made

between vomiting and retching for data collection. Nausea was defined as an unpleasant sensation indicative of a desire to vomit but not associated with expulsive muscular movement. Vomiting was defined as the forceful expulsion of gastric contents from the mouth. Retching was defined as an involuntary attempt to vomit that did not result in the expulsion of stomach contents. A complete response was defined as the absence of postoperative nausea and vomiting (PONV) and no requirement for rescue antiemetic medication during the study interval. Nausea and vomiting were evaluated as:

Ponv score: Zero-Complete Response, 1-Nausea, 2-Vomiting, 3-Rescue antiemetic given rescue antiemetic-inj. dexamethasone 8 mg i.v.

Nausea scale visual analog scale (VAS): Zero No nausea 10 = nausea at worst, score <5 Mild nausea, score = 5 Moderate nausea, score >5 severe nausea. Also assessed for adverse drug reaction like headache, constipation, dizziness and rashes post-operatively. Continuous data were expressed as mean and SD. The comparison of data among the two groups was performed using chi-square, Fisher exact test and two tailed unpaired t-test. Level of significance was accepted at $p<0.05$. Statistical data were analysed by using SPSS version 22 software.

RESULTS

Demographic data: Patients in both groups were demographically comparable. There was no statistically significant difference in age, weight and gender distribution between the groups (Table 1).

Type of surgery and duration: The patients in our study underwent either vaginal hysterectomy or abdominal hysterectomy The number of each surgery in both groups was comparable. Duration of surgery and duration of anesthesia were statistically significant (Table 1).

Hemodynamic parameters: Hemodynamic parameters at various time periods did not show any statistical or clinical difference in both the groups (Table 2).

Emesis and ponv score: Nausea and vomiting assessments were conducted using the PONV SCORE system, with assignments of 0 for Complete Response, 1 for Nausea, 2 for Vomiting, and 3 for the first Rescue antiemetic requirement (Inj. Dexamethasone 8 mg I.V.), observed at various time intervals. In the 0-6 hrs. time interval the incidence of nausea and vomiting was 10-0%, respectively, in the Ramosetron group, compared to 26.66-6.66% in the Ondansetron group. The PONV score was 10% in the Ramosetron group and 33.33% in the Ondansetron group, with comparable results statistically nonsignificant ($p>0.1066$) (Table 3). In the 6-12 hrs. time interval, the incidence of nausea and vomiting was lower with Ramosetron compared to Ondansetron at 6.66-3.33%, respectively, while it was 36.33-13.33%, respectively, in the Ondansetron group. The PONV score was significantly lower in the Ramosetron group (10%) compared to the Ondansetron group (46.66%) and this difference was statistically significant ($p>0.0019$). The discrepancy was primarily due to a higher incidence of nausea in patients receiving Ondansetron (33%) compared to Ramosetron (6.66%), while patients with vomiting were comparable in both groups (Table 3).

In the 12-24 hrs time interval the incidence of nausea and vomiting was 10.00-10%, respectively, in the Ramosetron group, compared to 33.33% and 16.66% in the Ondansetron group. The PONV score was 20% in the Ramosetron group and 50% in the Ondansetron group. The results were comparable in both groups, and the difference was statistically significant (p-0.0303). Although the overall PONV score and the incidence of nausea-vomiting were lower with Ramosetron, it was notably more effective during the 12-24 hrs time interval (Table 3).

These findings underscore the efficacy of both drugs in preventing postoperative emesis. The duration of the therapeutic effect appears more closely associated with the drug's binding affinity for the 5-HT3 receptors, with Ramosetron exhibiting higher receptor affinity and a longer half-life, conferring a prolonged duration of action.

