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Effectiveness of Ondansetron Alone Versus Ondansetron-Dexamethasone in the Prevention of Postoperative Nausea and Vomiting Following Laparoscopic Cholecystectomy

Dr. Harleen Kaur[1], Dr. Melchisedec Singh[2], Dr. Valsamma Abraham[3]

[1]MD Anaesthesia, Senior Resident, Department of Anaesthesia and Critical Care, Christian Medical College and Hospital, Ludhiana, Punjab, India.
Email: *harleenk824[at]gmail.com*

[2] MBBS, MD Anaesthesia, Professor, Department of Anaesthesia and Critical Care, Christian Medical College and Hospital, Ludhiana, Punjab. Address: Doctor's Colony, CMC campus, Ludhiana 141008, India.
Email: *melchisedec.singh[at]cmcludhiana.in*

[3] MBBS, DA, MD Anaesthesia, Professor, Department of Anaesthesia and Critical Care, Christian Medical College and Hospital, Ludhiana, Punjab. Address: Doctor's Colony, CMC campus, Ludhiana 141008, India.
Email: *dr_valsa[at]yahoo.com*

Abstract: ***Postoperative nausea and vomiting (PONV) continue to be generally observed and troubling side effects of general anaesthesia, especially after laparoscopic surgeries. Ondansetron, a selective 5-HT$_3$ receptor antagonist, is frequently implemented for the prophylaxis of PONV. However, concomitant medication may increase its efficacy. This prospective, randomized, double-blind study was performed over 18 months at a tertiary care teaching hospital to assess the efficacy of ondansetron monotherapy compared to a combination of ondansetron-dexamethasone is preventing PONV after laparoscopic cholecystectomy. There were 60 patients having ASA physical status I and II, and their age lied between 18 and 60 years. They were split into two groups of 30 people each at random. Group A was provided 4 mg of ondansetron. A visual analogue scale was used to compute the frequency and intensity of nausea, retching, and vomiting at 0, 2, 4, 8, 12, and 24-hours following surgery. The combined group showed a significantly reduced incidence of nausea, retching, and vomiting, necessitating substantially less rescue antiemetic medication in comparison to the ondansetron-only group ($p<0.05$). The negative effects were similar in both groups. The study shows that taking ondansetron and dexamethasone together works better than just taking ondansetron to stop nausea and vomiting after laparoscopic cholecystectomy.***

Keywords: Dexamethasone, General anaesthesia, Laparoscopic cholecystectomy, Ondansetron, Postoperative nausea and vomiting

1. Introduction

One of the most common and unpleasant side effects of general anaesthesia is PONV. It happens to 20% to 30% of people who have surgery and up to 70% of people who are at high risk (1). PONV is often thought of as a minor problem after surgery, but it can cause a lot of pain for patients, delay their recovery, lengthen their hospital stay, and raise their healthcare costs. In extreme cases, it can cause problems like dehydration, an imbalance of electrolytes, wound dehiscence, bleeding, aspiration, and higher pressure in the brain or eyes (1,5).

PONV is the state when you fill sick, throw up, or feel sick to your stomach within the first 24 hours after surgery (2). It is complex disease that is influenced by things about the patient, like women, not smoking, being younger, and having a history of motion sickness or PONV. Things that have to do with anaesthesia consisting utilizing volatile anaesthetics, nitrous oxide, opioids after surgery, and being under anaesthesia for a long time. Surgical factors are also very essential. Laparoscopic treatments, abdominal surgeries, cholecystectomy, gynaecological surgery, and neurosurgery procedures are correlated with a heightened occurrence of PONV. Risk stratification methods, such as Apfel risk score, are sometime used to find people who are more likely to get sick and the help doctors choose the right antiemetic medicine (3,4).

Laparoscopic cholecystectomy is related with significantly enhanced incidence of PONV, because of factors like pneumoperitoneum with carbon dioxide insufflation, peritoneal irritation, and the requirement for postoperative opioids. Laparoscopic surgery is better than open surgery as it is better than open surgery because it hurts less afterward, you do not have to stay in the hospital as long, and it helps in healing faster. But it is still very essential to stop PONV to get the better results after surgery and make patients happy (5, 6).

