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Inhaled isopropyl alcohol vs. intravenous ondansetron for postoperative nausea following laparoscopic cholecystectomy under general anaesthesia: A comparative study

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Abstract

Introduction: Postoperative nausea (PON) and vomiting remain common and distressing problems, affecting up to 30% of surgical patients globally. While intravenous ondansetron is a widely used antiemetic, inhaled isopropyl alcohol offers a rapid, low-cost alternative. This study compared the effectiveness of inhaled isopropyl alcohol versus intravenous ondansetron for PON.

Method: After ethical approval, this prospective, randomised comparative study included ASA I–II adults (18–50 years) undergoing elective laparoscopic cholecystectomy under general anaesthesia during Mar 2024–Mar 2025 at Chitwan Medical College, Nepal. Patients developing PON in the post-anaesthesia care unit were randomised to receive either inhaled isopropyl alcohol (Gr-IPA) or 4 mg intravenous ondansetron (Gr-O). Nausea severity was measured using a verbal numeric rating scale (VNRS) at baseline and at 5-minute intervals for 30 minutes. Data were checked for normality, and analysed using IBM SPSS v-20 (independent t-test/Mann-Whitney U for numerical data; Chi-square/Fisher exact for categorical data). A $p<0.05$ was considered significant.

Result: Of 94 enrolled patients, 91 completed the study. Mean age was 34.86±9.00 years in Gr-IPA and 36.89±8.27 years in Gr-O ($p>0.05$). In Gr-IPA, 24(54.5%) were females; in Gr-O, 29(61.7%) females ($p>0.05$). Gr-IPA showed significantly lower median VNRS scores at 5 and 10 minutes ($p<0.001$), indicating faster relief. From 20 minutes onward, Gr-O demonstrated more sustained nausea reduction ($p<0.001$).

Conclusion: Our findings suggest that inhaled isopropyl alcohol may serve as a rapid, simple, and cost-effective alternative to intravenous ondansetron for initial management of post-operative nausea.

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Introduction

Post-operative nausea and vomiting (PONV) is described as nausea and/or vomiting or retching in the immediate 24 postoperative hours.[1] Globally, it affects around 30% of patients, while in Nepal, incidence rates of 14% - 49% have been reported.[2-4] Factors like female sex, non-smoker, history of motion sickness, previous PONV, laparoscopic surgeries, opioid use, etc. are risks for development of PONV.[1]

Postoperative nausea (PON) and PONV are significant causes of patient dissatisfaction, with some patients rating them as distressing as postoperative pain.[5] It can lead to a range of complications, including dehydration, electrolyte disturbances, wound dehiscence, aspiration pneumonia, and elevated intraocular and intracranial pressures which contributes to delayed recovery and prolonged hospital stay.[6]

Ondansetron, a 5HT3 antagonist, is widely used for prophylaxis and management of PON/PONV. However, it is associated with common side effects such as headache, constipation, and dizziness, and rarely serious risks of QT interval prolongation and serotonin syndrome.[7] Inhalational therapy with isopropyl alcohol (IPA) has been emerging as a non-pharmacological modality for attenuation of PON with advantages like low cost, ease of administration, and minimal side effects. It is hypothesised to be effective, likely through olfactory distraction and trigeminal stimulation that modulates central emetic pathways, though the exact mechanism remains unclear.[8-11]

This study was therefore conducted to compare the effectiveness of inhaled isopropyl alcohol versus intravenous ondansetron in the treatment of postoperative nausea, with the aim of evaluating isopropyl alcohol as a potential alternative to ondansetron in local clinical setting.

Method

This prospective, hospital-based, randomised, comparative study was conducted from Mar 2024 to Mar 2025 in the operation theatre of Chitwan Medical College and Teaching Hospital, Nepal. Ethical approval was obtained from CMC-IRC (CMC/ADM/079/0801910) before the study.

The sample size was calculated based on a previous study, which reported a 14% prevalence of PONV in laparoscopic cholecystectomy under general anaesthesia.[3] Using the formula, $n=Z^2*p*q/e^2$; Z=1.96 for a 95% confidence level, p=0.14, q=1−p=0.86, margin of error (e) of 7%. The n=94 was equally divided into two groups, 47 each, in Group IPA (inhaled isopropyl alcohol) and Group O (intravenous ondansetron).