Nausea severity (visual analog scale): Severity of nausea was assessed by visual analog scale (VAS).It is described and scored as 0-No nausea, score <5 Mild nausea, score = 5 Moderate nausea, score >5 Severe nausea. It was also observed at different time intervals. In 0-6 hrs. Time interval, incidence of none, mild, moderate and severe nausea were 90%,10%. 0% and 0% respectively for Ramosetron group while it was 73.3%, 16.66%, 10-0% in Ondansetron group. These findings were statistically not significant (Table 4).

In 6-12 hrs. Time interval, incidence of none, mild, moderate, severe nausea were 93.33%, 3.33%, 3.33%, 0% in Ramosetron group respectively while it was 63.33%, 30%, 6.66-0% in ondansetron group found. None of the patients in both the groups had severe nausea. The result was statistically significant for patients having none and mild nausea (p-0.0122 and 0.01533 respectively), while number of patients having moderate nausea is comparable in both groups (p value-1) (Table 4). In 12-24 hrs time interval, incidence of none, mild, moderate and severe nausea were 90%,3.33-3.33-3.33% respectively for Ramosetron group while it was 66.66%, 26.66%, 3.33-

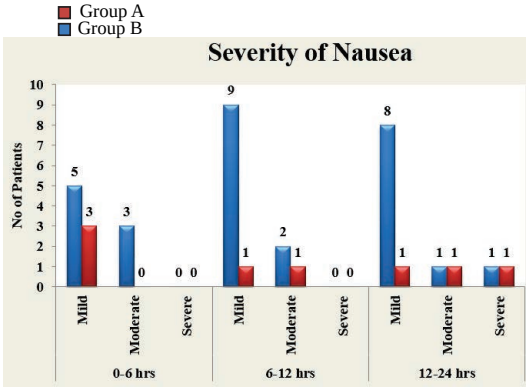

Fig. 1: Severity of Nausea among study groups

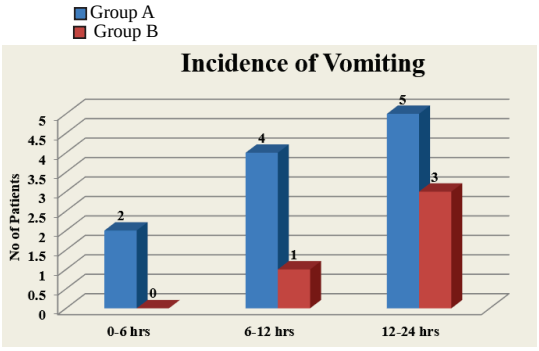

Fig. 2: Incidence of vomiting among study groups

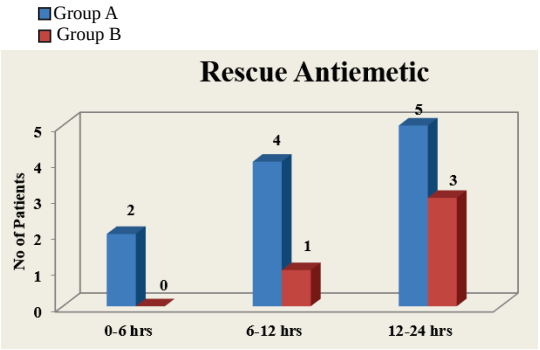

Fig. 3: Rescue Antiemetic required among study groups

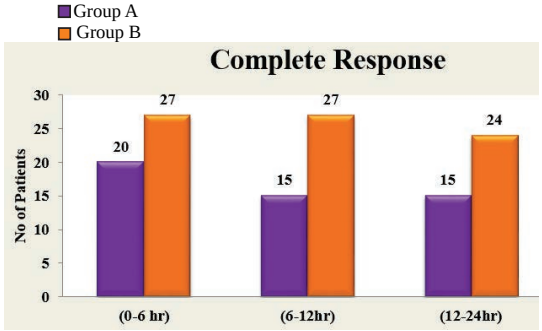

Fig. 4: Complete response among study groups

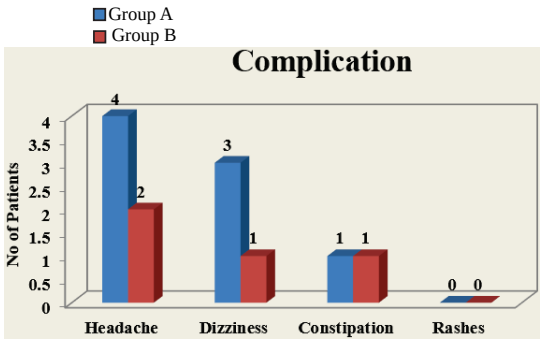

Fig. 5: Complications among study groups

3.33% in Ondansetron group (Table 4) (Fig. 1). Table 5 summarizes the incidence of vomiting and related metrics in two study groups, A and B, across three-time intervals. In the 0-6 hrs period, Group A experienced 2 cases (6.66%), while Group B had none (p = 0.4720) (Fig. 2). Rescue antiemetic use, especially in the (0-6) hrs period, showed notable differences (p = 0.4720) (Fig. 3).

Complete response rates varied, with Group B exhibiting higher percentages, notably in the (0-6 hrs) period (90% vs. 66.6% for Group A, p = 0.0599) (Fig. 4). Complications, including headache and dizziness, were observed with varying percentages in both groups, with corresponding p-values indicating statistical significance (Fig. 5).

