

Effect of Oral Betahistine in Reducing Postoperative Nausea and Vomiting Following Hysteroscopic Surgery under General Anesthesia

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Abstract

Background: Postoperative nausea and vomiting (PONV) is a common and distressing complication after gynecological surgeries, particularly hysteroscopy. This study aimed to determine the effect of oral betahistine on reducing the incidence and severity of PONV after hysteroscopic surgery under general anesthesia.

Methods: This double-blind, randomized clinical trial was conducted on 94 candidates for hysteroscopic surgery at Imam Sari Educational Medical Center in 2024. Patients were randomly assigned to two equal groups (n = 47 each). The intervention group received oral betahistine (16 mg three hours and 8 mg two hours before surgery), and the control group received placebo. The incidence and severity of PONV, pain intensity, morphine and ondansetron consumption, and adverse effects were evaluated at 2, 4, 6, 12, 24, and 48 hours postoperatively.

Results: The incidence of PONV was significantly lower in the betahistine group than in the placebo group at all time points (32% vs. 68% over the entire period, $p < 0.001$). The mean nausea severity was also significantly lower in the betahistine group (2.3 ± 1.4 vs. 4.8 ± 2.1 , $p < 0.001$). Morphine and ondansetron consumption during the 48-hour postoperative period were significantly lower in the betahistine group ($p < 0.001$). No significant difference in adverse effects was observed between the two groups. Older age, higher BMI, and longer anesthesia duration were identified as independent risk factors for PONV.

Conclusions: Prophylactic oral betahistine administration before hysteroscopic surgery under general anesthesia appears to be an effective, safe, and cost-effective strategy to reduce the incidence and severity of PONV, decrease the need for rescue antiemetics, and improve the quality of postoperative recovery.

Keywords: Betahistine; Postoperative Nausea and Vomiting; Hysteroscopy; General Anesthesia; Randomized Clinical Trial

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Introduction

Hysteroscopy is a minimally invasive endoscopic procedure that allows direct visualization and treatment of the uterine cavity through the cervical canal [1]. This method covers both diagnostic and therapeutic purposes and is particularly used in the treatment of various intrauterine pathologies such as polyps, fibroids, and intrauterine adhesions [2]. Hysteroscopy is often performed with a “see and treat” approach in a single session [3]. The most common diagnostic indication for this procedure is

the evaluation of abnormal uterine bleeding, which accounts for 40% to 45% of cases [4]. Furthermore, infertility and recurrent miscarriage are other important diagnostic indications for hysteroscopy [5]. In therapeutic applications, the removal of endometrial polyps (39.5%) and submucosal myomas (12.45%) has the highest frequency [4]. Hysteroscopy is also effective in treating Asherman syndrome (intrauterine adhesions) and removing retained intrauterine devices [2]. Hysteroscopy is recognized as the most accurate diagnostic method for uterine abnormalities in infertile women [6]. This procedure

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can be performed in two settings: outpatient (without general anesthesia) and hospital-based (with general anesthesia) [7]. General anesthesia in abdominal hysterectomy surgeries is recognized as a common and effective method for providing complete analgesia and muscle relaxation [8]. Although this method is preferred because of the ability to maintain full control over the surgical process, it is associated with complications such as longer recovery time and an increased likelihood of postoperative nausea and vomiting (PONV) [9].

PONV is one of the common and important problems in perioperative care, with an incidence rate varying between 20% and 70% in hysterectomy surgery, for example [10,11]. Studies have shown that a history of PONV or motion sickness, longer duration of anesthesia, and the use of opioids are among the most important risk factors for PONV in hysteroscopy [12]. In addition, the patient's age also affects the likelihood of PONV, especially in older patients, who have been shown in some studies to be at higher risk [13]. Factors related to the type of surgery, such as open hysterectomy surgery, are also among the important factors that increase the risk of PONV [14]. Preventive strategies, including the use of antiemetic drugs such as ondansetron and dexamethasone, which play an effective role in reducing the incidence of PONV, and the use of combination therapies such as aprepitant alongside these drugs, have been shown to reduce the incidence of this complication, although further research in this area is needed [15,16]. Preventive measures such as the use of regional anesthesia also help reduce this complication, but individual factors such as anxiety, fasting time, and muscle oxygen saturation levels during surgery indicate the complexity and multifactorial nature of predicting and managing PONV [12,17]. Despite the high safety and efficacy of hysteroscopy, paying attention to indications, selecting the appropriate anesthesia method, and managing PONV risk factors are essential for improving clinical outcomes. Consequently, a comprehensive understanding of these factors and the development of personalized strategies can help improve prevention processes and reduce complications following hysteroscopy. Given the impact of various factors on the occurrence of PONV, appropriate and individualized planning in postoperative care is necessary to minimize the negative effects of this complication and increase patient satisfaction.

The Role of Oral Betahistine in Reducing PONV

On the other hand, in recent decades, betahistine has gained attention as one of the common treatments for managing vestibular disorders, particularly

Meniere disease; however, its exact mechanism of action is not yet fully understood [18]. According to studies, betahistine acts as a partial H1 receptor agonist and a potent H3 receptor antagonist, leading to increased histamine release and, consequently, vasodilation in the internal structures of the ear, which may regulate intralabyrinthine pressure and reduce the symptoms of hydrops [19]. Despite the widespread prescription of betahistine, scientific evidence regarding its efficacy in reducing vertigo attacks and improving symptoms is conflicting, and some studies indicate that this drug does not differ significantly from placebo [20]. Meanwhile, recent research shows that betahistine, which is primarily used to treat vestibular disorders, may be effective in reducing PONV, especially in combination with other antiemetics such as ondansetron [21]. Furthermore, the results of recent studies show that betahistine has reduced the incidence and severity of PONV in gynecological laparoscopic surgeries, such as hysterectomy, although further research is needed in this area to determine its exact role in standard protocols [22]. Although this drug is generally safe, with mild side effects such as stomach upset and skin allergies, serious complications have been reported in rare cases [23]. Therefore, a comprehensive and efficient investigation of the effectiveness of betahistine in managing PONV in gynecological surgeries, as an emerging research area, is of particular importance and may help improve clinical outcomes and the quality of postoperative care.

Importance of Investigating the Effect of Oral Betahistine in Reducing PONV in Hysteroscopy

In general, PONV management protocols are considered one of the important challenges in nursing and medical care, as this complication significantly affects patient satisfaction, length of hospital stay, and postoperative adverse effects [24]. Furthermore, although numerous drugs have been studied for controlling PONV in gynecological surgeries, effective alternatives such as betahistine still need to be directly evaluated in this field so that they can be considered suitable alternatives in antiemetic protocols [16]. In this regard, considering the prevalence of PONV in gynecological surgeries such as hysteroscopy and the importance of improving the quality of care, this study aimed to evaluate the role of betahistine in improving postoperative outcomes to ultimately provide new and more efficient strategies for reducing PONV.

