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Original Research Article

Comparative effectiveness of ondansetron, dexamethasone, and their combination in preventing postoperative nausea and vomiting in ear nose and throat surgeries under general anaesthesia

Allen Joe Rodrigues[1]*, Abhishek CP[1], Eshanu H Shastry[1], Abhishek Acharya[1], Susheela S Halemani[1]

[1]Dept. of Pharmacology, Subbaiah Institute of Medical Sciences, Shivamogga, Karnataka, India

Abstract

Background: Postoperative nausea and vomiting (PONV) is a frequent complication following general anaesthesia, particularly in patients undergoing Ear, Nose, and Throat (ENT) surgeries. Vestibular stimulation and middle ear manipulation increase the risk of PONV. Ondansetron and dexamethasone are commonly used antiemetic agents, and combination therapy may improve prophylaxis.

Objectives: To compare the efficacy of ondansetron, dexamethasone, and their combination in preventing postoperative nausea and vomiting in patients undergoing elective ENT surgeries under general anaesthesia.

Materials and Methods: This prospective, randomized, double-blinded study included 104 adult patients with American Society of Anaesthesiologists physical status I–II scheduled for elective ENT surgeries. Patients were randomly allocated to receive intravenous ondansetron 4 mg, dexamethasone 8 mg, or a combination of ondansetron 4 mg and dexamethasone 8 mg before induction of anaesthesia. The incidence of nausea and vomiting was assessed during the early (0–1 hour) and late (1–6 hours) postoperative periods, and the requirement for rescue antiemetic therapy was recorded.

Results: The overall incidence of vomiting was significantly lower in the combination group (14%), compared with ondansetron alone (53%) and dexamethasone alone (60%). 33% patients in ondansetron group, 45% in dexamethasone group and 3% in combination group required rescue antiemetic therapy. Ondansetron alone showed reduced efficacy against late postoperative nausea and vomiting, while dexamethasone alone was less effective during the early postoperative period.

Conclusion: Combination prophylaxis with ondansetron and dexamethasone provides superior control of postoperative nausea and vomiting compared with either agent alone in patients undergoing ENT surgeries under general anaesthesia safely.

Keywords: Postoperative Nausea and Vomiting, Ondansetron, Dexamethasone, Otolaryngologic Surgical Procedures, General Anesthesia, Antiemetics

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1. Introduction

Postoperative nausea and vomiting (PONV) remains one of the most frequently encountered and distressing adverse events following general anaesthesia. Although improvements in anaesthetic pharmacology, airway management, and perioperative monitoring have enhanced overall surgical safety, the occurrence of nausea and vomiting during recovery continues to challenge clinicians. In the general surgical population, the reported incidence ranges between 20% and 30%.[1,2] However, in individuals with multiple predisposing risk factors, the probability may rise dramatically, approaching 70–80% when no prophylactic intervention is administered.[1,3] This high variability underscores the multifactorial nature of PONV and the need for individualized preventive strategies.

The aetiology of PONV is complex and involves interplay of patient-related characteristics, anaesthetic techniques, surgical factors, and postoperative influences. Patient-specific predictors such as female gender, non-smoking status, prior history of motion sickness or PONV, and postoperative opioid use have been consistently identified as independent determinants of risk.[3,4] The simplified risk scoring system proposed by Apfel et al. has gained widespread acceptance because of its practical utility in stratifying patients and guiding prophylaxis.[3] Nevertheless, risk scoring alone does not eliminate the

*Corresponding author: Allen Joe Rodrigues
Email: drallen.rodrigues15@gmail.com

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incidence of PONV, particularly in procedures inherently associated with high emetogenic potential.

ENT surgeries, especially those involving the middle ear and mastoid region are recognized as high-risk operations for the development of postoperative emesis. Manipulation of the vestibular apparatus can directly stimulate labyrinthine pathways that project to the vomiting centre via the vestibulocochlear nerve. Even minimal perturbations in semicircular canal function may evoke nausea similar to motion sickness. Additionally, blood ingestion during surgery, prolonged operative duration, and exposure to volatile anaesthetic agents collectively increase emetogenic stimuli.[4,5] Volatile anaesthetics, in particular, have been identified as major contributors to early postoperative vomiting. Randomized controlled trials have demonstrated that these agents are more strongly associated with early emetic episodes than with delayed symptoms.[6]

The neurophysiology underlying nausea and vomiting involves coordinated activity between peripheral and central structures. The chemoreceptor trigger zone (CTZ), located in the area postrema, is sensitive to circulating emetogenic substances. Peripheral serotonin release from enterochromaffin cells in the gastrointestinal tract activates vagal afferent fibres through 5-hydroxytryptamine-3 (5-HT_3) receptors. Signals are subsequently transmitted to the nucleus tractus solitarius and higher cortical centres. Additional neurotransmitters, including dopamine, histamine, acetylcholine, and substance P, modulate these pathways. The involvement of multiple receptor systems explains why blockade of a single pathway frequently results in incomplete prophylaxis.[4]