Post-hoc power analysis to assess sample size adequacy for comparative study to detect a clinically meaningful difference. For a 1.5 points difference in VNRS scores with a standard deviation of 2.0, the sample size could achieve approximately 80% power at a 5% significance level (two-tailed). This supports the study's ability to detect significant differences between the groups, although initially sample size was estimated using a prevalence formula.[12]

Adult patients aged 18 to 50 years belonging to ASA physical status I or II undergoing elective laparoscopic cholecystectomy under general anaesthesia who developed nausea and provided informed written consent were included. Patients were excluded from the study if they had pre-existing nausea, a known allergy to study drugs, history PONV requiring multiple prophylactic agents, nasal obstruction, pregnancy, chronic alcoholism, or were on disulfiram or medications known to cause disulfiram-like reactions when combined with alcohol.

A day before the date of surgery, a detailed pre-anaesthetic assessment was performed. They were educated about possibility of PON/PONV and were instructed to report the occurrence and severity of nausea using a verbal numeric rating scale (VNRS) ranging from 0 (no nausea) to 10 (worst possible nausea). The study procedure, with risks and benefits, was explained to the understanding of the patients and informed written consent was taken. Patients were kept nil per oral for 8 hours for a solid meal and 2 hours for clear liquid prior to the surgery.

On the day of surgery, in the preoperative area, patients were assessed for any complaint of nausea and were excluded from the study if present. In the operating room, routine monitors according to ASA standards were attached, and baseline vital parameters were recorded. Induction of GA was done with intravenous fentanyl (2 µg/kg) and titrated doses of propofol until loss of verbal response, followed by rocuronium (1 mg/kg) to facilitate tracheal intubation. An orogastric tube was inserted to evacuate gastric contents and improve surgical visualisation. Anaesthesia was maintained with isoflurane in a mixture of oxygen and air. At the end of surgery, orogastric tube was removed then neuromuscular blockade was reversed with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg) intravenously for extubation.

In the postoperative period, in post-anaesthesia care unit (PACU), upon the first complaint of nausea, patients were assessed for the severity of PON using VNRS. The PON was defined as a subjective unpleasant sensation associated with the urge to vomit. Patients with a VNRS score ≥3 were sequentially randomised into either Gr-IPA or Gr-O using a computer-generated randomisation sequence.

Patients in Gr-IPA received inhalational therapy with a 70% isopropyl alcohol preparation pad (Lifeline) held approximately 2 cm from the nares, with instructions to take three deep breaths. Patients in Gr-O were administered intravenous ondansetron, 4 mg.

A pre-intervention VNRS for PON was recorded by the anaesthesiologists involved in the study on a structured proforma then repeated every 5 minutes for up to 30 minutes following treatment. If there was no reduction in the severity of nausea, the assigned treatment was repeated once after 15 minutes. Rescue therapy with intravenous promethazine 12.5 mg was administered to patients who experienced worsening of nausea severity at any time during the observation period, including those who initially improved but subsequently showed increased severity, as well as to patients who showed no improvement by the 30-minute observation point. Patients who developed vomiting at any point during the study were excluded from further analysis and subsequently managed as per institutional protocol.

Data were tested for normality using the Shapiro–Wilk test and Levene's test for homogeneity of variances. Measure of central tendency (mean, median) was used to express numerical data (continuous variable age and ordinal VNRS), and compared between groups (independent sample t-test for normally distributed data, or Mann-Whitney U test for non-normal distribution). Categorical variables (gender, ASA physical status and need for repeat intervention, rescue therapy) were expressed in n(%) and analysed using the Chi-square or Fisher exact test. Statistical analysis was performed using IBM SPSS Statistics version 20. A $p<0.05$ was considered statistically significant.

Result

Out of the 94 patients initially enrolled, 91 completed the study. Three patients from the isopropyl alcohol (IPA) group were excluded due to vomiting during the intervention period.

Data were normally distributed. In Gr-IPA, out of 44 patients, 24(54.5%) were females. In Gr-O, out of 47 patients, 29(61.7%) were females. The mean age was 34.86±9.00 years in the Gr-IPA and 36.89±8.27 years in Gr-O.

Baseline characteristics, including age, gender, and ASA physical status, were comparable between the two groups ($p>0.05$), Table 1.

The pre-intervention median VNRS scores for PON were similar in both groups, with no statistically significant difference ($p=0.77$). At 5- and 10-minute time points, Gr-IPA demonstrated significantly lower median VNRS scores compared to Gr-O, ($p<0.05$), Table 2.