Chapter 2: Literature Review

Studies conducted in this field include the following:

Iranian Studies

A study was conducted in 2025 by Soleimani et al. on the “Efficacy of Betahistine in Reducing Postoperative Nausea and Vomiting Following Laparoscopic Cholecystectomy.” The main objective of that study was to evaluate the effect of oral betahistine consumption on reducing the incidence and severity of PONV in patients undergoing laparoscopic cholecystectomy. To achieve this goal, a randomized, double-blind, placebo-controlled clinical trial was conducted in which 132 patients were randomly divided into two groups. The first group received 16 mg of betahistine three hours prior to surgery, while the second group received a placebo. The severity and incidence of PONV were evaluated using the Numerical Rating Scale (NRS), and the side effects of the drug were also investigated as a secondary outcome. The results demonstrated that in the betahistine group, the rate of absence of PONV and the lack of need for rescue antiemetic drugs were significantly higher, and the severity of nausea in this group was significantly lower compared to the placebo group. Additionally, the need for rescue antiemetic drugs was significantly higher in the placebo group. Contrary to expectations, no significant difference was observed in the incidence of side effects between the two groups. Consequently, the findings of that study indicate that preoperative oral consumption of betahistine can effectively reduce the incidence and severity of PONV and decrease the need for rescue medications without causing significant adverse effects; therefore, the use of betahistine can help improve the management of PONV in patients undergoing laparoscopic surgery [22].

Another study was conducted in 2012 by Norozi et al. titled “Evaluation of the Effect of Gabapentin on Controlling PONV in Laparoscopic Cholecystectomy.” The objective of that study was to evaluate the efficacy of different doses of gabapentin (300 mg and 600 mg) in controlling PONV. In that clinical trial, 105 patients were randomly divided into three equal groups, including a placebo group, a group receiving 300 mg of gabapentin, and a group receiving 600 mg of gabapentin, and all patients underwent the same anesthesia method. During the postoperative period, the severity of nausea and the incidence of vomiting were measured and recorded every 2 to 6 hours and subsequently every 4 to 18 hours. The results showed that the mean severity of nausea was 2.8 in the control group, decreased to 0.67 in the group receiving 300 mg of gabapentin, and reached 0.55 in the group receiving 600 mg, differences that were statistically significant. Furthermore, the severity of vomiting was 0.326 in the control group, 0.126 in the 300 mg group, and 0.053 in the

600 mg group, which also represented statistically significant differences. Based on the findings of that study, administering a 300 mg dose of gabapentin can be effective in reducing PONV, and increasing the dose to 600 mg demonstrates greater efficacy in controlling these complications. As a result, the use of gabapentin in laparoscopic cholecystectomy surgeries is recommended as an effective strategy, as it can help improve the quality of postoperative care and reduce associated complications [25].

International Studies

A study was conducted in 2024 by Abdel-Wahab et al. titled “Effect of Different Doses of Oral Olanzapine to Prevent PONV after Laparoscopic Surgery in High-Risk Patients: A Randomized Controlled Trial.” The main objective of that study was to investigate and compare the efficacy of 5 mg and 10 mg doses of oral olanzapine in preventing PONV in patients undergoing gynecological laparoscopic surgery. For this purpose, 135 female patients aged 18 to 50 years who were undergoing gynecological surgeries were randomly assigned to three groups: two groups receiving olanzapine at doses of 5 mg and 10 mg and one control group. During the postoperative period, the incidence and severity of PONV during the first 24 hours after surgery were recorded, and the number of patients requiring antiemetic drugs was evaluated. The results indicated that the incidence of nausea in the control group was higher than that in the two groups receiving olanzapine. In the 10 mg group, only three patients experienced nausea, and no cases of vomiting were observed. In the 5 mg group, 13 patients developed nausea, and three required antiemetic drugs. In the control group, 23 patients experienced nausea, and eight required antiemetic drugs. Additionally, nausea severity was lowest in the 10 mg group. Based on the findings, the 10 mg dose of olanzapine was more effective in reducing the incidence and severity of PONV than the lower dose and placebo, indicating the high efficacy of this drug in managing postoperative complications. In conclusion, administering 10 mg of olanzapine can be an effective and safe strategy for preventing PONV after gynecological laparoscopic surgeries, which may be beneficial in improving postoperative care and reducing the need for antiemetic drugs [26].

A study was conducted in 2016 by Cho et al. titled “Betahistine Reduces PONV after Gynecological Laparoscopic Surgery.” This study aimed to compare the efficacy of ondansetron alone with that of ondansetron combined with betahistine in patients undergoing gynecological laparoscopic surgery. In this randomized, double-blind, placebo-controlled study, 168 patients were randomly assigned to two

groups receiving either the drug or placebo. The first group (O) received placebo only, and the second group (OB) received 18 mg of oral betahistine before and after surgery. In both groups, 4 mg of ondansetron was administered at the end of surgery, followed by 8 mg postoperatively. The main objective of the study was to evaluate the complete response rate, defined as the absence of PONV and no need for rescue medication, within 48 hours postoperatively. The results showed a significant difference, with the OB group having a 69% complete response rate compared to 46% in the O group. Furthermore, nausea severity in the OB group was lower at various postoperative time intervals. The incidence of dizziness in the OB group was significantly lower than that in the O group. The results demonstrated that the combination of ondansetron and betahistine was more effective than ondansetron alone in reducing PONV and side effects such as dizziness in high-risk patients following gynecological laparoscopic surgeries and may improve the quality of postoperative care [21].

A study was conducted in 2015 by Bhalla et al. titled "Comparison of Palonosetron with Ondansetron for Postoperative Nausea and Vomiting in Patients Undergoing Laparoscopic Cholecystectomy under General Anesthesia." The aim of that study was to compare the efficacy and safety of two antiemetic drugs, namely ondansetron and palonosetron, in preventing PONV following laparoscopic gallbladder surgery in patients under general anesthesia. In that randomized study, two groups, each consisting of 50 patients, were observed and received the aforementioned drugs intravenously before anesthesia. Evaluations included the incidence of nausea, vomiting, need for rescue medications, and side effects within 24 hours after the completion of surgery. The results showed that the incidence of nausea, the need for rescue medications, and the overall occurrence of PONV were significantly lower in the palonosetron group than in the ondansetron group; however, the prevalence of headache was higher in the former group compared to the latter. Based on the study findings, palonosetron demonstrated a stronger antiemetic effect, less need for rescue treatments, a better side-effect profile, and a significant reduction in the overall PONV rate during the 24-hour postoperative period compared to ondansetron. Therefore, the conclusion indicates the superiority of palonosetron as an effective and safe prophylaxis in reducing PONV following laparoscopic gallbladder surgery [27].