The pathophysiology of PONV encompasses different neurotransmitter pathways and systems of receptor, consisting of serotonin (5-HT$_3$), dopamine (D_2), histamine (H_1), muscarinic (M_1), neurokinin-1 (NK_1), and gamma-aminobutyric acid (GABA) receptors. This complex method explains why single-agent therapy does not work for patients at high risk and backs up the idea of using combined antiemetic therapy to target various pathways (7).

Ondansetron is a type of selective 5-HT$_3$ receptor antagonist, commonly used antiemetic drugs to prevent PONV at it works fast, has low side effects, and is effective. It works by stopping serotonin receptors in chemoreceptor trigger zone and the

digestive system. Dexamethasone, a synthetic corticosteroid, has represented significant antiemetic properties, particularly when administered prophylactically (10). It is thought that its method of action includes blocking the brain from making prostaglandins, reducing the amount of serotonin released in the gut, and having anti-inflammatory effects. When used together, ondansetron and dexamethasone work on various pathways that cause vomiting, which makes both early and late PONV less likely to happen (9).

Even though ondansetron is widely used, researchers are still trying to figure out what the best antiemetic regimen is for people having laparoscopic cholecystectomy. The objective of this study is to compare ondansetron monotherapy with ondansetron–dexamethasone combination therapy for the prevention of nausea and vomiting in patients undergoing laparoscopic cholecystectomy under general anaesthesia.

2. Literature Survey

PONV have been thoroughly studied because it happens a lot and makes recovery after surgery much harder, especially after laparoscopic procedures done with general anaesthesia. There are a number of risk factor that are related to the patient and the procedure. (1) Stated that being a woman, not smoking, using opioids after surgery and having laparoscopic surgery are all major risk factors for PONV. They also stressed the importance of multimodal antiemetic prophylaxis for patients who are at high risk. (2) Similarly showed that serotonin ($5\text{-}HT_3$) receptor antagonists are effective at reducing early postoperative emetic symptoms, which shows that they should be the first choice for preventing PONV.

Ondansetron, a selective $5\text{-}HT_3$ receptor antagonist, has undergone extensive research regarding its efficacy and favourable safety and tolerability in preventing PONV. Nevertheless, despite its prevalent application, ondansetron as a solitary agent may not offer sufficient protection in high-risk surgical interventions. Bhattarai et al. examined a comparison between ondansetron monotherapy and its conjunction with dexamethasone in patients having laparoscopic surgery, revealing a markedly reduced incidence of PONV in the combination cohort. In a comparable study, Rajeeva et al. (11) identified that adding dexamethasone to ondansetron increase antiemetic effectiveness without elevating side effects, showing a synergistic benefit.

Dexamethasone is a common add-on antiemetic because it lasts a long time, doesn't cost much, and can make another antiemetic perform better. McKenzie et al. identified that using ondansetron and dexamethasone together greatly reduced the vomiting risk after surgery, both in the early and the late stages, compared to using ondansetron alone. Sanjowal et al. (12) further validated these findings by demonstrating a reduced requirement for rescue antiemetic medicine in patients undergoing laparoscopic cholecystectomy when combination therapy was employed.

3. Problem Definition

Despite advancements in anaesthetic techniques and the consistent administration of prophylactic antiemetics, PONV continues to be a significant therapeutic challenge following laparoscopic cholecystectomy. The complex pathophysiology of PONV, involving serotonergic, dopaminergic, histaminergic, and neurokinin pathways, limits the effectiveness of single-drug prophylaxis. Persistent postoperative nausea, retching, or vomiting adversely affects patient comfort, obstructs oral intake and ambulation, prolongs recovery room length and may lead to problems like dehydration, imbalance of electrolyte, dehiscence of wound, aspiration, and increased healthcare costs. Numerous studies support the effectiveness of combination antiemetic therapy; however, there is considerable diversity regarding patient demographics, surgical techniques, pharmaceutical dosages, and assessment intervals.

Furthermore, there is a paucity of data from single-centre randomized controlled trials specifically examining laparoscopic cholecystectomy in the Indian population using standardized assessment instruments. This underscores the necessity for additional controlled clinical trials in tertiary care environments to ascertain the efficacy safety and influence on rescue antiemetic needs of ondansetron alone compared to ondansetron in conjunction with dexamethasone within this particular surgical subgroup.