By 15 minutes, the difference between the groups was no longer statistically significant ($p=0.276$), Table 2.

From 20 minutes onward (i.e., at 20, 25, and 30 minutes), Gr-O showed progressively lower

median VNRS scores compared to the Gr-IPA with statistical significance (p<0.05), Table 2.

The trend of VNRS score from baseline to different points of time at 5-minute intervals showed an initial faster fall in Gr-IPA, but less sustained over time compared to Gr-O, Figure 1.

The need for repeat intervention was higher in Gr-IPA, with 12(27.27%) patients requiring additional dosing compared to 3(6.38%) in Gr-O (p=0.007), Figure 2.

Following the repeat intervention, a progressive decrease in VNRS scores was noted at subsequent time points of 20, 25, and 30 minutes in both groups. A significantly higher proportion of patients in Gr-IPA required rescue antiemetic therapy, 12(27.27%), compared to Gr-O, 6(12.77%), p=0.042, Figure 2.

Table 1. Characteristics of LC patients receiving inhaled isopropyl alcohol (IPA) vs. intravenous ondansetron (O) for PON, n=91

Variable	Gr-IPA (n=44)	Gr-O (n=47)	p-value
Age (mean±SD)	34.86±9.00	36.89±8.27	0.265*
Gender (Male / Female)	20 / 24	18 / 29	0.489**
ASA Class (I / II)	22 / 22	30 / 17	0.183**

LC-Laparoscopic cholecystectomy, PON-postoperative nausea, ASA-American Society of Anaesthesiologists physical status, *independent sample t-test, **Chi-square test

Table 2: Pre- and post-intervention median VNRS scores PON in Gr-IPA vs. Gr-O after LC, n=91

Observation time points	Median VNRS for PON		p-value
	Gr-IPA (n=44)	Gr-O (n=47)	Mann-Whitney U test
Pre-intervention	6	6	0.77
5 minutes	5	6	0.001
10 minutes	3	6	0.001
15 minutes	4	4	0.224
20 minutes	4	3	0.001
25 minutes	3	2	0.001
30 minutes	1	0	0.001

VNRS- visual numerical rating scale

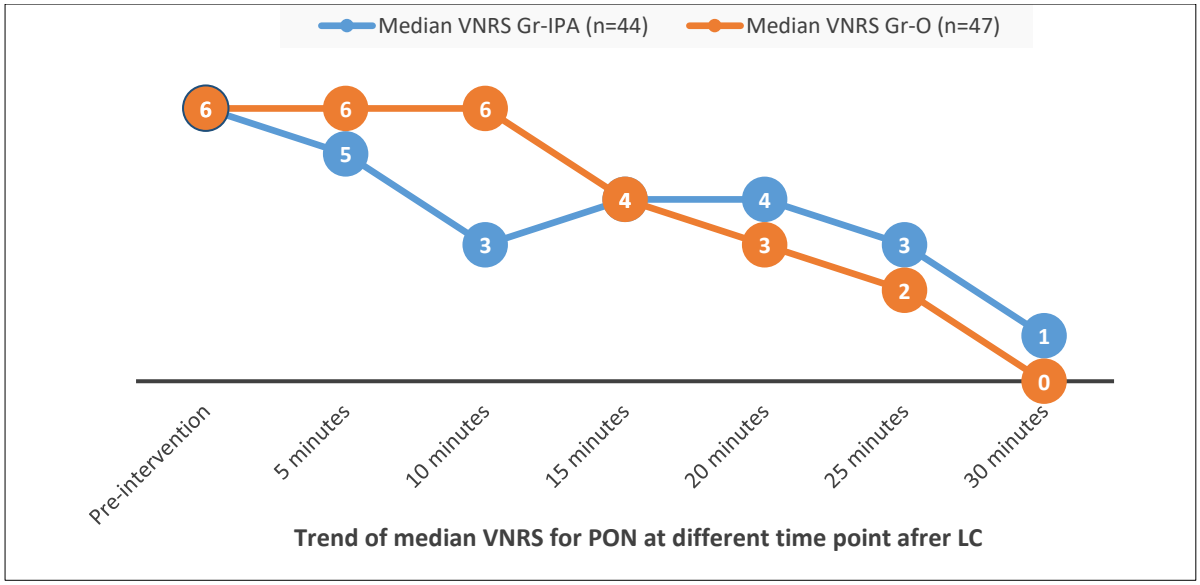

Figure 1. Median VNRS for PON at pre- and post-intervention time points after LC, n=91