This Table provides a concise overview of vomiting incidence and associated outcomes, offering insights into the comparative effectiveness of interventions in Groups A and B.

DISCUSSIONS

We conducted a comparative assessment of the prophylactic antiemetic efficacy between Ramosetron and ondansetron in patients undergoing hysterectomy. A singular administration of Ramosetron exhibited superior efficacy compared to ondansetron in preventing postoperative nausea and vomiting (PONV) during the 24-48 hrs post-surgery period.

This finding aligns with the study by Choi *et al.*[10] where the overall incidence of nausea was comparable between the two groups. However, the ondansetron group exhibited a significantly higher incidence of moderate to severe nausea (34%) compared to the ramosetron group (13%) during the 6 to 24 hrs following surgery. Additionally, the incidence of vomiting and the use of antiemetics during the 6-24 hours post-surgery were lower in the ramosetron group (30% vs. 11-28% vs. 11%, respectively). Our study similarly identified a higher incidence of nausea in the ondansetron group at 6-24 hrs compared to the

Table 1: Demographic Data of two groups

Parameters	Group A (ondan.)	Group B (ramose.)	p-value
Age (years)	44.2±9.95	45.43±9.26	0.6220
Weight (kg)	55.26±4.77	55.1±5.99	0.9093
Type of surgery			
Abdominal hysterectomy	16 (53.33%)	12 (40%)	0.791
Vaginal hysterectomy	14 (46.66%)	18 (60%)	
Duration of anesthesia	82.33±8.06	86.33±9.64	0.1031
Duration of surgery	62.33±7.03	65.83±9.01	0.0988

Table 2: Hemodynamic parameters comparison between two groups

Parameters	Group A (ondan.)	Group B (ramose.)	p-value
Pulse rate			
Intra-operative	92.36±8.05	93.8±7.65	0.481
0-6 hrs	95.5±9.12	95.36±9.05	0.952
6-12 hrs	93.3±5.29	92.23±9.57	0.594
12-24 hrs	91.16±7.01	92.96±10.03	0.423
Systolic blood pressure			
Intra-operative	119.33±9.82	120.6±10.46	0.629
0-6 hrs	122.93±7.03	123.46±4.89	0.310
6-12 hrs	119.93±5.03	119.2±4.94	0.572
12-24 hrs	121.73±4.29	119.53±4.80	0.066
Diastolic blood pressure			
Intra-operative	75.40±5.37	74.6±7.53	0.637
0-6 hrs	81.33±4.21	82.73±4.40	0.213
6-12 hrs	81.26±3.69	81.53±5.27	0.819
12-24 hrs	80.6±5.12	81.66±5.33	0.435

