J Surg Med. 2026;10(6):e8412.
https://doi.org/10.28982/josam.8412

JOSAM

Research Article
https://jsurgmed.com/

Journal of Surgery and Medicine
e-ISSN: 2602-2079

The effect of total intravenous versus inhalation anesthesia on early postoperative pain after laparoscopic cholecystectomy: A randomized controlled trial from Eastern Libya

Hamza M. Alhussadi[1], Saja S. Noisari[2], Esraa M. Alhassi[2], Salim M. Makhlouf[1]

[1] Department of Anesthesia and Critical Care, College of Medical Technology, Derna, Libya
[2] The College of Medical Technology, Derna, Libya

ORCID of the author(s)

HMA: https://orcid.org/0009-0000-1941-0980
SSN: https://orcid.org/0009-0002-1635-4957
EMA: https://orcid.org/0009-0007-0774-5637
SMM: https://orcid.org/0000-0002-1567-7757

Corresponding Author
Salim M. Makhlouf
Department of Anesthesia and Critical Care, College of Medical Technology, Yah Al Zuhor, Bab Tubrik, Derna, Libya
E-mail: leicester_2009@yahoo.com

Ethics Committee Approval
The study was approved by the Ethics Committee of the College of Medical Technology, Derna, Libya, on February 5, 2025 (CMTD 02-025). The research was conducted in accordance with the principles of the Declaration of Helsinki.

Conflict of Interest
No conflict of interest was declared by the authors.

Financial Disclosure
The authors declared that this study has received no financial support.

Published
2026 June 5

Abstract

Background/Aim: Effective postoperative pain (POP) control remains a major determinant of recovery after laparoscopic cholecystectomy (LC), particularly in resource-limited healthcare settings such as Libya. Although propofol-based total intravenous anesthesia (TIVA) may improve early analgesia compared with isoflurane-based inhalation anesthesia (IA), comparative evidence from these settings is limited. This trial compared acute POP trajectories during the first 24 hours after LC under these two anesthetic techniques in Eastern Libya.

Methods: This prospective, double-blind, randomized controlled trial was conducted at two public hospitals in Eastern Libya between February and May 2025. Fifty-nine patients scheduled for elective LC were analyzed after randomization to propofol-based TIVA (n = 29) or isoflurane-based IA (n = 30). The primary outcome was pain intensity measured with the Numerical Rating Scale (NRS; 0-10) at 2, 6, 12, and 24 hours postoperatively. Data were analyzed using SPSS version 26.

Results: A significant anesthesia-by-time interaction was observed for postoperative pain scores (F[2.92, 166.63] = 11.67, $P < 0.001$). Pairwise comparisons showed lower mean pain scores in the TIVA group at 2 hours [4.3 (0.8) vs. 4.8 (0.8), $P = 0.010$] and 12 hours [2.2 (0.5) vs. 2.7 (0.6), $P = 0.001$]. The 6-hour difference was smaller [3.2 (0.6) vs. 3.4 (0.7), $P = 0.028$], and no significant difference was observed at 24 hours [1.5 (0.3) vs. 1.7 (0.4), $P = 0.063$]. The main effect of anesthetic type was not significant (F[1, 57] = 2.21, $P = 0.143$).

Conclusion: Propofol-based TIVA was associated with modestly lower early postoperative pain scores after LC compared with isoflurane-based IA, but this benefit was not sustained at 24 hours. Selection of anesthetic technique should consider whether early POP control is a clinical priority within the broader multimodal analgesia strategy.

Keywords: propofol, isoflurane, laparoscopic cholecystectomy, postoperative pain, Libya

How to cite: Alhussadi HM, Noisari SS, Alhassi EM, Makhlouf SM. The effect of total intravenous versus inhalation anesthesia on early postoperative pain after laparoscopic cholecystectomy: A randomized controlled trial from Eastern Libya. J Surg Med. 2026;10(6):e8412.

Introduction

Postoperative pain (POP) is a key determinant of patient satisfaction, quality of recovery, and healthcare utilization after surgery. Although laparoscopic cholecystectomy (LC) is considered minimally invasive, it is frequently associated with moderate to severe acute pain, particularly during the first 24 postoperative hours [1, 2]. In Libya, where healthcare resources have been constrained by ongoing instability, POP management remains suboptimal, and approximately 55% of patients experience significant pain on the first postoperative day [3].