4. Methodology/Approach

This research was evaluated as prospective, randomized, double-blind clinical trial over 18 months, from August 2022 to January 2024, at a tertiary care teaching hospital. The Institutional Ethics Committee gave its approval ahead of time, and all participants gave their written well-versed agreement before being accepted. This study included sixty individuals who were going to have elective laparoscopic cholecystectomy performed under general anaesthesia.

Study Population
Individuals aged 18-60 years, classified as American Society of Anaesthesiologists (ASA) physical status I and II, regardless of gender were eligible for inclusion. Patients with a history of motion sickness or PONV, known hypersensitivity to the study drugs, chronic steroid or opioid use, significant renal or hepatic dysfunction, middle ear disease, gastrointestinal obstruction, or any condition associated with delayed gastric emptying were not allowed to participate.

Randomization and Blinding
Participants were assigned to two groups of 30 each through computer-generated randomization. Allocation concealment was preserved using sealed, opaque envelops prepared and overseen by personnel not involved in the study. An anaesthesiologist who was not in charge of patient care or data collection made the study drugs which made sure that both the patients and the investigators were blind to what was going on.

Intervention
Group A (Combination Group): Patients got 4mg of ondansetron and 4mg of dexamethasone through an IV, mixed with 100 ml of normal saline, 10 minutes before the start of anaesthesia.

Group B (Ondansetron Group): Patients received 4 mg of ondansetron through an IV, mixed with 100 ml of normal saline, 10 minutes before anaesthesia was started.

Anaesthesia Technique

Upon arrival at the operation room, the patient had standard monitoring, consisting of non-invasive blood pressure measurement, pulse oximetry, and ECG monitoring. The patient was put to sleep by intravenous fentanyl ($1\mu g$/kg) and propofol (2 mg/kg). Atracurium (0.5 mg/kg) was then administered to facilitate tracheal intubation. The patient was kept sleeping with isoflurane (0.8-1.5%) in a 2:2 mixture of oxygen and nitrous oxide. Following surgery, the neuromuscular blockade was reversed using glycopyrrolate (0.01 mg/kg) and neostigmine (0.05 mg/kg). After the defined extubation criteria were met, tracheal extubation was used.

Outcome Assessment

Nausea, retching, and vomiting after surgery were checked right after the surgery and then again at 2, 4, 8, 12, and 24 hours after the surgery. A visual analogue scale (VAS) from 0 to 10 was used to rate how bad the nausea was. A VAS score of 5 or higher or vomiting were treated with intravenous ondansetron (0.1 mg/kg) as a backup antiemetic. Patients were also watched for bad drug reactions such as headaches, dizziness, anxiety and constipation.

Statistical Analysis

The data was grouped and evaluated utilizing the Statistical Package for the Social Science (SPSS) version 28. Descriptive statistics were displayed data were reported as percentages for categorical variables and as mean ± standard deviation for continuous variables. Categorical data was evaluated using the χ^2-test or Fisher's exact test, as applicable. To identify if the data was normally distributed, the Kolmogorov-Smirnov test was employed. Results were regarded as statistically significant when the p-value was below 0.05.

5. Result & Discussion

Sixty patients who were going to have elective laparoscopic cholecystectomy were included in the study and randomly grouped into two equal groups. Group A was provided ondansetron and dexamethasone together, while Group B was only provided ondansetron. The demographic characteristics, including age, gender, and (Body Mass Index) BMI, were similar between the two groups, ASA physical status. The two group's baseline clinical and demographic features did not differ statistically significantly ($p > 0.05$), showing appropriate randomization and ensuring that observed differences in outcomes were attributable to the study interventions.

Postoperative Nausea

Patients who got both ondansetron and dexamethasone had a lot less nausea after surgery than those who only got ondansetron. Table 1 represents that 56.6% of patients in Group A had no nausea at all in the first 24 hours after surgery, while only 26% of patients in Group B had no nausea ($p = 0.018$). The temporal analysis also showed that nausea was more common and lasted longer at various times after surgery in Group B. Figure 1 shows this trend in a graph.