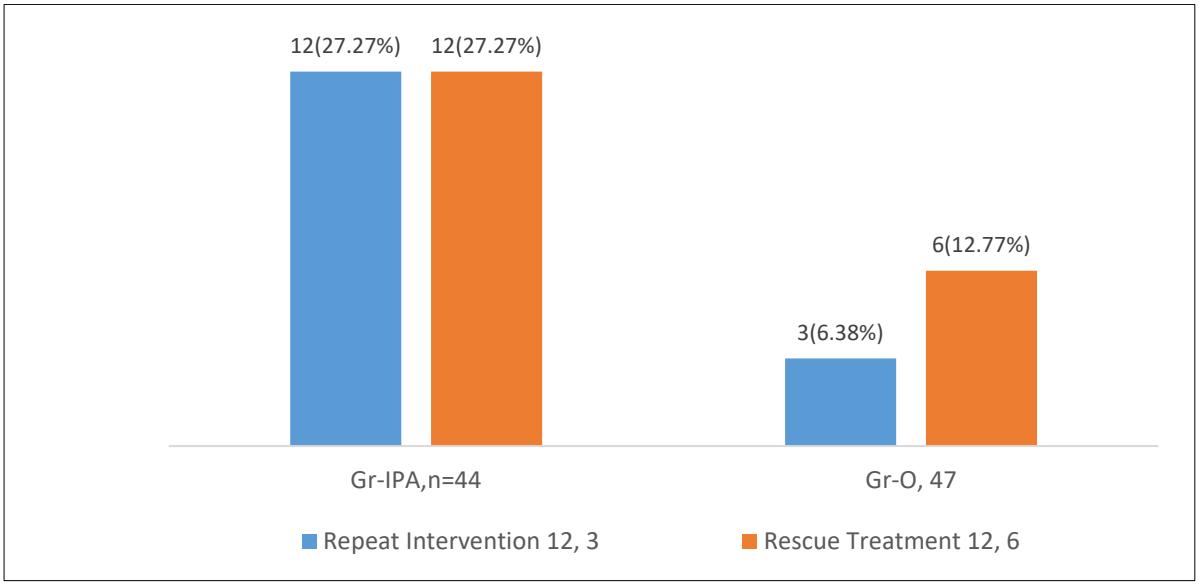

Figure 2. Patients requiring repeat intervention and rescue treatment for PON in Gr-IPA and Gr-O, n=91

Discussion

This study demonstrates that IPA provides a rapid reduction in nausea after general anaesthesia in laparoscopic cholecystectomy patients compared to ondansetron.

Our findings demonstrated that inhaled IPA provides a faster relief for PON, with significantly lower median VNRS scores at 5- and 10-minute compared to intravenous ondansetron. Although, ondansetron had a slower onset, the therapeutic effect was there was more sustained. It showed median VNRS scores progressively decreasing from 20 minutes onwards and complete relief of postoperative nausea (median VNRS score of 0) in most patients by the 30-minute observation point.

Despite advances in antiemetic therapy, PON/PONV remains a significant concern, particularly in high-risk surgical populations. Various pharmacological agents such as ondansetron, dexamethasone, droperidol, and metoclopramide are commonly employed, and each carries potential side effects including headache, dizziness, QT prolongation, and extrapyramidal symptoms.[1]

Ondansetron, a selective 5-HT3 receptor antagonist, acts by blocking serotonin both peripherally on vagal nerve terminals and centrally in the chemoreceptor trigger zone of the area postrema and is a widely used for treatment of PON/PONV in our clinical setting.[7]

Isopropyl alcohol is a common ingredient in products such as antiseptic solutions, topical disinfectants, hand sanitisers, and detergents. Interestingly, it has emerged as a simple, inexpensive and non-invasive alternative in the treatment of nausea in the emergency as well as postoperative setting.[13]

Consistent with our findings, a comparative study demonstrated that IPA achieved a 50% reduction in VNRS scores in 15±10.6 minutes versus 33.9±23.2 minutes with ondansetron (p=0.001). They advocated IPA's utility as a rapid, non-invasive first-line agent alongside traditional antiemetics.[10]

Another study conducted on female patients undergoing laparoscopic surgeries reported that mean times from initiation of therapy to a 50% reduction in nausea between the ondansetron and alcohol groups were 6.3 minutes and 27.7 minutes, respectively (p=0.022). Similar to our observation, no statistically significant differences were seen beyond the initial 15 minutes.[11]

A recent meta-analysis including four randomised controlled trials, inhaled IPA was

associated with a significantly faster reduction in nausea, achieving a 50% reduction in mean nausea time approximately 20 minutes earlier than 5-HT3 antagonists.[8] Contrary to our findings, their study demonstrated significantly lower nausea scores at 30 minutes post-treatment in the Gr-IPA and a reduced need for rescue antiemetics compared to 5-HT3 antagonists.