Table 3: PONV score of two groups

	Group A (n = 30)	Group B (n = 30)	p-value
0-6 hrs			
Nausea	08 (26.66%)	3 (10.00%	0.1821
Vomiting	02 (06.66%)	0 (0)	0.4720
PONV	10 (33.33%)	3 (10.00%)	0.0602
6-12 hrs			
Nausea	11 (36.66%)	2 (06.66%)	0.0122
Vomiting	04 (13.33%)	1 (03.33%)	0.351
PONV	15 (50%)	3 (10.00%)	0.0019
12-24 hrs			
Nausea	10 (33.33%)	3 (10.00%)	0.0599
Vomiting	05 (16.66%)	3 (10.00%)	0.7083
PONV	15 (50%)	6 (20.00%)	0.0303

Table 4: Distribution of severity of nausea

	Group A (n = 30)	Group B (n = 30)	p-value
0-6 hrs		22 (73.33%)	27(90.00%)
None	0.1821		
Mild	05 (16.66%)	03 (10.00%)	0.7083
Moderate	03 (10.00%)	0 .00	0.2367
Severe	0.00	0.00	
6-12 hrs			
None	19 (63.33%)	28 (93.33%)	0.0122
Mild	09 (30.00%)	01 (03.33%)	0.1533
Moderate	02 (06.66%)	01 (03.33%)	1.0000
Severe	0.00	0.00	
12-24 hrs			
None	20 (66.66%)	27 (90.00%)	0.0599
Mild	08 (26.66%)	01 (03.3	

Table 5: Incidence of Vomiting and related measurements of study groups

Parameters	Group A	Group B	p-value
Incidence of vomiting			
0-6 hrs	02 (6.66%)	0	0.4720
6-12 hrs	04 (13.33%)	01 (3.33%)	0.3520
12-24 hrs	05 (16.66%)	03 (10%)	0.7083
Rescue antiemetic			
(0-6) hrs	2(06.66%)	0 (0.00%)	0.4720
(6-12) hrs	4(13.33%)	1 (3.33%)	0.3502
(12-24) hrs	5(16.66%)	3 (10%)	0.7083
Complete response			
(0-6 hr)	20 (66.6%)	27 (90%)	0.0599
(6-12hr)	15 (50%)	27 (90%)	0.0019
(12-24hr)	15 (50%)	24 (80%)	0.0303
Complications			
Headache	4 (13.3%)	2 (6.66%)	0.6670
Dizziness	3 (10%)	1 (3.33%)	0.6048
Constipation	1 (3.33%)	1 (3.33%)	0.4720
Rashes	0	0	0

ramosetron group. Numerous investigations have consistently reported the superior or comparable efficacy of ramosetron in preventing postoperative nausea and vomiting (PONV) in comparison to other 5-HT3 receptor antagonists. Ramosetron exhibited heightened effectiveness in averting nausea and vomiting compared to ondansetron across diverse clinical scenarios, encompassing spinal surgery[10], chemotherapy[11] and total knee replacement surgery [12].

According to Fujii *et al*.[13-14] ramosetron demonstrates effectiveness in preventing PONV following major gynecological surgery, with a defined effective dose of 0.3 mg. Furthermore, the manufacturer's recommended dose is 0.3 mg administered intravenously once daily. Consequently, the present study adopted the 0.3 mg dose of ramosetron. Our findings conclusively demonstrated the efficacy of ramosetron 0.3 mg in significantly reducing the incidence of PONV by 30% during the 24-hrs postoperative period, from an initial 80-90%. Notably, this efficacy was comparable to that of ondansetron in PONV prevention.