Effective POP control requires multimodal strategies and may also be influenced by the choice of anesthetic maintenance technique. The two main approaches for maintaining general anesthesia are total intravenous anesthesia (TIVA) with propofol and inhalation anesthesia (IA) with volatile agents such as isoflurane [4]. Recent evidence suggests that these approaches may have different effects on postoperative nociception and inflammatory responses [5].

Beyond its hypnotic effects, propofol has anti-inflammatory and potential analgesic-sparing properties that may modulate early POP [6]. In contrast, volatile anesthetics may contribute to nociceptive sensitization through receptor-mediated pathways [7]. Clinical studies comparing these techniques have produced conflicting results. Some studies have reported lower early pain scores and reduced opioid consumption with propofol-based TIVA [8, 9], whereas others have found no significant differences in overall pain outcomes [10, 11]. These discrepancies may reflect differences in surgical procedures, analgesic protocols, and timing of pain assessment.

The analgesic efficacy of propofol-based TIVA may depend on several factors, including surgical technique and perioperative analgesic management [12]. Although the comparative effects of TIVA and IA on POP have been studied [13, 14], findings regarding the temporal pattern of analgesia remain inconsistent. Moreover, no study has evaluated this question in the Libyan healthcare context or in similar resource-constrained settings, where postoperative care pathways may differ. This randomized controlled trial (RCT) aimed to compare the trajectory of acute POP during the first 24 hours after LC in patients receiving either propofol-based TIVA or isoflurane-based IA in Eastern Libyan hospitals.

Materials and methods

Study design and setting

We conducted a prospective, double-blind, parallel-group RCT at two public hospitals in Eastern Libya, Derna and Shahat, between February and May 2025. The study protocol was approved by the Ethics Committee of the College of Medical Technology, Derna (CMTD 02-025), and was registered locally (The Libya Clinical Research Registry, LCRR/2025/02/003270). Written informed consent was obtained from all participants. The trial was reported in accordance with the CONSORT guidelines [15]. All study procedures complied with the Declaration of Helsinki.

Participants

Eligible participants were adults aged 18 years or older who were scheduled for elective LC and had an American Society of Anesthesiologists (ASA) physical status of I or II. Exclusion criteria were psychiatric disorders, known drug allergies, planned discharge within 24 hours, chronic pain conditions requiring regular analgesics, anticipated intensive care unit (ICU) admission, concomitant surgical procedures, pregnancy, and inability to provide informed consent. The primary outcome was the between-group difference in NRS pain score trajectories during the first 24 postoperative hours. A key secondary outcome was the 24-hour pain score. Rescue analgesic timing, 24-hour tramadol consumption, and postoperative nausea and vomiting (PONV) were also recorded.

Randomization and blinding

Eligible participants were randomly assigned in a 1:1 ratio using computer-generated block randomization with a block size of four. Sealed, opaque envelopes prepared by an independent statistician were opened immediately before induction by an anesthetist who was not involved in postoperative assessment. Participants, postoperative outcome assessors, and data analysts were blinded to group allocation.

Anesthesia protocol

All patients received intravenous atropine 0.5 mg and midazolam 0.03 mg/kg as premedication ten minutes before induction. Anesthesia was induced with fentanyl 1.5 micrograms/kg, propofol 1.5 mg/kg, and rocuronium 0.5 mg/kg, followed by tracheal intubation and orogastric tube insertion.

The intervention group received propofol-based intravenous anaesthesia maintained with a continuous propofol infusion (6 mg/kg/hour) together with a gas mixture of 50% oxygen and 50% nitrous oxide. No volatile anaesthetic agent was administered. The IA group received 1.2% isoflurane with the same gas mixture. Anesthetic depth was adjusted to maintain hemodynamic stability. All port sites were infiltrated with 0.25% bupivacaine before incision. Dexamethasone 8 mg intravenously was administered for PONV prophylaxis. Neuromuscular blockade was reversed with neostigmine 2.5 mg and atropine 0.5 mg, and patients were extubated after adequate recovery.

Postoperative analgesia

The standardized postoperative analgesic regimen consisted of intravenous paracetamol 1 g every 6 hours and ketorolac 30 mg every 8 hours for 24 hours. Rescue analgesia with intravenous tramadol 50 mg was available on patient request or when the NRS score was 4 or higher. Total rescue analgesic consumption was recorded.