Table 1: Comparison of two group's postoperative nausea at various points in time

Nausea	Ondansetron + Dexamethasone (n=30)	Ondansetron (n=30)	p-value
No nausea	17 (56.6%)	8 (26.6%)	0.018
0 hour	5 (16.6%)	5 (16.6%)	0.319
2 hours	3 (10%)	7 (23.3%)	0.580
4 hours	1 (3.3%)	4 (13.3%)	0.391
8 hours	0	3 (10%)	—
12 hours	1 (3.3%)	3 (10%)	0.593
24 hours	3 (10%)	0	—
Total patients with nausea	13 (43.3%)	22 (73.3%)	0.018

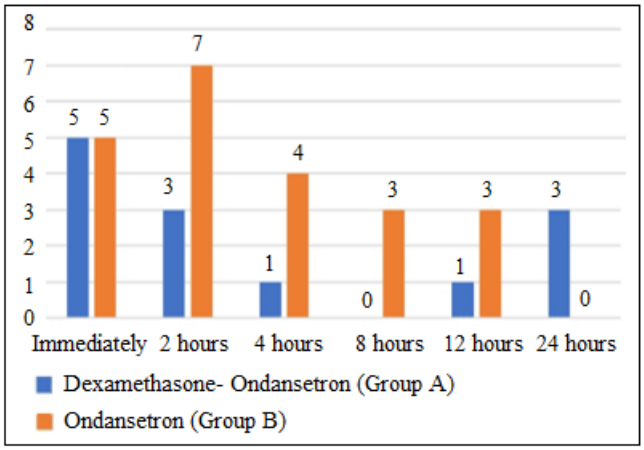

Figure 1: Comparison of the group's post-operative nausea at various time points

These results align with prior research conducted by Ahsan et al. and Sanjowal et al., which illustrated enhanced nausea management through combination antiemetic therapy post-laparoscopic cholecystectomy (6,12). The enhanced efficacy is due to the combined effects of ondansetron, which blocks both peripheral and central 5-HT_3 receptors, and dexamethasone, which works against nausea, inflammation, and prostaglandins in the brain.

Postoperative Retching

Retching happened significantly less often in the ondansetron-dexamethasone group. Table 2 shows that only one patient (3.3%) in Group A had retching, while seven patients (23.3%) in Group B did, which was statistically significant difference ($p = 0.022$). Figure 2 shows how many times people retched at different times after surgery.

Table 2: Comparison of postoperative retching between two groups

Retching	Ondansetron + Dexamethasone (n=30)	Ondansetron (n=30)	p-value
No retching	29 (96.6%)	23 (76.6%)	0.022
Immediate	0	1 (3.3%)	—
2 hours	1 (3.3%)	1 (3.3%)	—
4 hours	0	2 (6.6%)	—
8 hours	0	2 (6.6%)	—
12 hours	0	1 (3.3%)	—
24 hours	0	0	—
Total patients with retching	1 (3.3%)	7 (23.3%)	0.022

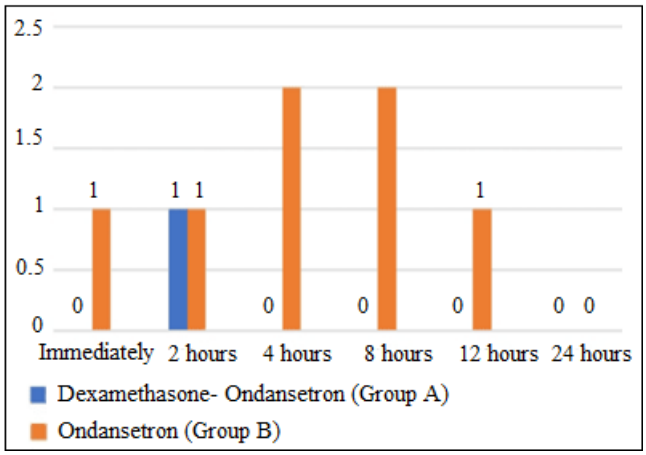

Figure 2: Comparison of post operative retching between the groups at various intervals.

These finding support the hypothesis that combination therapy more effectively inhibits the intricate neural mechanisms associated with retching. Shivanna et al. and McKenzie et al. have reported analogous finding, noting a diminished occurrence of retching with ondansetron-dexamethasone combination therapy in patients undergoing laparoscopic and other surgical procedures (13, 14).