In a conducted study involving highly susceptible patients undergoing abdominal hysterectomy[15], ramosetron at a dose of 0.3 mg exhibited superior efficacy in preventing delayed postoperative nausea and vomiting (PONV). This enhanced effectiveness can be rationalized by considering the extended elimination half-life of ramosetron, lasting 9 hrs, in contrast to the shorter half-life of ondansetron (3.5 hrs). Ramosetron, characterized by a higher affinity and slower dissociation rate for 5-HT3 receptors compared to other 5-HT3 receptor antagonists[16], demonstrates increased potency and prolonged duration of action[17,28]. This attribute may potentially reduce the necessity for an additional rescue antiemetic within the initial 24 hrs post-operation[19]. However, in the present investigation, the comparative effectiveness of ramosetron (0.3 mg) and ondansetron (4 mg) in preventing PONV and the requirement for a rescue antiemetic were found to be similar during both the early (0-6 hrs) and late (6-24 hrs) postoperative periods. Notably, the severity of nausea differed significantly, with ramosetron showing less severe nausea compared to ondansetron during the 6-24 hrs time frame. Although the demand for a rescue antiemetic was lower in the ramosetron group over the 24-hrs period, this difference did not reach statistical significance. Fewer patients in the ondansetron group experienced nausea in the 6-24 hrs period compared to the ramosetron group. However, a statistically significant difference in the severity of nausea between the two groups was observed only during the 6-12 hrs and 12-24 hrs periods.

While the efficacy of ramosetron demonstrated similarity to ondansetron in reducing the incidence of postoperative nausea and vomiting (PONV), ramosetron exhibited a potential superiority over ondansetron in diminishing the requirement for additional rescue antiemetic within the initial 24 hrs after the operation and in mitigating the severity of nausea, although these distinctions did not attain statistical significance. Ramosetron significantly decreased the necessity for additional rescue antiemetic administration throughout the 24-hrs postoperative period, specifically during the 0-6 hrs and 6-24 hrs intervals. Ondansetron also significantly lowered the need for additional rescue antiemetic within the first 6 hrs after the operation, however, it failed to achieve a statistically significant reduction in rescue antiemetic requirement during the 6-24 hrs postoperative period, consequently not significantly impacting the overall 24-hrs postoperative duration. These results suggest that ramosetron may possess a more potent and enduring antiemetic effect compared to ondansetron, despite the absence of statistical significance in the treatment effect difference. Consequently, we posit that ramosetron is a more favorable antiemetic option than ondansetron for preventing PONV.

The most commonly reported adverse events associated with 5-HT3 receptor antagonists included headache, and dizziness. These findings align with a study conducted by Cho *et al*.[20] which reported similar side effects.

CONCLUSION

The study demonstrated that Ramosetron is more effective than Ondansetron in preventing and reducing the severity of nausea. Both drugs significantly reduced postoperative emesis, with Ramosetron showing high efficacy, especially in the initial 24 hrs. Ramosetron also yielded a significantly higher complete response rate during the first 24 hrs compared to Ondansetron. Importantly, both medications were deemed safe, with no clinically significant adverse effects observed. Furthermore, all patients maintained hemodynamic stability, highlighting the overall efficacy, safety and stability of both Ramosetron and Ondansetron in postoperative care.

REFERENCES

1. Khanna, S., M.M. Abdul, U. Fatima, H. Garlapati, M. Qayyum and S. Gulia, 2022. Role of general anesthetic agents in postoperative nausea and vomiting: A review of literature. Nat. J. Maxillofacial Surg., 13: 190-190.
2. Apfel, C.C., E. Läärä, M. Koivuranta, C.A. Greim and N. Roewer, 1999. A simplified risk score for predicting postoperative nausea and vomiting. Anesthesiology., 91: 693-693.

