



Anaesthesiology

COMPARISON OF POSTOPERATIVE ANALGESIA FOLLOWING PREOPERATIVE ORAL ADMINISTRATION OF VITAMIN C VERSUS PARACETAMOL IN PATIENTS UNDERGOING ELECTIVE LAPAROSCOPIC CHOLECYSTECTOMY UNDER GENERAL ANAESTHESIA: A RANDOMISED PROSPECTIVE COMPARATIVE STUDY

Dr Vyshnavi S	Associate Professor, Department of Anaesthesiology, JSS Academy of Higher Education and Research, Mysuru.
Dr Snigdha Kavali	Junior Resident, Department of Anaesthesiology, JSS Academy of Higher Education and Research, Mysuru.
Dr Girish B K	Associate Professor, Department of Anaesthesiology, JSS Academy of Higher Education and Research, Mysuru.
Dr Mamatha V*	Assistant Professor, Department of Anaesthesiology, JSS Academy of Higher Education and Research, Mysuru. *Corresponding Author
Dr Pratibha Matche	
Dr Manjula B P	Professor and Head, Department of Anaesthesiology, JSS Academy of Higher Education and Research, Mysuru.

ABSTRACT **Background:** Postoperative pain remains common after laparoscopic cholecystectomy. Multimodal analgesia minimizes opioid use and related adverse effects. Paracetamol is an established component while vitamin C is a potential drug with antioxidant, anti-inflammatory, and analgesic properties. However, evidence directly comparing oral vitamin C with paracetamol remains limited. **Objective:** To compare the postoperative analgesic efficacy of preoperative oral administration of vitamin C with oral paracetamol in patients undergoing elective laparoscopic cholecystectomy under general anaesthesia. Secondary objectives were to compare the time to first rescue analgesia, total rescue analgesic doses, and severity of postoperative sore throat in the first 24 hours. **Methods:** This prospective randomized study included 110 ASA I–II patients aged 18–60 years undergoing elective laparoscopic cholecystectomy. Group C received oral vitamin C 2 g and Group P oral paracetamol 1 g one hour preoperatively. VAS pain scores at 1, 6, and 24 hours, time to first rescue analgesia, total rescue analgesic consumption, and postoperative sore throat severity were assessed. **Results:** Baseline demographic characteristics were comparable between groups. Pain scores at 1, 6, and 24 hours were similar ($p = 0.099$), as were time to first rescue analgesia (2.56 ± 1.75 vs. 2.82 ± 1.60 h; $p = 0.428$) and total rescue analgesic use ($p = 0.600$). Vitamin C significantly reduced postoperative sore throat ($p < 0.001$). **Conclusions:** Preoperative oral vitamin C provided postoperative analgesia comparable to paracetamol and significantly reduced postoperative sore throat, supporting its use as an effective analgesic after laparoscopic cholecystectomy.

KEYWORDS : Vitamin C; Paracetamol; Postoperative Pain; Postoperative Sore Throat.

INTRODUCTION

Laparoscopic cholecystectomy has emerged as the preferred surgical treatment for symptomatic cholelithiasis because of its minimally invasive approach, which is associated with reduced surgical trauma, shorter hospital stay, faster recovery, and fewer postoperative complications than open cholecystectomy. Despite these advantages, postoperative pain remains a common clinical problem, with 30–80% of patients experiencing moderate to severe pain during the first 24–48 hours after surgery.¹ Pain following laparoscopic cholecystectomy is multifactorial, arising from port-site incisions, visceral irritation at the gallbladder bed, chemical irritation due to generation of reactive oxygen species (ROS), and referred shoulder pain secondary to diaphragmatic irritation caused by residual carbon dioxide. Inadequately controlled pain delays ambulation, prolongs hospital stay, reduces patient satisfaction, and may contribute to the development of chronic postoperative pain.²

Current postoperative pain management relies on multimodal analgesia incorporating paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs), opioids, and regional anaesthetic techniques. Although intravenous or oral paracetamol is widely accepted as a baseline non-opioid analgesic because of its favourable safety profile, it may provide insufficient analgesia when used alone in patients with moderate-to-severe postoperative pain. Opioids remain effective rescue analgesics but are associated with adverse effects such as postoperative nausea and vomiting, respiratory depression, sedation, pruritus, and ileus. NSAIDs and selective cyclooxygenase-2 inhibitors effectively reduce postoperative pain but may be unsuitable for patients with renal dysfunction, peptic ulcer disease, bleeding disorders, or cardiovascular risk factors.³ Regional anaesthetic techniques, while effective, require expertise and resources that may not be universally available. Consequently, there is continued interest in identifying simple, safe, inexpensive adjuncts that enhance multimodal analgesia while minimizing opioid consumption and adverse effects.