Postoperative Vomiting

Patients who got combination therapy had a lot less vomiting after surgery. Table 3 highlight that 86.6% of patients in Group A did not vomit at all, while only 33.3% among Group patients. A highly significant statistical difference was observed (p = 0.000025). Figure 2 shows the pattern of vomiting incidence over various postoperative intervals. It shows that the combination group had a consistently lower incidence.

Table 3: Comparison of Postoperative Vomiting

Vomiting	Ondansetron + Dexamethasone (n=30)	Ondansetron (n=30)	p-value
No vomiting	26 (86.6%)	10 (33.3%)	0.000025
Immediate	0	4 (13.3%)	—
2 hours	3 (10%)	2 (6.6%)	—
4 hours	0	5 (16.6%)	—
8 hours	0	4 (13.3%)	—
12 hours	0	5 (16.6%)	—
24 hours	1 (3.3%)	0	—
Total patients with vomiting	4 (13.3%)	20 (66.6%)	0.000025

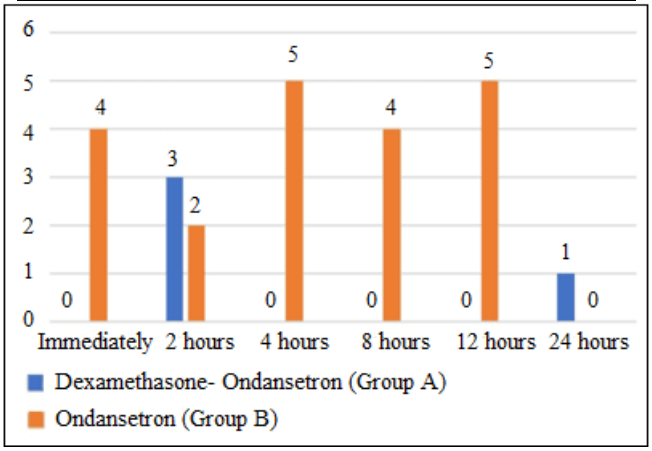

Figure 3: Comparison of post operative vomiting of the groups at various intervals

The noted reduced occurrence of vomiting in Group A corresponds with previous findings by Rajeeva et al. and Sanjowal et al., which showed the efficacy of ondansetron-dexamethasone combination therapy over ondansetron monotherapy in mitigating postoperative vomiting (11, 12). The improved efficacy is likely due to the dual mechanism of action that targets both peripheral serotonergic pathways and central inflammatory mediators.

Adverse Drug Reactions

The adverse drug reactions were mild and similar in both groups. Table 4 shows that 20% in Group A and 30% of patients in Although side effects were reported in Group B, the comparison between the two groups did not show statistical significance (p = 0.371). Figure 4 shows how common side effects such as dizziness, anxiety, and headaches are.

Table 4: Comparison of adverse drug reactions

Adverse Effect	Ondansetron + Dexamethasone	Ondansetron	p-value
No reaction	24 (80%)	21 (70%)	0.371
Dizziness	3 (10%)	2 (6.6%)	0.263
Anxiety	2 (6.6%)	4 (13.3%)	0.669
Headache	1 (3.3%)	2 (6.6%)	0.792
Constipation	0	1 (3.3%)	—
Total ADR	6 (20%)	9 (30%)	0.371

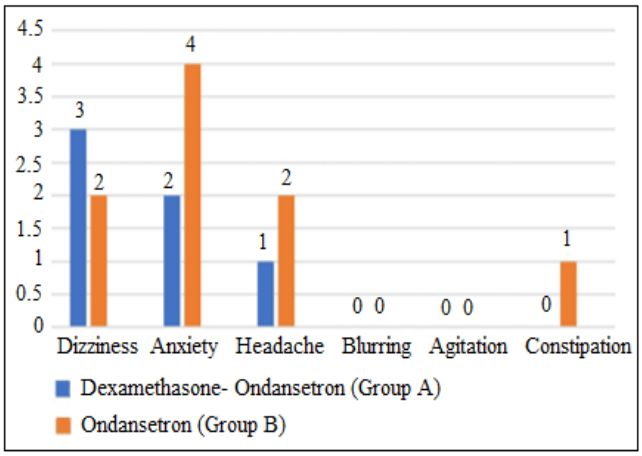

Figure 4: Comparison of rescue medication requirement between the groups at 24 hours

These findings are consistent with the systematic study by Henzi et al., which concluded that the incorporation of dexamethasone into 5-HT3 receptor antagonists does not significantly increase the probability of adverse effects (15). It is important to record that neither group had any big issues or drug-related illnesses, which represents that the combination regimen is safe.