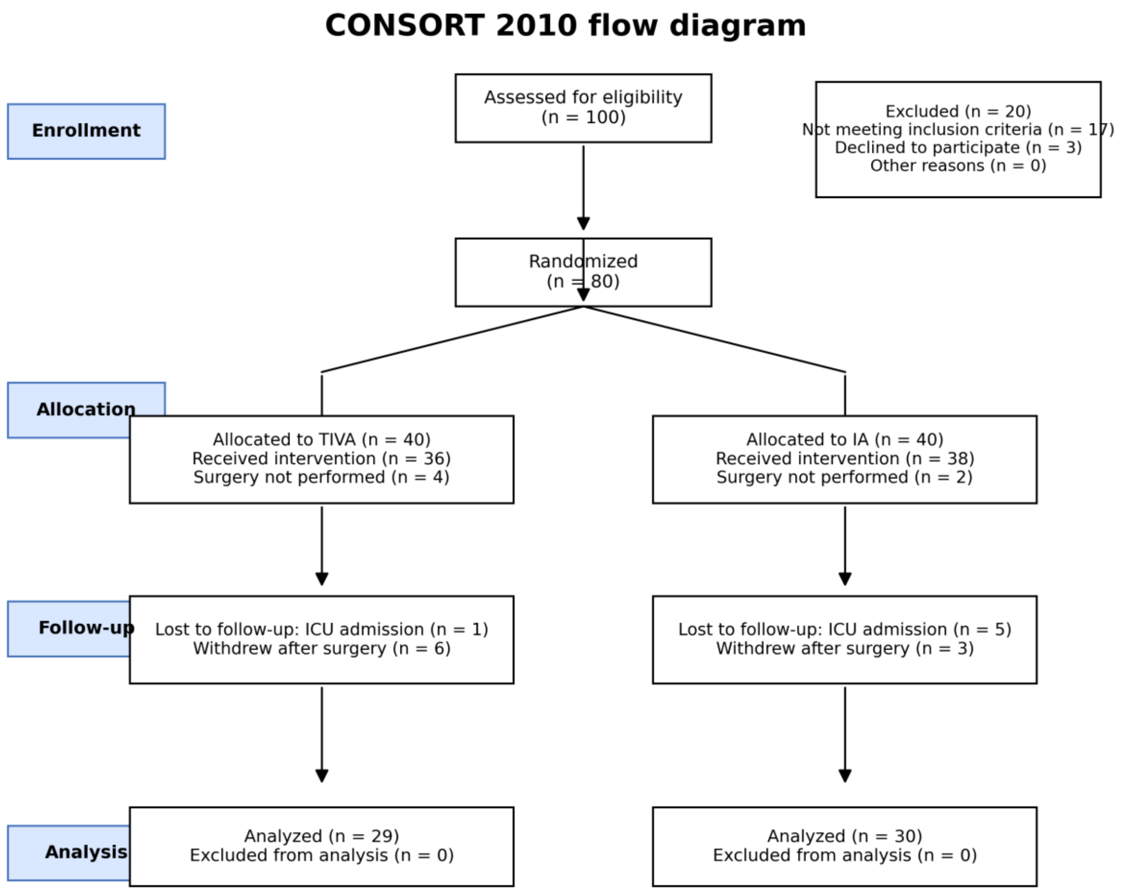
Sample size calculation

Based on data from Wong et al. [9], detecting a mean difference of 1.0 point on the NRS with an SD of 1.5, 80% power, and an alpha level of 0.05 required 36 patients per group. After allowing for a 15% attrition rate, the target recruitment was 80 patients, with 40 participants per group.

Statistical analysis

Data were analyzed using SPSS version 26. Normality was assessed with the Shapiro-Wilk test. Descriptive statistics are presented as mean (SD) or frequency (n). The primary analysis used repeated-measures analysis of variance to examine the interaction between anesthetic type and time on postoperative pain scores. When appropriate, Greenhouse-Geisser-corrected degrees of freedom were reported. Post hoc comparisons were performed using independent-samples t tests with Bonferroni correction. A

Figure 1. CONSORT flow diagram for the study



two-tailed P-value less than 0.05 was considered statistically significant, except where a Bonferroni-adjusted threshold was specified.