Vitamin C has emerged as a potential perioperative analgesic adjunct owing to its antioxidant, anti-inflammatory, neuromodulatory, and neuroprotective properties⁴. Previous studies have demonstrated opioid-sparing effects and improved postoperative pain scores following perioperative vitamin C administration⁵; however, evidence comparing preoperative oral vitamin C with oral paracetamol in patients undergoing laparoscopic cholecystectomy remains limited.

The present study was therefore undertaken to compare the effectiveness of preoperative oral vitamin C and oral paracetamol in controlling postoperative pain following elective laparoscopic cholecystectomy under general anaesthesia. In addition to postoperative pain scores, the study evaluated the time to first rescue analgesia, total rescue analgesic requirement, and severity of postoperative sore throat during the first 24 hours after surgery.

Materials and Methods**Study Design and Setting**

This prospective, randomized, comparative study was conducted at a tertiary care centre after obtaining approval from the Institutional Ethics Committee and registration with the Clinical Trials Registry (CTRI/2025/09/094825). The study was conducted between March 2024 and August 2026

Study Population

A total of 110 adult patients were enrolled for the study. Written informed consent was obtained from all participants before inclusion in the study.

Inclusion Criteria

- Aged between 18 and 60 years.
- ASA physical status I or II.
- Patients undergoing elective laparoscopic cholecystectomy under general anaesthesia.

Exclusion Criteria

- Known allergy to Vitamin C or Paracetamol.

- Pregnant or lactating women
- Glucose-6-phosphate dehydrogenase deficiency.
- Patients receiving analgesics for other indications, such as cancer-related pain or chronic pain conditions.
- Patients receiving intraoperative dexamethasone.

Methodology

Participants were randomly allocated in a 1:1 ratio into two equal groups (55 patients each) using a shuffled opaque sealed-envelope randomization technique.

- Group C: Oral vitamin C 2 g administered one hour before induction of anaesthesia.
- Group P: Oral paracetamol 1 g administered one hour before induction of anaesthesia.

Anaesthetic management was according to institutional protocols. Standard monitoring included electrocardiography, non-invasive blood pressure, pulse oximetry, end-tidal carbon dioxide and heart rate monitoring. Following intravenous access, patients received routine premedication with Ondansetron 0.1 mg/kg, and Fentanyl 2 µg/kg. General anaesthesia was induced with propofol 2 mg/kg and neuromuscular blockade was achieved using vecuronium 0.1 mg/kg to facilitate endotracheal intubation. Anaesthesia was maintained as required by treating anaesthesiologist while abiding to hospital protocol.

Outcome Measures :

Primary Outcome

- The primary outcome was postoperative pain severity measured using the Visual Analogue Scale (VAS; 0–10) at 1, 6, and 24 hours after surgery.

Secondary Outcomes

- Time to first rescue analgesia
- Total rescue analgesic requirement during the first 24 hours postoperatively
- Severity of postoperative sore throat at 1, 6, and 24 hours using a four-point grading scale:
 - Grade 0: No sore throat.
 - Grade 1: Mild sore throat (complains only on questioning).
 - Grade 2: Moderate sore throat (complains spontaneously).
 - Grade 3: Severe sore throat (associated with hoarseness or voice change).

Rescue analgesia was given with IV tramadol 50 mg for VAS >3. Severe sore throat (>3) was treated with 2 mL of 1% lignocaine nebulisation