The sustained antiemetic effect of ondansetron observed in our study aligns with multiple previous reports demonstrating its prolonged efficacy in preventing/treating PON/PONV.[14,15] However, some patients experience refractory nausea despite ondansetron prophylaxis, necessitating adjunctive therapies.[16]

In our study, although the effect of inhaled IPA was not statistically significant when compared to ondansetron beyond 15 minutes, most patients continued to show lower VNRS scores compared to preintervention levels, with a median VNRS score of 1 at the 30-minute observation point. Notably, only 27.3% of patients required rescue therapy, while the remainder experienced sustained relief without requesting further treatment during the study period.

The cost of medications used in our study highlights a significant economic advantage of IPA aromatherapy. A single IPA prep pad (Lifeline) costs approximately 1 Nepali rupee, which is substantially lower than the cost of a dose of intravenous ondansetron (National Healthcare), priced at 36 Nepali rupees. Even after accounting for the cost of rescue treatment, intravenous promethazine (National Healthcare) at 15 Nepali rupees, which was administered to 12 patients in the Gr-IPA, the overall treatment cost remained lower in the Gr-IPA compared to the Gr-O. Moreover, inhalational therapy with IPA does not require intravenous access and can be administered at any setting, as no systemic side effects have been reported.[8-11]

Despite these benefits, a Cochrane systematic review which analysed 16 randomised controlled trials examining the use of aromatherapy, including IPA, for the management of PONV concluded that while IPA offers rapid symptom relief and is associated with minimal adverse effects, its overall efficacy compared to standard antiemetics remains inconsistent.[17]

A systematic review concluded that while IPA provided rapid relief of nausea, particularly within the first 5 to 10 minutes, its effects were not sustained beyond 15 to 30 minutes in most trials, limiting its long-term utility.[18]

Even though it was not of statistical significance, our patients in inhaled Gr-IPA did show an effect for up to 30 minutes, with a median VNRS of 1 compared to 6 at the pre-intervention period.

The discrepancy between our finding and other studies may be due to loss of follow up in our study beyond 30 minutes. Nonetheless, the studies have noted IPA to be a safe, inexpensive, and easily administered, making it a first-line or a viable adjunct to standard antiemetics, especially in settings where rapid symptom relief and resource optimisation are priorities, which aligns with our experience.[17,18]

Our study has several limitations that should be acknowledged. The sample size was calculated based on PONV prevalence, rather than an estimated comparative effect size. However, a post-hoc power analysis using the observed VNRS difference (Δ=1.5, SD=2.0) confirmed that the study was adequately powered (80%) to detect clinically meaningful effect. Another limitation of present study may be a follow-up period up to a limited time point of 30 minutes, restricting assessment of sustained antiemetic efficacy beyond the immediate PACU stay. Future research should address these limitations by including larger sample, and longer follow-up durations for further subgroup analysis, like high-risk patients for PON (e.g., females, non-smokers). Multicentre trials incorporating various anaesthetic agents are also warranted to further clarify the role of IPA within multimodal PON/PONV management strategies.

Conclusion

Our study suggests that inhaled isopropyl alcohol is a viable, non-invasive, and low-cost alternative for initial management leading to

rapid relief of postoperative nausea after general anaesthesia. Ondansetron was found to be more effective for sustained therapeutic effect. Although a subset of patients receiving inhaled isopropyl alcohol required repeat or rescue interventions, many achieved satisfactory relief with a single administration. Its ease of use and favourable safety profile make receiving inhaled isopropyl alcohol a practical first-line agent or an adjunct in multimodal PONV strategies.

Author contribution

Concept design: BSR, SR, GPD, RP; Literature search: BSR, SR, GPD; Data collection: BSR, SR, RP; Data analysis: BSR, SR, GPD; Draft manuscript: BSR, SR, GPD, RP; Final manuscript and accountability: All

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Conflict of interest

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Supplementary material

The data and supplementary material that support the findings of this study are available from the corresponding author upon reasonable request.

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