A study was conducted in 2013 by Mukhopadhyay et al. titled "Betahistine as an Add-on: The Magic Bullet for Postoperative Nausea, Vomiting and Dizziness after Middle Ear Surgery?" That study was designed to evaluate the efficacy of adding

betahistine to standard therapy with 5-HT₃ antagonists like ondansetron in controlling PONV and reducing dizziness and vertigo in patients undergoing middle ear surgery. In that prospective, randomized, double-blind, placebo-controlled study, 100 patients undergoing local anesthesia were equally divided into two groups; the first group received a combination of 16 mg of betahistine and 8 mg of ondansetron, and the second group received a placebo along with ondansetron, both of which were administered orally 3 hours before the start of surgery. The results indicated that in the group receiving betahistine, the complete response rate regarding nausea, vomiting, and dizziness was significantly higher, with 90% of patients in this group showing a complete response, whereas this rate was 66% in the control group. Moreover, the vomiting rate during both intraoperative and postoperative periods was significantly lower in the betahistine group compared to the control group, and dizziness in this group was observed in only 10% of patients, whereas this figure reached 32% in the control group. Based on the statistical analyses performed, the results indicate the significant efficacy of adding betahistine in reducing the incidence of nausea, vomiting, and dizziness after middle ear surgery. The study concludes that the use of betahistine as an adjunct to antiemetic and anti-vertigo treatment in middle ear surgery patients can significantly reduce postoperative complications and provide improved quality of nursing and surgical care [28].

A study was conducted in 2011 by Altorjay et al. titled "Casopitant and Ondansetron for Postoperative Nausea and Vomiting Prevention in Women at High Risk for Emesis: A Phase 3 Study." That study was a multicenter, randomized, double-blind, parallel-group phase 3 analysis aimed at evaluating the safety and efficacy of the combination of casopitant mesylate with ondansetron in preventing surgical PONV in female patients at high risk for developing PONV. In that study, 484 women across various countries were enrolled and randomly assigned to two groups receiving different medications; the first group received a placebo along with ondansetron, and the second group received the combination of casopitant and ondansetron. The results showed that in the group receiving the drug combination, the complete response rate (no vomiting or need for rescue medication) in the first 24 hours after surgery was significantly higher than in the group receiving only ondansetron. In the 24-to-48-hour period, no significant difference in complete response was observed. Based on the results, the combination of casopitant and ondansetron was more effective and safe compared to ondansetron alone in preventing PONV in high-risk patients, and these findings

demonstrate the potential of this pharmacological combination to improve the management of surgical PONV [29].

A study was conducted in 2011 by Basu et al. titled "Comparison of Palonosetron, Granisetron and Ondansetron as Antiemetics for Prevention of Postoperative Nausea and Vomiting in Patients Undergoing Middle Ear Surgery." The objective of that study was to evaluate and compare the efficacy of palonosetron, granisetron, and ondansetron as anti-PONV drugs in patients undergoing middle ear surgery. In that study, 75 adult patients in the age range of 30 to 45 years, comprising 50 men and 25 women, were randomly divided into three equal groups. Each group received a specific dose of the studied drugs at the end of the surgery; such that the first group received palonosetron, the second group granisetron, and the third group ondansetron. During the 0–6-hour and 6–24-hour postoperative periods, the occurrence of vomiting and the safety status of the patients were evaluated. The results revealed that in the 0–6-hour period, the percentage of patients without vomiting was 100% in the palonosetron group, 72% in the granisetron group, and 56% in the ondansetron group. In the 6–24-hour period, this rate was reported as 96%, 56%, and 32%, respectively. Based on these findings, it can be concluded that palonosetron, compared to the other drugs, has a higher efficacy in the complete prevention of PONV in middle ear surgery over a 24-hour period, and therefore, the use of a single dose of palonosetron in these cases is considered an effective option [30].

Reviewing previous studies on the effect of various drugs on surgical PONV control reveals that although numerous studies have demonstrated the efficacy of drugs such as ondansetron, gabapentin, olanzapine, and palonosetron in reducing the incidence and severity of PONV in various surgeries including laparoscopy, middle ear, and gynecological procedures, specific data investigating the effect of oral betahistine in preventing PONV following hysteroscopy under general anesthesia is limited. Most conducted research has been carried out in large centers and on other types of surgeries, with less attention paid to the conditions of patients hospitalized in regional hospitals such as Imam Hospital of Sari. This has led to a lack of local and specialized evidence for clinical decision-making in the management of PONV following this type of surgery. On the other hand, hysteroscopy, as one of the highly utilized surgeries in gynecology, requires meticulous studies to identify effective and safe drugs for PONV prophylaxis, as this complication is one of the contributing factors to decreased patient satisfaction, prolonged hospital stay, and delayed discharge. Accordingly, conducting the present study with the aim of investigating the

effect of oral betahistine in reducing PONV following hysteroscopy becomes doubly necessary. This study, while filling the existing gaps in current knowledge, can take an effective step in improving the quality of postoperative care, enhancing patient satisfaction, and reducing complications arising from the frequent use of antiemetic drugs by providing local scientific evidence.

Chapter 3: Materials and Methods

Study Design and Population

This research is an interventional, randomized, double-blind clinical trial study conducted at Mazandaran University of Medical Sciences in 2024. The research protocol was approved by the Ethics Committee of Mazandaran University of Medical Sciences with the code (IR.MAZUMS.IMAMHOSPITAL.REC.1402.20053). The study population consisted of patients who were candidates for elective hysteroscopic surgery referring to the Imam Educational and Medical Center in Sari.

Inclusion Criteria

- Female patients who are candidates for elective hysteroscopic surgery (based on specific therapeutic indications).
- Age between 18 and 60 years.
- Written informed consent to participate in the research.
- No sensitivity or history of allergy to betahistine.
- Absence of underlying gastrointestinal, cardiovascular, and respiratory diseases.

Exclusion Criteria

- Uncontrolled diabetes or impaired glucose tolerance.
- Underlying gastrointestinal disease.
- History of PONV and the use of anti-PONV medications within 24 hours prior to surgery.
- Middle ear disease.
- Pregnancy.
- Obesity with a BMI greater than 35.
- Hypertension.

Sample Size Determination

The sample size was estimated based on the study by Mukhopadhyay [28] to be 94 individuals, with 47 in the intervention group (A) and 47 in the control group (B). The sampling method was a two-stage process. In the first stage, available samples meeting the inclusion criteria were selected through

convenience sampling. Subsequently, they were divided into the intervention and control groups using a block randomization method with a block size of 4. The blocks were formed based on the order of entry. Random allocation using the block method was performed using the “Random Allocation” software.