Requirement of Rescue Antiemetic

The group who took ondansetron and dexamethasone needed rescue antiemetic drugs substantially less often. Table 5 highlights that only one patient (3.3%) from Group A required rescue antiemetic medication, but eleven patient (36.6%) from Group B did (p = 0.0012). Figures represent this difference very clear.

Table 5: Requirements of rescue antiemetic within 24 hours

Rescue medication	Ondansetron + Dexamethasone	Ondansetron	p-value
Yes	1 (3.3%)	11 (36.6%)	0.0012
No	29 (96.6%)	19 (63.3%)	

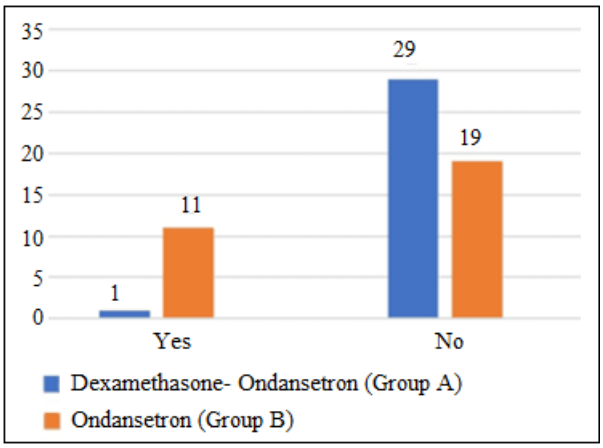

Figure 5: Comparison of rescue medication requirement between the groups at 24 hours

The diminished requirements for rescue medication signifies enhanced prophylactic efficacy of the combination therapy, bearing significant ramifications for patient comfort, expedited postoperative recovery, and healthcare resource allocation. Bhattarai et al. and Shivanna et al. have both reported similar decreases in the need for rescue antiemetics in patients receiving combination antiemetic prophylaxis (8, 14).

6. Conclusion

Postoperative nausea and vomiting persist as prevalent and clinically significant complications subsequent to laparoscopic cholecystectomy performed in presence of general anaesthesia. The finding of this research shows that the prophylactic administration of ondansetron in conjunction with dexamethasone is substantially more effective than ondansetron alone in mitigating postoperative nausea, retching, vomiting. The combination therapy not only lowered the overall number and severity of PONV cases but it also greatly cut down on the need for rescue antiemetic medication. There was no statistically significant difference in the number of adverse drug reactions between the two groups, so both treatment plans were well tolerated. Adding dexamethasone did not cause more side effects, which shows that it is safe to use as an extra antiemetic agent. In conclusion, the ondansetron-dexamethasone combination offers superior and safe prophylaxis against PONV and should be regarded as the preferred antiemetic strategy for patients undergoing laparoscopic cholecystectomy under general anaesthesia.

7. Future Scope

The present study indicates the improved effectiveness of ondansetron-dexamethasone combination therapy in alleviating PONV following laparoscopic cholecystectomy; however, further investigation is required to strengthen and expand these findings. Future research utilizing larger sample sizes and multicentric designs may improve the applicability of the results across various patient populations and healthcare environments. Comparative studies assessing the ondansetron-dexamethasone combination against newer antiemetic agents or multimodal antiemetic protocols may clarify the most cost-effective and clinically efficient strategies for the prophylaxis of PONV. Furthermore, assessing the effectiveness of combination therapy in high-risk patient populations, including individuals with elevated Apfel risk scores or those undergoing extended and intricate laparoscopic procedures, may aid in the formulation of customized antiemetic approaches.

Additional research concentrating on optimal drug dosing, administration, timing, and long-term outcomes- encompassing patient satisfaction, recovery quality, and hospital resource utilization- may aid in the development of evidence-based, standardized protocols for the management of PONV in laparoscopic surgeries.

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