Ondansetron, a selective 5-HT_3 receptor antagonist, is widely used because of its favourable safety profile and effectiveness in controlling early postoperative emesis.[3,7] By blocking serotonin-mediated stimulation at both peripheral vagal terminals and central receptors, ondansetron reduces the incidence of acute nausea and vomiting during emergence from anaesthesia. However, its elimination half-life of approximately 3–5 hours may limit prolonged efficacy in procedures associated with sustained vestibular stimulation. Pharmacological management of PONV has evolved toward multimodal strategies targeting different receptor systems simultaneously.[1,2,8]

Dexamethasone, a synthetic corticosteroid, has demonstrated significant antiemetic properties despite its primary classification as an anti-inflammatory agent.[9] The exact mechanism remains incompletely understood, but several hypotheses have been proposed. These include inhibition of prostaglandin synthesis, reduction of inflammatory mediator release, modulation of serotonin turnover, and potential central effects on the nucleus tractus solitarius.[9,10] Unlike ondansetron, dexamethasone exhibits a longer duration of action and is particularly effective in preventing delayed postoperative vomiting. In addition, perioperative dexamethasone administration has been associated with improved analgesia and decreased tissue oedema, which may indirectly influence nausea severity.[10]

International consensus guidelines recommend that prophylaxis be tailored to individual risk profiles, often advocating the use of combination therapy in moderate- and high-risk patients.[1,2] Evidence from large randomized analyses demonstrates additive benefits when antiemetics with differing mechanisms are administered concurrently.[11] Such findings are particularly relevant in ENT surgeries, where single-agent prophylaxis frequently proves insufficient. ENT-specific investigations have reported improved outcomes when serotonin antagonists are combined with corticosteroids or other antiemetic classes.[12]

Despite these advances, real-world clinical practice often varies in terms of drug selection, timing of administration, and risk stratification. Therefore, continued evaluation of combination regimens in specific surgical populations remains valuable. The present observational study was undertaken to compare the effectiveness of ondansetron alone, dexamethasone alone, and their combination in preventing PONV among patients undergoing elective ENT surgeries under general anaesthesia.

2. Materials and Methods

This randomized, prospective, double-blind clinical study was conducted after obtaining approval from the Institutional Ethical and Scientific Committee (IEC-SUIMS/8/2021-22). Written informed consent was obtained from all participants prior to enrolment. A total of 104 patients (distributed equally among three groups) of either sex, aged 18–75 years, belonging to American Society of Anesthesiologists (ASA) physical status I and II, scheduled for elective otorhinolaryngological (ENT) surgeries under general anesthesia, were included in the study.

Patients were excluded if they had a history of motion sickness or previous postoperative nausea and vomiting, diabetes mellitus or pregnancy, active gastrointestinal disorders, psychiatric illness, smoking or chronic alcohol use, use of antiemetics, opioids, antihistamines, sedatives, or anxiolytics within 48 hours before surgery, known hypersensitivity to the study drugs, active vestibular disorders, or preoperative nausea or vomiting.

2.1. Sample size calculation

Sample size estimation was performed using OpenEpi software, based on an expected incidence of postoperative nausea and vomiting (PONV) of 12% in the unexposed group and 28% in the exposed group, with a 95% confidence level and 80% study power.[13]

2.2. Randomization

Participants were randomly allocated into three groups (1:1:1) using a computer-generated randomization table. All

patients underwent standardized pre-anesthetic evaluation. No sedative premedication was administered. Patients were kept nil per oral from midnight prior to surgery.

In the operating room:

1. Group O+D received ondansetron 4 mg IV and dexamethasone 8 mg IV
2. Group D received dexamethasone 8 mg IV
3. Group O received ondansetron 4 mg IV

All study drugs were administered one minute before induction of anesthesia. Following preoxygenation with 100% oxygen, anesthesia was induced with fentanyl 2 µg/kg IV and propofol 2 mg/kg IV. Tracheal intubation was facilitated using atracurium 0.5 mg/kg IV. Anesthesia was maintained with isoflurane in nitrous oxide and oxygen, with intermittent doses of atracurium (0.2 mg/kg) for muscle relaxation. Mechanical ventilation was adjusted to maintain end-tidal carbon dioxide between 35–40 mmHg. At the end of surgery, anesthetic agents were discontinued and residual neuromuscular blockade was reversed using neostigmine 0.05 mg/kg IV and glycopyrrolate 0.01 mg/kg IV. Patients were transferred to the post-anesthesia care unit and observed for 6 hours postoperatively for:

1. Incidence of nausea and vomiting were assessed at 0–1 hour and 1–6 hours postoperatively
2. Time to first emetic episode
3. Requirement of rescue antiemetic medication

3. Rescue Antiemetic Protocol

Metoclopramide 10 mg IV was administered as rescue antiemetic if:

1. Nausea persisted for more than 15 minutes, or
2. Any episode of vomiting occurred

The primary outcome was the incidence of postoperative nausea and vomiting within 6 hours. Secondary outcomes included time to first emetic event and requirement of rescue antiemetic medication. The prophylactic regimen was considered effective if the patient experienced no nausea or vomiting during the 6-hour postoperative period and did not require rescue antiemetic therapy.

4. Statistical Analysis and Significance

Continuous variables (age and weight) were expressed as mean values and compared among the three groups using one-way analysis of variance (ANOVA). Categorical variables, including gender distribution, type of surgery, incidence of postoperative nausea and vomiting, and requirement of rescue antiemetic medication, were analyzed using the Chi-square test or Fisher's exact test, as appropriate. A p value < 0.05 was considered statistically significant.

5. Results

Baseline demographic variables including age, gender, and body weight were comparable among the three groups, with no statistically significant difference observed (**Table 1**). The distribution of various ENT surgical procedures was also similar across the groups, indicating adequate randomization and homogeneity of the study population (**Table 2**) (P value 0.12).

Table 1: Demographic details

Particulars	Ondensetron	Dexamethasone	Ondensetron + Dexamethasone	P value
Age	38.52 ± 11.2	35.84 ± 10.6	36.08 ± 9.8	0.41
Gender (Male)	12	10	12	0.83
Weight	71.21 ± 9.4	61.51 ± 8.1	64.34 ± 7.6	0.09

Table 2: Type of surgery

Type of Surgery	Ondensetron	Dexamethasone	Ondensetron + Dexamethasone
Tympanoplasty	11	19	16
MRM &Tympanoplasty	11	6	3
MRM+Occiculoplasty &Tympanoplasty	0	0	1
CRM with tympanoplasty	10	4	9
MRM	3	2	6
Excision	1	2	0
**MRM – Modified radical mastoidectomy, CRM – Cortical radical mastoidectomy*			

Table 3: Incidence of vomiting

Medication	Total	Yes	
Ondensetron	36	19	53%
Dexamethasone	33	20	60%
Ondensetron + Dexamethasone	35	5	14%

Table 4: Use of rescue antiemetic

Medication	Rescue antiemetic			
	Metoclopramide		Nil	
	N	%	N	%
Ondensetron	12	33	24	67
Dexamethasone	15	45	18	55
Ondensetron + Dexamethasone	1	3	34	97

The requirement for rescue antiemetic medication differed significantly among the groups. The ondansetron–dexamethasone combination group demonstrated a significantly lower requirement for rescue metoclopramide compared with both ondansetron and dexamethasone alone ($p < 0.001$).

Table 5: Incidence of nausea & vomiting during 0-6 hrs

		Ondensetron	Dexamethasone	Ondensetron + Dexamethasone
Incidence of nausea	0-1 hrs	4	8	1
	1-6 hrs	8	3	3
Incidence of vomiting	0-1 hrs	2	6	1
	1-6 hrs	7	4	0

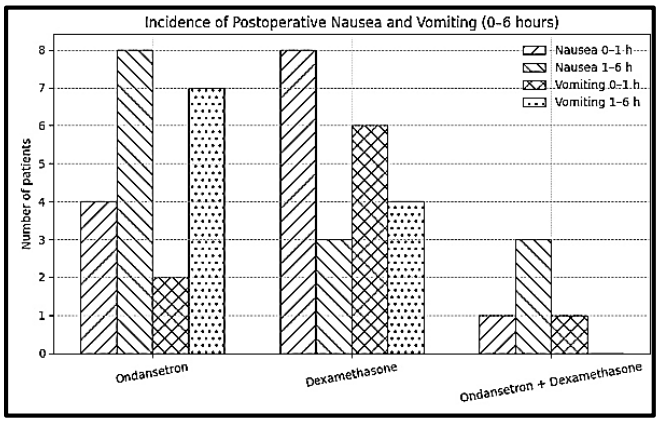

Figure 1: Incidence of nausea and vomiting (0-6 hours)

The overall incidence of postoperative nausea and vomiting (0–6 hours) was significantly reduced in the combination group compared to the individual drug groups ($p < 0.001$). When analyzed temporally, both early (0–1 hour) and late (1–6 hours) episodes of nausea and vomiting were significantly less frequent in the ondansetron–dexamethasone group ($p < 0.05$). Late postoperative vomiting was absent in the combination group, whereas it persisted in both monotherapy groups.