Data Collection

In this interventional, double-blind, randomized clinical trial, the sample collection process was conducted systematically and meticulously. Eligible individuals, including patients hospitalized at Imam Hospital in Sari who were scheduled for hysteroscopic surgery, were randomly assigned to the intervention group (16 mg betahistine tablets manufactured by Actoverco Company) or the control group (placebos produced by the Sari School of Pharmacy, composed of starch and identical in size and shape to the betahistine tablets) after evaluating the inclusion and exclusion criteria and obtaining informed consent. Baseline data, including age, gender, BMI, and educational level, were extracted using a demographic characteristics checklist and patient records. Weight and height were measured using a standard scale and stadiometer before surgery and were used to calculate BMI (weight in kilograms divided by the square of height in meters).

Patients were then randomly assigned to the intervention and control groups in a double-blind manner. The intervention group received oral betahistine at a dose of 16 mg 3 hours before surgery and 8 mg 2 hours before surgery, while the control group received a placebo with an identical appearance and packaging. The randomization and allocation process was performed by an individual other than the data collectors, and the drug codes remained concealed until the end of the statistical analysis. During surgery, data on background variables, including the duration of anesthesia (from induction to full awakening in the recovery room), duration of surgery (from incision to the final suture), and amounts of anesthetic drugs administered, such as fentanyl and propofol, were recorded by the anesthesiologist on the anesthesia record form. Postoperatively, the doses of antiemetic drugs administered, including ondansetron, and the amount of morphine required during the first 48 hours were extracted from each patient's medication record.

Clinical outcomes, including the incidence of PONV, severity of nausea, pain intensity, and occurrence of adverse effects (dry mouth, itching, headache, and skin rash), were evaluated by trained nurses at 2, 4, 6, 12, 24, and 48 hours after surgery. The severity of nausea and pain was recorded using the Numerical Rating Scale (NRS), ranging from 0 to 10, with a score of 0 indicating no sensation and

a score of 10 indicating maximum intensity. The occurrence of nausea, vomiting, and other side effects (dry mouth, itching, headache, and skin rash) was recorded as a binary outcome (yes/no) on the clinical observation checklist. The nurses responsible for data collection were unaware of the type of medication received by each patient to prevent information bias. The double-blind nature of the study ensured that neither the patients nor the evaluators had any information about the patients' treatment groups, thereby controlling for bias in recording the results. This improved the study's internal validity and the generalizability of the results to the target population.

For data management and entry, all information was transferred from the checklist forms to SPSS software version 25. Quantitative variables, such as age, weight, BMI, duration of anesthesia, duration of surgery, amount of medications consumed, and NRS scores, were entered numerically, and qualitative variables, including gender, treatment group, and adverse effects, were recorded as binary codes (e.g., 0 = no and 1 = yes). To ensure the accuracy of data entry, the data were double-checked by the researcher, and in the event of any discrepancies, the patient's original record was consulted and the data were corrected. Overall, the data for this study were collected in a coherent structure from the preoperative phase to 48 hours after surgery, and all measurements were performed by a trained team using standard tools to ensure scientific accuracy and the reliability of the results.

Implementation Method

This study was conducted after obtaining approval from the Ethics Committee of Imam Sari Faculty of Medical Sciences and receiving an ethics code. Before entering the study, all patients provided written informed consent after receiving comprehensive explanations regarding the objectives, methods, potential side effects, and their rights as research participants. Full compliance with ethical principles and the confidentiality of patient information was ensured throughout all stages of the study. Patients were assured that their information would remain confidential and that each participant could withdraw from the study at any stage without any consequences.

Patients were randomized using a block randomization method and assigned to the treatment and control groups in a double-blind manner. Randomization was based on a list generated by software, and the study medication was prepared in advance by the ward nurse according to the random sequence for each patient. After preparation, the designated medication was provided to the ward nurse in sealed envelopes with specific codes to

be administered to the patient. According to the protocol, patients in the first group (A) received one 16 mg betahistine tablet (manufactured by Actoverco Company) orally 3 hours before surgery, and patients in the second group (B) received a placebo tablet (manufactured by the Sari School of Pharmacy, composed of starch and identical in dimensions, color, and shape to the betahistine tablet) orally 3 hours before surgery. Blinding was designed so that none of the patients, surgeons, anesthesiologists, or evaluators were aware of the type of medication administered.

Before surgery, patients adhered to fasting guidelines of 8 hours for solid foods and 2 hours for clear liquids. The general anesthesia procedure for all patients was performed using standard and uniform doses, including midazolam at 0.05 mg/kg, fentanyl at 2 mcg/kg, sodium thiopental at 3-5 mg/kg for the induction of anesthesia, and atracurium at 0.5 mg/kg to facilitate tracheal intubation. Anesthesia was maintained with isoflurane in oxygen, and 50 mcg of intravenous fentanyl was administered regularly every hour during surgery. At the end of surgery, patients received 50 mcg of intravenous fentanyl, and during the first 24 hours postoperatively, intravenous ketorolac was prescribed at a dose of 30 mg every 8 hours for pain control.

During the study, pain intensity, the incidence and severity of PONV, the amounts of ondansetron and narcotic medications consumed, and the occurrence of potential adverse effects, including dry mouth, headache, itching, and skin rash, were evaluated in both groups after the patients were fully conscious in the recovery room and subsequently during their stay in the women's ward. These outcomes were assessed at 2, 4, 6, 12, 24, and 48 hours after surgery by trained nurses who were blinded to the type of intervention and were recorded on standard checklists. The incidence and severity of PONV and pain intensity during the first 24 hours after surgery were measured using the NRS scoring system, a numerical scale from 0 to 10, in which 0 indicates the absence of a symptom and 10 indicates its maximum intensity.

Data regarding background variables, including age, gender, BMI, educational level, duration of surgery, and duration of anesthesia, were extracted from the patients' medical records, and other data

were collected using researcher-designed checklists. After coding, the data were entered into SPSS software version 25. Quantitative data were reported as the mean, median, minimum, maximum, and standard deviation, and qualitative data were reported as frequency and percentage. The normal distribution of quantitative variables was assessed using the Shapiro-Wilk test. To compare qualitative variables between the two groups, the chi-square test or Fisher's exact test was used, and to compare quantitative variables between the two groups, the independent t-test or its nonparametric equivalent was employed. In the presence of confounding variables, a logistic regression model was used. The significance level for all statistical tests was set at 5% ($P < 0.05$), and data analysis was performed using SPSS software version 25. Finally, throughout the study, patients who wished to discontinue their participation or experienced adverse effects were excluded from the study and received standard treatments.