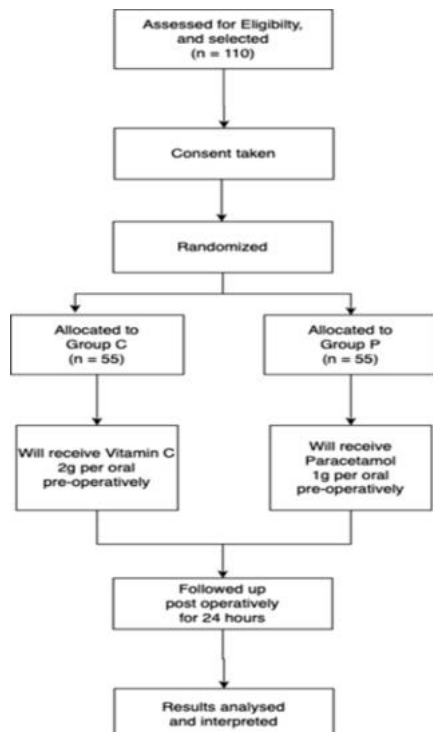


Figure 1 : Flow Chart Showing Study Conduct

Statistical Analysis

Data was analysed using IBM SPSS Statistics 27.0. Continuous variables were expressed as mean ± SD and categorical variables as frequency and percentage. The *t*-test and Chi-square test were used for comparisons, while RM-ANOVA assessed changes in pain and sore throat scores over time. $p < 0.05$ was considered significant.

RESULTS

A total of 110 patients were randomized equally to Group C (vitamin C) and Group P (paracetamol), with 55 patients each; all enrolled participants completed the study and were included in the final analysis.

Postoperative pain severity, time to first rescue analgesia, and total rescue analgesic requirement were comparable between groups, while postoperative sore throat was significantly less severe with vitamin C.

Table 1: Baseline Demographic Characteristics of Study Participants

Characteristic	Group C (N = 55)	Group P (N = 55)	Total (N = 110)	p-value
Age (years)				0.874
Mean m SD	43.73 ± 12.08	44.09 ± 11.87	43.91 ± 11.92	
Range	20.0 - 60.0	21.0 - 60.0	20.0 - 60.0	
Age Group, n (%)				0.548
< 30	10(18.2%)	7(12.7%)	17(15.5%)	
31–40	12(21.8%)	18(32.7%)	30(27.3%)	
41–50	13(23.6%)	10(18.2%)	23(20.9%)	
51–60	20(36.4%)	20(36.4%)	40(36.4%)	
Sex, n (%)				0.113
Male	24(43.6%)	16(29.1%)	40(36.4%)	
Female	31(56.4%)	39(70.9%)	70(63.6%)	

Table 2. Primary Outcome: Comparison of Postoperative VAS Scores

Category	Metric	Group C (n = 55) Mean ± SD / n (%)	Group P (n = 55) Mean ± SD / n (%)
Descriptive statistics of VAS scores $p = 0.099$	VAS 1hr	4.78 ± 1.52	4.29 ± 1.38
	VAS 6hr	3.67 ± 1.25	3.75 ± 1.32
	VAS 24hr	2.15 ± 0.80	2.16 ± 1.21

Table 3. Secondary Outcomes

Category	Metric	Group C (n = 55) Mean ± SD / n (%)	Group P (n = 55) Mean ± SD / n (%)
Comparison of time to first rescue analgesia $p = 0.428$	Time to first rescue analgesia (In hours)	2.56 ± 1.75	2.82 ± 1.60
Number of rescue analgesic doses required $p = 0.6$	1 dose	1 (1.8%)	0 (0%)
	2 doses	23 (41.8%)	24 (43.6%)
	3 doses	31 (56.4%)	31 (56.4%)
Descriptive statistics of postoperative sore throat scores $p < 0.001$	Sore throat 1hr	0.75 ± 0.84	1.09 ± 0.87
	Sore throat 6hr	0.31 ± 0.54	0.58 ± 0.69
	Sore throat 24hr	0.24 ± 0.51	0.11 ± 0.37

DISCUSSION

This study compared preoperative oral vitamin C with oral paracetamol to determine whether vitamin C provides comparable postoperative analgesia following laparoscopic cholecystectomy under general anaesthesia.

Baseline demographic characteristics were comparable between the groups, minimizing potential confounding. Most participants were 51–60 years of age, with no significant difference in age distribution (Pearson $\chi^2 = 2.121$, $p = 0.548$). Females predominated in both groups, reflecting the higher prevalence of cholelithiasis among women, while mean age and sex distribution remained comparable. Similar demographic characteristics have been reported by Kalim et al.,⁶ KRV Singh et al.,⁷ Awwanna et al.,⁸ Matsushima et al.,⁹ and Mędrzycka et al.¹⁰

Postoperative VAS pain scores declined significantly over the first 24 hours in both groups. Although Group C had slightly higher pain

scores at 1 hour, scores at 6 and 24 hours were comparable. The absence of a significant group-by-time interaction indicates that vitamin C and paracetamol produced similar postoperative analgesia. These findings are consistent with the findings in the study by Awwanna et al.⁸ and the systematic review by Mędrzycka et al.,¹⁰ which reported reduced postoperative pain with perioperative vitamin C in several surgical settings. Bijalwan et al.¹¹ and Choi et al.⁴ likewise reported similar efficacy of oral vitamin C compared to the control in laparoscopic cholecystectomy.