6. Discussion

The findings of this study indicate that concurrent administration of ondansetron and dexamethasone provides superior prophylaxis against PONV compared with monotherapy using either agent. The combination group demonstrated a lower overall incidence of nausea and vomiting, fewer breakthrough episodes, and reduced requirement for rescue antiemetic medication. ENT procedures represent a unique clinical context due to direct vestibular stimulation and heightened susceptibility to motion-related emetic pathways.[12] The relatively elevated baseline incidence observed in this study is therefore consistent with previously published data. Even subtle manipulation of the middle ear may activate neural circuits analogous to motion sickness, thereby amplifying nausea during the recovery phase.

Patients receiving ondansetron alone exhibited effective early-phase control of symptoms. This observation aligns with its established pharmacodynamic profile targeting 5-HT_3 receptors implicated in serotonin-mediated vagal transmission.8[8] However, the protective effect appeared to diminish during later postoperative intervals, likely reflecting its relatively short half-life. Comparable temporal patterns have been described in previous ear surgery studies comparing ondansetron with alternative agents such as droperidol.[7]

Dexamethasone monotherapy displayed a contrasting pattern, with relatively improved control during later postoperative periods. Corticosteroids exert genomic and anti-inflammatory effects that require time to manifest, which may explain the delayed onset of antiemetic action.[9,10] Systematic reviews and meta-analyses have confirmed dexamethasone's particular effectiveness in preventing late PONV rather than immediate postoperative nausea.[9]

The enhanced outcomes observed with combination therapy can be interpreted through the lens of complementary pharmacology. Ondansetron primarily attenuates acute serotonin-mediated stimulation, whereas dexamethasone modulates inflammatory processes and central neurotransmitter activity over a longer duration. The integration of these mechanisms broadens the temporal coverage of prophylaxis and reduces the likelihood of breakthrough symptoms. Large-scale analyses have consistently demonstrated incremental reductions in PONV when antiemetic agents from different pharmacological classes are combined.[11] Contemporary consensus recommendations reflect this evidence base and endorse multimodal prophylaxis in patients presenting with two or more risk factors.[1,2] ENT surgeries frequently meet criteria for high-risk categorization, thereby supporting routine consideration of combination therapy in such cases.

Beyond pharmacologic interventions, modification of anaesthetic techniques also influences PONV incidence. Avoidance of nitrous oxide and minimization of volatile anaesthetic exposure have been shown to reduce early postoperative vomiting.[6,14] Economic evaluations further indicate that effective prophylaxis in high-risk populations is cost-efficient by decreasing unplanned admissions and enhancing patient satisfaction.[15]

Another clinically relevant finding in the present study was the lower necessity for rescue antiemetics in the combination group. Recurrent vomiting following ENT surgery may increase postoperative discomfort, compromise wound integrity, and elevate the risk of aspiration or bleeding.[16] Thus, preventing breakthrough episodes contributes not only to symptomatic relief but also to improved surgical outcomes.

Although the observational design limits definitive causal inference, the study benefitted from standardized anaesthetic protocols and consistent surgical populations, reducing variability. Nevertheless, certain limitations merit consideration. Assessment was primarily confined to the early postoperative window, potentially underestimining delayed symptoms occurring beyond 24 hours. Additionally, nausea severity was not quantified using a validated numerical scale, which might have provided more granular insights.

Despite these limitations, the findings align closely with established evidence supporting multimodal prophylaxis.[1,2,11,17] Rational management algorithms emphasize individualized, risk-based strategies rather than uniform single-agent approaches.[17,18] The collective data suggest that targeting multiple receptor pathways simultaneously yields more comprehensive symptom control.

Overall, PONV following ENT surgery is driven by both immediate serotonergic stimulation and sustained inflammatory or central mechanisms.[5,9] Addressing these distinct yet overlapping pathways through combination therapy appears to offer the most effective strategy for minimizing postoperative emesis in this high-risk population.

7. Conclusion

Combined prophylaxis with ondansetron and dexamethasone offers more consistent and sustained protection against postoperative nausea and vomiting than either agent alone in elective ENT surgeries. The dual regimen effectively reduces early and late emetic episodes and minimizes the need for rescue antiemetics. Given the high emetogenic potential associated with vestibular and middle ear procedures, a multimodal antiemetic strategy should be considered in appropriately risk-stratified patients to enhance postoperative comfort and recovery quality.

8. Source of Funding

None.

9. Conflict of Interests

None.

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