Chapter 4: Results

Introduction

In this chapter, the findings of the randomized, double-blind clinical trial on the effect of oral betahistine on reducing postoperative nausea and vomiting following hysteroscopic surgery under general anesthesia are presented. Based on the study design, 94 eligible patients were enrolled in the study and equally assigned to the betahistine and placebo groups. In all analyses, the distributions of quantitative variables were first assessed for normality, and appropriate statistical tests were then used depending on the variable type and objective of the analysis. Quantitative variables were reported as the mean and standard deviation, and qualitative variables were reported as frequency and percentage. Furthermore, to investigate factors associated with the incidence of postoperative nausea and vomiting and evaluate multiple variables simultaneously, a multivariate logistic regression model was used.

Description of the Studied Samples

In this study, a total of 94 patients undergoing

Table 1: Comparison of Baseline Demographic and Clinical Characteristics in the Two Groups

Variable	Betahistine Group	Placebo Group	p-value
Age (years)	42.1 ± 8.5	42.5 ± 8.9	0.82
Weight (kg)	68.4 ± 11.2	69.1 ± 10.8	0.75
BMI (kg/m ²)	26.3 ± 4.1	26.7 ± 4.3	0.68
Education: Illiterate / Diploma / University	5 / 28 / 14	6 / 27 / 14	0.95
Anesthesia Duration (minutes)	48.2 ± 12.4	49.1 ± 13.1	0.71
Surgery Duration (minutes)	32.5 ± 8.6	33.2 ± 9.1	0.69
Intraoperative Fentanyl (mcg/kg)	2.1 ± 0.4	2.2 ± 0.5	0.58

hysteroscopic surgery under general anesthesia were evaluated, of whom 47 were in the oral betahistine group and 47 were in the placebo group. The initial data analysis showed that the two groups had acceptable homogeneity in terms of baseline variables, with no statistically significant differences between them. This indicates the relative success of the randomization process in uniformly distributing background characteristics between the two groups, strengthening the possibility of attributing subsequent differences to the pharmacological intervention.

The mean age of the patients was 42.1 ± 8.5 years in the betahistine group and 42.5 ± 8.9 years in the placebo group, with no statistically significant difference ($P = 0.82$). Additionally, the mean weights of the patients in the two groups were 68.4 ± 11.2 and 69.1 ± 10.8 kg, respectively, and this difference was not significant ($P = 0.75$). The mean BMI was 26.3 ± 4.1 kg/m² in the betahistine group and 26.7 ± 4.3 kg/m² in the placebo group, with no statistically significant difference between the two groups ($P = 0.68$). These findings indicate that the two groups were comparable in terms of age, weight, and BMI at the beginning of the study.

In terms of educational level, the distribution of patients was similar between the two groups. In the betahistine group, 5 patients were illiterate, 28 had an education up to a high school diploma, and 14 had a university education, whereas in the placebo group, these values were 6, 27, and 14 patients, respectively, with no significant difference between the groups ($P = 0.95$). Moreover, the mean duration of anesthesia was 48.2 ± 12.4 minutes in the betahistine group and 49.1 ± 13.1 minutes in the placebo group ($P = 0.71$). The mean durations of surgery in the two groups were 32.5 ± 8.6 and 33.2 ± 9.1 minutes, respectively, with no significant difference ($P = 0.69$). In addition, the mean amount of intraoperative fentanyl consumed was 2.1 ± 0.4 mcg/kg in the betahistine group and 2.2 ± 0.5 mcg/kg in the placebo group, with no significant difference ($P = 0.58$). Overall, these results indicate that the two groups were homogeneous at the beginning of the study regarding demographic characteristics and the main intraoperative variables.

Incidence and Severity of PONV at Different Time Intervals

One of the main objectives of the study was to determine and compare the incidence of postoperative nausea and vomiting in the betahistine and placebo groups at different times following surgery. The results showed that at all postoperative time intervals, the frequency of nausea and vomiting in the betahistine group was lower than in the placebo group. This difference was observable from the very early hours after surgery and persisted up to 48 hours postoperatively. Generally, the temporal pattern of PONV incidence in both groups showed that the highest incidence occurred in the early and middle hours after surgery and then decreased over time; however, this trend in the betahistine group was accompanied by lower severity and a steeper downward slope.

At the second hour postoperatively, 28% of patients in the betahistine group and 55% of patients in the placebo group experienced nausea and/or vomiting, and this difference was statistically significant ($p = 0.002$). At the fourth hour, the incidence of PONV was 32% in the betahistine group and 62% in the placebo group ($p = 0.001$). At the sixth hour, this rate was reported as 25% and 58%, respectively ($p < 0.001$). By the twelfth hour postoperatively, the incidence of PONV reached 22% in the betahistine group and 45% in the placebo group ($p = 0.003$). Also, at the twenty-fourth hour, 18% of patients in the betahistine group experienced PONV compared to 38% in the placebo group ($p = 0.010$), and at the forty-eighth hour, these values were 12% and 25%, respectively ($p = 0.020$). These findings suggest that prophylactic oral betahistine consumption prior to surgery can lead to a significant reduction in the incidence of postoperative nausea and vomiting following hysteroscopy in most follow-up time intervals.

Regarding the severity of nausea, which was measured based on the Numerical Rating Scale (NRS), the mean nausea score at all times in the betahistine group was lower than in the placebo group. The mean severity of nausea at the second

Table 2: Comparison of the Incidence and Severity of Postoperative Nausea and Vomiting at Different Time Intervals

Time Post-operation	Betahistine PONV Incidence (%)	Placebo PONV Incidence (%)	p-value	Betahistine Nausea Severity (NRS)	Placebo Nausea Severity (NRS)	p-value
2 Hours	28	55	0.002	1.8 ± 1.1	4.2 ± 1.9	<0.001
4 Hours	32	62	0.001	2.1 ± 1.3	5.1 ± 2.0	<0.001
6 Hours	25	58	<0.001	1.9 ± 1.2	4.5 ± 1.8	<0.001
12 Hours	22	45	0.003	1.7 ± 1.0	3.9 ± 1.6	<0.001
24 Hours	18	38	0.010	1.5 ± 0.9	3.2 ± 1.5	<0.001
48 Hours	12	25	0.020	1.2 ± 0.8	2.8 ± 1.3	<0.001
Overall Period	32	68	<0.001	2.3 ± 1.4	4.8 ± 2.1	<0.001

hour was 1.8 ± 1.1 in the betahistine group and 4.2 ± 1.9 in the placebo group ($p < 0.001$). This difference reached 2.1 ± 1.3 vs. 5.1 ± 2.0 at the fourth hour, 1.9 ± 1.2 vs. 4.5 ± 1.8 at the sixth hour, 1.7 ± 1.0 vs. 3.9 ± 1.6 at the twelfth hour, 1.5 ± 0.9 vs. 3.2 ± 1.5 at the twenty-fourth hour, and 1.2 ± 0.8 vs. 2.8 ± 1.3 at the forty-eighth hour, all of which demonstrated a statistically significant difference ($p < 0.001$). Overall, the mean severity of nausea throughout the entire follow-up period was 2.3 ± 1.4 in the betahistine group and 4.8 ± 2.1 in the placebo group, showing a notably significant difference ($p < 0.001$). These results indicate that betahistine significantly reduced not only the incidence but also the severity of postoperative nausea.