Vitamin C may reduce postoperative pain by scavenging reactive oxygen species generated during surgical trauma and pneumoperitoneum-induced oxidative stress, thereby limiting nociceptor sensitization and NMDA mediated central sensitization; it may also enhance descending inhibitory pain pathways and suppress pro-inflammatory cytokines such as TNF- α and IL-6.¹²

Postoperative sore throat decreased significantly in both groups, with patients receiving vitamin C demonstrating a greater reduction over time than those receiving paracetamol. Similar findings were reported by Hossein et al.¹³ and Jaiswal et al.,¹⁴ who demonstrated reduced incidence and severity of post-intubation sore throat with perioperative vitamin C. The improved airway comfort observed in our study may be attributable to the antioxidant and anti-inflammatory effects of vitamin C on the airway mucosa.

The mean time to first rescue analgesia was comparable between groups (2.56 vs. 2.82 hours), with no statistically significant difference. These findings agree with the findings of Awwanna et al.,⁸ Bijalwan et al.,¹¹ and the review by Mędrzycka et al.,¹⁰ which reported variable effects of vitamin C on prolonging rescue analgesia. In contrast, Ranjan et al.¹⁵ and the meta-analysis by Moraes et al.¹⁶ demonstrated greater analgesic benefit, particularly with intravenous vitamin C, suggesting that the route of administration and comparator drug may influence outcomes.

Total postoperative rescue analgesic requirement was also similar between groups, with no significant difference in tramadol consumption. While Ranjan et al.,¹⁵ Mahajan et al.,¹⁷ and Garg et al.¹⁸ reported reduced postoperative analgesic consumption with vitamin C, these studies largely involved placebo comparators and different surgical populations. In contrast, our study compared vitamin C with oral paracetamol, an established non-opioid analgesic, which may explain the comparable outcomes. Overall, our findings demonstrate that preoperative oral vitamin C provides postoperative analgesia comparable to oral paracetamol, while offering the additional benefit of reducing postoperative sore throat following laparoscopic cholecystectomy.

Limitations

The present study has limitations. First, single-centre design limiting generalizability. Only ASA I–II patients aged 18–60 years undergoing elective laparoscopic cholecystectomy were included, limiting applicability to elder, comorbid, emergency and other surgical populations. The outcomes were assessed only for 24 hours, without longer-term recovery assessment. It was not possible to blind the patient to the drug they received since paracetamol and Vitamin C come in different formulations as a tablet. Finally, oxidative and inflammatory markers were not measured, limiting confirmation of vitamin C's proposed mechanism.

CONCLUSION

Preoperative oral vitamin C (2 g) provided analgesia comparable to paracetamol (1 g), with similar pain scores, rescue analgesic requirements, and time to first rescue analgesia, while significantly reducing postoperative sore throat, supporting its use as an alternative non-opioid analgesic in laparoscopic cholecystectomy. Larger multicentre studies with longer follow-up are needed to confirm findings for broader applicability.

Declarations

Ethics Approval:

The study was approved by the Institutional Ethics Committee of JSS Medical College and Hospital, Mysuru, and conducted in accordance with the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all participants before enrolment.

Clinical Trial Registration:

Clinical Trials Registry–India (CTRI): CTRI/2025/09/094825

Consent to Participate:

Written informed consent was obtained from all study participants before enrolment.

Availability of Data:

The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest:

The authors declare that they have no competing interests.

Funding:

No external funding was received for this study.