3. Gan, T.J., 2006. Risk factors for postoperative nausea and vomiting. Anesth. Analg., 102: 1884-1898.
4. Apfel, C.C., P. Kranke, L.H.J. Eberhart, A. Roos and N. Roewer, 2002. Comparison of predictive models for postoperative nausea and vomiting. Elsevier BV, Br. J. Anaesth., 88: 234-240.
5. Pierre, S., H. Benais and J. Pouymayou, 2002. La cotation d'apfel simplifiée peut prédire favorablement le risque de nausées et de vomissements postopératoires. Can. J. Anesthesia/J. canadien d'anesthésie, 49: 237-242.
6. Gan, T.J., P. Diemunsch, A.S. Habib, A. Kovac and P. Kranke et al., 2014. Consensus guidelines for the management of postoperative nausea and vomiting. Anesth. Analg., 118: 85-113.
7. Gan, T.J., T. Meyer, C.C. Apfel, F. Chung and P.J. Davis *et al*., 2003. Consensus guidelines for managing postoperative nausea and vomiting. Anesth. Analg., 97: 62-71.
8. Rabasseda, X., 2002. Ramosetron, a 5-HT3 receptor antagonist for the control of nausea and vomiting. Drugs. Today .(Barc)., 38: 75-89.
9. Frost, F., F. Dailler and F. Duflo, 2010. Méta-analyse : Ondansétron en prophylaxie des nausées et vomissements postopératoires chez l'adulte et l'enfant après craniotomie. Ann. Françaises d'Anesthésie Réanimation, 29: 19-24.
10. Choi, Y.S., J.K. Shim, D.H. Yoon, D.H. Jeon, J.Y. Lee and Y.L. Kwak, 2008. Effect of ramosetron on patient-controlled analgesia related nausea and vomiting after spine surgery in highly susceptible patients. Spine, 33:
11. Shi, Y., X. He, S. Yang, B. Ai and C. Zhang *et al*., 2007. Ramosetron versus ondansetron in the prevention of chemotherapy-induced gastrointestinal side effects: A prospective randomized controlled study. Chemotherapy, 53: 44-50.
12. Hahm, T.S., J.S. Ko, S.J. Choi and M.S. Gwak, 2010. Comparison of the prophylactic anti-emetic efficacy of ramosetron and ondansetron in patients at high-risk for postoperative nausea and vomiting after total knee replacement. Anaesthesia, 65: 500-504.
13. Fujii, Y., Y. Saitoh, H. Tanaka and H. Toyooka, 2000. Ramosetron for preventing postoperative nausea and vomiting in women undergoing gynecological surgery. Anesthe. Analg., 90: 472-475.
14. Fujii, Y. and H. Tanaka, 2002. Retracted: Double-blind, placebo-controlled, dose-ranging study of ramosetron for the prevention of nausea and vomiting after thyroidectomy. Clin. Ther., 24: 1148-1153.
15. Lee, J.W., H.J. Park, J. Choi, S.J. Park, H. Kang and E.G. Kim, 2011. Comparison of ramosetron's and ondansetron's preventive anti-emetic effects in highly susceptible patients undergoing abdominal hysterectomy. Korean J. Anesthesiol., 61: 488-492.
16. Hirata, T., Y. Keto, T. Funatsu, S. Akuzawa and M. Sasamata, 2007. Evaluation of the pharmacological profile of ramosetron, a novel therapeutic agent for irritable bowel syndrome. J. Pharmacol. Sci., 104: 263-273.
17. Kim, W.O., B.N. Koo, Y.K. Kim and H.K. Kil, 2011. Ramosetron for the prevention of postoperative nausea and vomiting (PONV): A meta-analysis. Korean J. Anesthesiol., 61: 405-412.
18. Kim, S.I., S.C. Kim, Y.H. Baek, S.Y. Ok and S.H. Kim, 2009. Comparison of ramosetron with ondansetron for prevention of postoperative nausea and vomiting in patients undergoing gynaecological surgery. Br. J. Anaesth., 103: 549-553.
19. Cho, J.S., S.W. Kim, S. Lee and Y.C. Yoo, 2019. Dose-ranging study of ramosetron for the prevention of nausea and vomiting after laparoscopic gynecological surgery: A prospective randomized study. J. Clin. Med., Vol. 8. 10.3390/jcm8122188