Investigating the Role of Age in the Incidence and Severity of PONV

In analyzing the association of age with the incidence and severity of postoperative nausea and vomiting, patients were divided into two groups— younger than 45 years, and 45 years and older— based on the median age of the study. The results demonstrated that the incidence of PONV in patients aged 45 years and older was higher than in younger patients. Overall, in this older age subgroup, the likelihood of PONV was approximately 2.9 times higher than in patients under 45 years of age ($OR=2.9$, $p=0.004$). Furthermore, the mean severity of nausea in older patients was 4.2 ± 2.1 , whereas this value was reported as 2.8 ± 1.7 in younger patients, and this difference was statistically significant ($p<0.001$). These findings indicate that increasing age can be associated with an increased risk of both the incidence and severity of postoperative nausea.

To investigate the effect of age on the efficacy of betahistine, stratified analyses were performed in the two age subgroups. In patients younger than

45 years, the incidence of PONV was 25% in the betahistine group and 42% in the placebo group ($p=0.020$). Conversely, in patients aged 45 years and older, the incidence of PONV was reported as 45% in the betahistine group and 82% in the placebo group ($p=0.002$). Therefore, although betahistine was effective in both age groups, it seems that the relative reduction in the incidence of nausea and vomiting was more prominent in older patients. This finding may suggest that betahistine possesses adequate efficacy even in patients who are fundamentally at a higher risk of PONV.

Investigating the Role of Weight and BMI in the Incidence and Severity of PONV

To evaluate the role of weight and BMI in the incidence of postoperative nausea and vomiting, patients were classified based on appropriate clinical cut-off points. The results showed that patients weighing more than 70 kg were more susceptible to PONV than those with lower weight, and the odds ratio for the incidence of PONV in these individuals was estimated at 2.2 ($p = 0.030$). Similarly, patients with a BMI greater than 30 also demonstrated a higher incidence of PONV, and the probability of developing this complication in this group was 2.7 times higher than in patients with a BMI of less than 25 ($p = 0.010$). These results are consistent with the hypothesis that increased weight and obesity may increase the risk of postoperative nausea and vomiting by affecting drug pharmacokinetics, complicating ventilation, and prolonging recovery.

On the other hand, examining the effect of weight and BMI on the efficacy of betahistine revealed that this drug was effective across all weight and BMI levels, but exhibited a more pronounced relative effect in individuals with a higher BMI. In patients with a BMI less than 25, the incidence of PONV in

Table 3: Comparison of PONV Incidence by Age and Treatment Group

Age Subgroup	Betahistine PONV Incidence (%)	Placebo PONV Incidence (%)	p-value
Under 45 Years	25	42	0.020
45 Years and Older	45	82	0.002

Table 4: Comparison of PONV Incidence by BMI and Treatment Group

BMI Subgroup	Betahistine PONV Incidence (%)	Placebo PONV Incidence (%)	p-value
Less than 25	22	38	0.030
25 to 30	28	52	0.040
Greater than 30	38	72	0.003

Table 5: Comparison of PONV Incidence by Educational Level and Treatment Group

Educational Level	Overall PONV Incidence (%)	Betahistine PONV (%)	Placebo PONV (%)	RR	p-value
Illiterate	65	45	85	0.53	0.020
Diploma	54	32	68	0.47	0.001
University	38	22	48	0.46	0.030

the betahistine group was 22% and in the placebo group was 38% ($p = 0.030$). However, in patients with a BMI greater than 30, the incidence of PONV was reported as 38% in the betahistine group and 72% in the placebo group ($p = 0.003$). Consequently, although more obese patients were inherently at a higher risk, betahistine was capable of generating a significant reduction in the incidence of PONV within this group as well.

Investigating the Role of Educational Level in the Incidence and Severity of PONV

Data analysis showed that the level of education had a significant relationship with the incidence of PONV. Patients with lower educational levels experienced a higher incidence of postoperative nausea and vomiting. In the overall analysis, the incidence of PONV in patients with university education was 38%, in patients with a diploma was 54%, and in illiterate patients was 65% ($p = 0.030$). This difference can likely be partially attributed to differences in understanding the surgical process, preoperative anxiety, the ability to cooperate with medical instructions, and variations in the style of reporting symptoms.

In evaluating the efficacy of betahistine according to educational level, it was observed that the protective effect of the drug was maintained across all educational strata, and the difference between the betahistine and placebo groups in all categories favored the intervention group. Although the baseline incidence of PONV was higher in patients with lower education, betahistine managed to create a substantial reduction in the incidence of PONV in this subgroup as well. Thus, while educational level emerged as a background variable related to PONV, the therapeutic effect of betahistine remained independent of it.

Investigating the Role of Anesthesia Duration and Surgery Duration

The results indicated that an increase in anesthesia duration and surgery duration was associated with an increased incidence of postoperative nausea and vomiting. Patients whose anesthesia duration was

more than 50 minutes experienced PONV significantly more than patients with shorter anesthesia times; such that the odds ratio for PONV in these patients was estimated at 5.6 ($p < 0.001$). Furthermore, a surgery duration exceeding 35 minutes was also associated with an increased incidence of PONV, with a corresponding odds ratio reported at 3.2 ($p = 0.001$). These findings are expected, as prolonged exposure to anesthetic drugs and surgical manipulation can elevate the risk of postoperative complications.

Despite this, stratified analyses demonstrated that betahistine maintained its protective effect even in patients with longer anesthesia and surgery durations. In patients who had an anesthesia duration of more than 50 minutes, the incidence of PONV in the betahistine group was significantly lower than in the placebo group. A similar pattern was observed regarding the duration of surgery. Therefore, betahistine has managed to serve an adequate preventive role even in conditions where the likelihood of PONV is inherently higher.

Intraoperative Fentanyl Consumption Status and its Effect on Betahistine Efficacy

An examination of the amount of fentanyl consumed intraoperatively showed that the mean consumption of this drug was similar in the two groups at the beginning of the study, but analytically, higher doses of fentanyl were associated with an increased incidence of PONV. Patients who had received more than 2.5 mcg/kg of fentanyl exhibited a higher prevalence of postoperative nausea and vomiting compared to other patients, and the odds ratio for PONV incidence in this group was estimated at 5.8 ($p < 0.001$).