REFERENCES

- DeVitis J, Flom E, Cooper-Roth T, Davis A, Krech L, Fisk C, Pounders S, Kwazneski D, Chapman A, Valdez C. The NOpioiD Project: a prospective observational feasibility study examining the implementation of a non-narcotic post-operative pain control regimen. *Surg Endosc*. 2022 Nov;36(11):8472–8480.
- Ayman Abd El-Salam Hassan, AbdEl-Mohsen El-Shiekh Mansour Aly, Mohamed Monir Khalil Ebrahim, Heba Mohamed Fathi. Prevention and Management of Postoperative Pain in Laparoscopic Cholecystectomy. *IJCBS*. 24(10) (2023): 965–968.
- Cao L, Yang T, Hou Y, Yong S, Zhou N. Efficacy and safety of different preemptive analgesia measures in pain management after laparoscopic cholecystectomy: a systematic review and network meta-analysis of randomized controlled trials. *Pain Ther*. 2024;13(6):1471–97.
- Choi Y, Hong TH. High-dose Oral Vitamin C Supplementation and Acute Pain Control Following Laparoscopic Cholecystectomy: A Randomized Controlled Study. *J Perianesth Nurs*. 2026 Apr;41(2):286–290.
- Hung KC, Lin YT, Chen KH, Wang LK, Chen JY, Chang YJ, Wu SC, Chiang MH, Sun CK. The Effect of Perioperative Vitamin C on Postoperative Analgesic Consumption: A Meta-Analysis of Randomized Controlled Trials. *Nutrients*. 2020 Oct 12;12(10):3109.
- Kalim M, Asjad M, Ahmed J, Qureshi MA, Bhatti TA, Khan R. Comparative Analysis of Pain Management Strategies Following Laparoscopic Cholecystectomy. *J Neonatal Surg* [Internet]. 2025 Jul. 3 [cited 2026 Apr. 26];14(32S):3449–54.
- K R V, Singh K, Sahay N, Sinha C, Kumar A, Kumar N. Opioid-free anesthesia using a combination of ketamine and dexmedetomidine in patients undergoing laparoscopic cholecystectomy: a randomized controlled trial. *Anesth Pain Med* (Seoul). 2024 Apr;19(2):109–116.
- Awwanna MB, Asha , Sagar GV, Shanthala Naik. Comparative study of high dose vit c and paracetamol in pain relief in patients undergoing laparoscopic cholecystectomy. *IJAR*. 2023;13(8):68–70.
- Matsushima K, Ciesielski KM, Mandelbaum RS, Matsuo K. Clinical Demographics of Laparoscopic Cholecystectomy: A Gender-Specific Analysis. *Am Surg*. 2024 Apr;90(4):528–532.
- Mędrzycka-Dąbrowska W, Lange S, Dąbrowski S, Dhugoborska K, Piotrkowska R. Vitamin C as an Adjuvant Analgesic Therapy in Postoperative Pain Management. *J Clin Med*. 2025 Jun 5;14(11):3994.
- Bijalwan, A., Singhal, P., & Altamash, S. (2019). A comparative evaluation of analgesic effects of using intravenous paracetamol versus intravenous diclofenac post-operatively in laparoscopic cholecystectomy patients in SMIIH, department of surgery, Dehradun. *International Surgery Journal*, 6(5), 1716–1722.
- Kanazi GE, El-Khatib MF, Yazbeck-Karam VG, Hanna JE, Masri B, Aouad MT. Effect of vitamin C on morphine use after laparoscopic cholecystectomy: a randomized controlled trial. *Can J Anaesth*. 2012;59(6):538–43.
- Hossein H, Mohammad Z Hamidreza, Elnaz. The efficacy of vitamin C infusion in reducing post-intubation sore throat in patients undergoing laparoscopic surgery *Med J (Krag)*. 2019; 53(3): 95–100.
- Jaiswal R, Ishan S Kagra, Vandna Arora. Effect of Vitamin C on Severity of Post-Operative Sore Throat Following Tracheal Intubation: A Randomised Controlled Trial. *International Journal of Pharmaceutical and Clinical Research* 2024;16(6): 430–435.
- Ranjan R, et al. Vitamin C premedication reduces postoperative rescue analgesic requirement after laparoscopic surgeries. *J Anaesth Crit Care Open Access*. 2016;6(3):00200.
- Moraes M, et al. The effect of perioperative vitamin C on postoperative analgesic consumption: a meta-analysis of randomized controlled trials. *Br J Anaesth*. 2020;125(5):e444–e454.
- Mahajan, N. P., Narvekar, M. A., Chandanwale, A. S., Gadod, L. L., & Prasannakumar, G. S. (2021). Vitamin C supplementation as adjuvant analgesic therapy in post-operative pain management in patients undergoing surgical decompression in a case of prolapsed intervertebral disc. *International Journal of Research in Medical Sciences*, 9(9), 2756–2760.
- Garg, R. N., Patil, H., Bajaj, S., & Vaje, S. S. (2023). Assessment of vitamin C supplementation as an adjuvant analgesic therapy and evaluating its efficacy in terms of clinical and functional outcomes in post-operative patients undergoing surgical decompression for prolapsed intervertebral lumbar disc. *International Journal of Research in Orthopaedics*, 9(6), 1241–1246.