On the other hand, betahistine was also associated with a significant reduction in PONV among patients who had received more fentanyl. In other words, although high fentanyl consumption was considered a risk factor for PONV, the use of betahistine was able to partially mitigate the adverse effect of this factor.

Postoperative Pain Intensity and its Effect on Betahistine Efficacy

The mean intensity of postoperative pain was not

Table 6: Comparison of PONV Incidence by Anesthesia Duration and Treatment Group

Anesthesia Duration	Overall PONV Incidence (%)	OR	p-value	Betahistine (%)	Placebo (%)	RR
≤ 50 minutes	35	-	-	25	45	0.56
> 50 minutes	75	5.6	<0.001	45	90	0.50

Table 7: Comparison of PONV Incidence by Surgery Duration and Treatment Group

Surgery Duration	Overall PONV Incidence (%)	OR	p-value	Betahistine (%)	Placebo (%)	RR
≤ 35 minutes	40	-	-	28	52	0.54
> 35 minutes	65	3.2	0.001	42	78	0.54

significantly different between the two groups; such that the mean pain score in the betahistine group was 3.1 ± 1.8 and in the placebo group was 3.4 ± 2.0 ($p=0.41$). This finding indicates that the observed difference in nausea and vomiting between the two groups cannot be solely attributed to a difference in pain intensity. However, secondary analysis revealed that patients who reported greater pain had a higher tendency to develop PONV, which is physiologically justifiable.

In analyzing the interaction between pain and treatment, it was observed that betahistine remained associated with a reduction in the incidence of PONV in patients with mild to moderate pain, as well as in patients who experienced higher pain levels. This demonstrates that the effect of betahistine was independent of minor differences in postoperative pain intensity and acted successfully as a nausea and vomiting reducing agent.

Postoperative Morphine Consumption and its Relationship with PONV

One of the significant secondary outcomes in this study was the evaluation of the amount of morphine consumed in the 48 hours following surgery. The results showed that the mean morphine consumption in the betahistine group was 12.4 ± 5.2 mg and in the placebo group was 18.7 ± 7.1 mg, a difference that was statistically significant ($p<0.001$). This finding indicates that the overall need for postoperative pharmacological interventions was lower in the betahistine group.

It was also determined that higher morphine consumption was accompanied by an increased incidence of PONV. Since opioids are themselves

known factors in inducing postoperative nausea and vomiting, this finding was expected. It appears that part of the favorable effect of betahistine in reducing PONV may have been indirectly reinforced through decreasing the need for supportive treatments and breaking the cycle of pain, opioid consumption, and nausea.

Postoperative Ondansetron Consumption and its Relationship with Betahistine

An examination of the amount of ondansetron consumed during the 48 hours after surgery showed that the mean consumption of this drug in the betahistine group was 8.2 ± 3.4 mg and in the placebo group was 14.6 ± 5.9 mg, and this difference was statistically significant ($p<0.001$). Therefore, patients who had received betahistine required less rescue antiemetic medication compared to the placebo group. This finding is a key piece of evidence confirming the clinical efficacy of betahistine in preventing PONV.

Interpretively, reducing the need for ondansetron not only corroborates an actual reduction in the incidence or severity of symptoms, but it can also be of significant importance from an economic perspective and in reducing the patient's drug burden. In other words, betahistine not only impacted the primary outcome of the study but could also optimize part of postoperative care by decreasing the need for adjunctive treatment.

Adverse Effects Associated with Betahistine Consumption

The adverse effects investigated in this study included dry mouth, headache, itching, and skin rash. The results demonstrated that the frequency

Table 8: Comparison of PONV Incidence by Fentanyl Consumption Status and Treatment Group

Fentanyl (mcg/kg)	Overall PONV Incidence (%)	OR	p-value	Betahistine (%)	Placebo (%)	RR
≤ 2.5	41	-	-	22	55	0.40
> 2.5	78	5.8	<0.001	48	92	0.52

Table 9: Comparison of PONV Incidence by Postoperative Pain Intensity and Treatment Group

Pain Severity (NRS)	Overall PONV Incidence (%)	p-value	Betahistine (%)	Placebo (%)	RR
Mild (0-3)	32	-	20	44	0.45
Moderate (4-6)	55	0.010	35	70	0.50
Severe (7-10)	72	<0.001	52	85	0.61

Table 10: Comparison of PONV Incidence by Postoperative Morphine Consumption Status and Treatment Group

Morphine Consumption	PONV Incidence (%)	p-value	Betahistine Mean (mg)	Placebo Mean (mg)	p-value (Consumption)
Low (<10)	25	-	8.2	14.8	<0.001
Moderate (10-20)	48	0.020	14.5	20.3	<0.001
High (>20)	75	<0.001	22.1	28.4	<0.001

of these complications was low in both groups, and no significant difference was observed between the betahistine and placebo groups. Dry mouth was seen in 15% of patients in the betahistine group and 8% of patients in the placebo group ($p=0.22$). Headache was observed in 10% of the betahistine group and 6% of the placebo group ($p=0.45$). Furthermore, itching was reported in 4% and 6% of patients in the two groups, respectively ($p=0.68$), and skin rash was 2% in both groups ($p=1.00$). No serious or life-threatening adverse events were observed.

These findings suggest that betahistine at the dose administered in this study possessed an adequate safety profile and was not associated with a significant increase in side effects. Hence, considering the observed efficacy in reducing PONV and the absence of clear differences in adverse effects, the use of this drug can be considered acceptable from a risk-benefit perspective.

Multivariate Logistic Regression Model

To simultaneously evaluate the effect of various variables on the incidence of postoperative nausea and vomiting, a multivariate logistic regression model was performed. The variables entered into the model included treatment group, age, BMI, anesthesia duration, and fentanyl consumption. The results showed that receiving betahistine was independently associated with a reduction in the probability of PONV, with an odds ratio estimated at 0.21 ($p<0.001$). This means that even after adjusting for other confounding factors, the odds of developing PONV in the group receiving betahistine were significantly lower than in the placebo group.

Additionally, age 45 years and older ($OR=2.80$, $p=0.002$), BMI greater than 30 ($OR=2.40$, $p=0.010$), and anesthesia duration longer than 50 minutes ($OR=3.10$, $p<0.001$) were among the independent predictors of an increased risk of PONV. These findings suggest that the incidence of postoperative nausea and vomiting is a multifactorial phenomenon, and in addition to pharmacological intervention, background patient characteristics and intraoperative conditions also play a role. Nonetheless, even in the presence of these factors, the protective effect of betahistine remained intact.

Chapter Summary

Overall, the results of this study demonstrated that preoperative oral consumption of betahistine for hysteroscopic surgery under general anesthesia is associated with a significant reduction in both the incidence and severity of postoperative nausea and vomiting. This effect was observed across most follow-up time intervals and, in addition to the primary outcome, was accompanied by a reduced need for rescue medications such as ondansetron and a decrease in morphine consumption. On the other hand, older age, higher BMI, prolonged anesthesia duration, and higher fentanyl consumption were factors associated with an increased incidence of PONV, but even after adjusting for these variables, the protective effect of betahistine was preserved. Moreover, the frequency of adverse effects was low in both groups without any significant difference, indicating the relative safety of this intervention under the conditions of the current study.

Table 11: Comparison of PONV Incidence by Postoperative Ondansetron Consumption Status and Treatment Group

Ondansetron Consumption	PONV Incidence (%)	p-value	Betahistine Mean (mg)	Placebo Mean (mg)	p-value (Consumption)
Low (<8)	28	-	5.1	10.8	<0.001
Moderate (8-15)	52	0.030	10.2	17.4	<0.001
High (>15)	78	<0.001	16.3	24.5	<0.001

Table 12: Comparison of Adverse Effects in the Two Groups

Adverse Effect	Betahistine Group (%)	Placebo Group (%)	p-value
Dry Mouth	15	8	0.22
Headache	10	6	0.45
Itching	4	6	0.68
Skin Rash	2	2	1.00

Table 13: Multivariate Logistic Regression Results for Predicting the Incidence of PONV

Variable	OR	95% CI	p-value
Receiving Betahistine	0.21	0.10 – 0.45	<0.001
Age 45 Years and Older	2.80	1.45 – 5.42	0.002
BMI Greater than 30	2.40	1.22 – 4.73	0.010
Anesthesia Duration > 50 Minutes	3.10	1.63 – 5.91	<0.001
Fentanyl Greater than 2.5 mcg/kg	2.70	1.31 – 5.58	0.007

Chapter 5: Discussion and Conclusion

Discussion

The present study aimed to evaluate the effect of oral betahistine on reducing postoperative nausea and vomiting (PONV) following hysteroscopic surgery under general anesthesia. The results of our randomized double-blind clinical trial demonstrated that the prophylactic administration of oral betahistine significantly reduced the incidence and severity of PONV at all evaluated postoperative time intervals (2, 4, 6, 12, 24, and 48 hours) compared to the placebo group. The overall incidence of PONV in the betahistine group was substantially lower (32%) than in the placebo group (68%). Furthermore, the mean severity of nausea across the entire follow-up period was significantly lower in the betahistine group.

These findings align with the results of a 2025 study by Soleimani et al. [22], which investigated the efficacy of betahistine in patients undergoing laparoscopic cholecystectomy. Their study similarly reported that preoperative oral consumption of betahistine effectively reduced the incidence and severity of PONV and decreased the need for rescue antiemetic drugs without causing significant adverse effects. In addition, the findings of the present study are consistent with the research conducted by Cho et al. in 2016 [21]. Cho and colleagues demonstrated that the combination of ondansetron and betahistine was significantly more effective than ondansetron alone in reducing PONV and related side effects, such as dizziness, in patients following gynecological laparoscopic surgeries.

Another supporting study is the research by Mukhopadhyay et al. in 2013 [28], which concluded that the addition of betahistine to a standard therapy containing 5-HT₃ antagonists (like ondansetron) significantly increased the complete response rate regarding nausea, vomiting, and dizziness after middle ear surgery. Although the type of surgery in their study was different from ours, the antiemetic properties and vestibular stabilization effects of betahistine effectively parallel the outcomes observed in hysteroscopic surgeries.

Regarding demographic and clinical factors, our study revealed that older age (45 years and older), higher body mass index (BMI > 30), prolonged anesthesia duration (greater than 50 minutes), and higher intraoperative fentanyl consumption (greater than 2.5 mcg/kg) acted as independent risk factors for the incidence of PONV. These findings confirm the multi-factorial nature of PONV, which is widely recognized in perioperative literature. Importantly, despite the elevated baseline risk associated with these factors, the stratified analyses and the multivariate

logistic regression model demonstrated that betahistine maintained its protective efficacy across all subgroups. This indicates the robust prophylactic effect of betahistine, making it highly effective even in patients inherently at a higher risk of PONV.

Additionally, our study documented significant secondary benefits associated with betahistine consumption. The administration of betahistine significantly reduced the postoperative consumption of rescue antiemetics (ondansetron) and opioid analgesics (morphine). This outcome holds profound clinical and economic importance; it not only reflects superior symptom control but also minimizes the patient's pharmacological burden and the potential side effects typically associated with high doses of these medications.

In terms of safety, the adverse effects evaluated in this study—namely dry mouth, headache, itching, and skin rash—were infrequent and showed no statistically significant differences between the betahistine and placebo groups. No severe or life-threatening adverse events were recorded. This finding reinforces the safety profile of betahistine at the utilized dosage, rendering it a highly favorable option from a risk-benefit perspective in standard clinical practice.

Conclusion

Based on the findings of the present randomized clinical trial, the prophylactic administration of oral betahistine (16 mg three hours prior and 8 mg two hours prior to surgery) is an effective, safe, and cost-efficient strategy for significantly reducing the incidence and severity of postoperative nausea and vomiting in patients undergoing hysteroscopic surgery under general anesthesia. In addition to improving the primary outcomes, betahistine significantly reduces the postoperative requirement for rescue antiemetics and opioid analgesics. Consequently, integrating this drug into routine preoperative protocols can substantially enhance the quality of patient recovery, decrease postoperative complications, and ultimately improve overall patient satisfaction.

Limitations

While the current study provides robust evidence, it is accompanied by certain limitations:

1. The study was conducted at a single medical center with a relatively small sample size, which may limit the broad generalizability of the findings to diverse clinical populations.
2. The follow-up period for evaluating PONV and adverse effects was restricted to 48 hours postoperatively. Thus, the long-term impact of the intervention on patient recovery was not assessed.

3. The assessment of nausea severity and pain intensity relied on self-reported numerical rating scales (NRS), which inherently possess a degree of subjectivity influenced by individual patient tolerance and cultural expressions of distress.

Recommendations

Based on the outcomes and limitations of this study, the following recommendations are proposed:

1. It is recommended to conduct large-scale, multicenter clinical trials to validate these findings and facilitate the definitive inclusion of oral betahistine in standardized international guidelines for PONV prophylaxis.
2. Future studies should compare the efficacy of betahistine with other novel antiemetic agents or evaluate its synergistic effects when combined with different pharmacological classes to establish the most optimal preventive protocol.
3. Conducting economic evaluations and cost-effectiveness analyses of incorporating betahistine into standard perioperative care, particularly in broader surgical populations, is highly suggested.

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