The primary analysis was conducted on a per-protocol basis, including participants who completed surgery and all scheduled postoperative pain assessments. Participants who were randomized but did not undergo surgery, required postoperative ICU admission, or withdrew before completion of follow-up were excluded from the final analysis.

Results

Participant flow and baseline characteristics

Of the 100 patients assessed for eligibility, 80 were randomized and 59 completed the study and were included in the final analysis (Figure 1). The main reasons for non-inclusion or postrandomization non-completion were failure to meet inclusion criteria (n = 17), declining participation (n = 3), surgery not performed after allocation (n = 6), postoperative ICU admission (n = 6), and withdrawal after surgery (n = 9).

Baseline demographic and clinical characteristics were comparable between the groups (Table 1). The mean age was 32.1 (11.5) years in the TIVA group and 29.9 (10.8) years in the IA group (P = 0.450). Overall, females comprised 57.6% of the sample and males comprised 42.4%. The distribution of anesthetic allocation was similar between groups, with 29 patients in the TIVA group and 30 patients in the IA group.

Table 1. Baseline characteristics of study participants

Characteristic	TIVA group (n = 29)	IA group (n = 30)	P-value
Female sex, n (%)	16 (55.2)	18 (60.0)	0.710
Age (years), mean (SD)	32.1 (11.5)	29.9 (10.8)	0.450
ASA score I/II, n (%)	20 (69.0)/9 (31.0)	22 (73.0)/8 (27.0)	0.790
Chronic pain history, n (%)	13 (44.8)	12 (40.0)	0.710
BMI (kg/m²), mean (SD)	26.8 (4.2)	27.1 (3.9)	0.770
Surgery duration (min), mean (SD)	68.5 (18.2)	71.3 (16.7)	0.530

ASA: American Society of Anesthesiologists, BMI: body mass index, IA: inhalation anesthesia, n: number, SD: standard deviation, TIVA: total intravenous anesthesia. P < 0.05 was considered statistically significant.

Primary repeated-measures analysis

There was no statistically significant main effect of anesthetic type on mean pain scores across the 24-hour assessment period. Mean pain scores across all time points were 5.2 (1.5) for TIVA and 5.5 (0.96) for IA (F[1, 57] = 2.21, P = 0.143, partial eta squared = 0.037), indicating a small effect size. However, the main effect of time and the time-by-anesthetic type interaction were statistically significant, indicating that pain scores changed over time and that the pattern of change differed between groups (Table 2).

Table 2. Repeated-measures analysis of pain scores by anesthetic group and time

Effect	df	F	P-value	Partial eta squared
Main effect of group	1, 57	2.21	0.143	0.037
Main effect of time	2.92, 166.63	32.52	<0.001	0.363
Time × group interaction	2.92, 166.63	11.67	<0.001	0.170

df: degrees of freedom. Greenhouse-Geisser-corrected degrees of freedom are shown for time and interaction effects. P < 0.05 was considered statistically significant.

Between-group comparisons by time point

Repeated-measures analysis of variance showed a significant interaction between anesthetic type and time (F[2.92, 66.63] = 11.67, P < 0.001, partial eta squared = 0.170). The main effect of time was also significant (F[2.92, 166.63] = 32.52, P <

0.001, partial eta squared = 0.363), whereas the main effect of group was not significant (F[1, 57] = 2.21, P = 0.143, partial eta squared = 0.037).

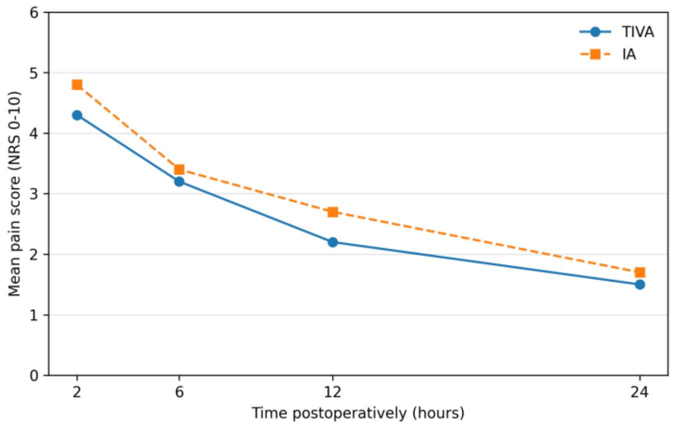
Mean pain scores were lower in the TIVA group at 2 hours [4.3 (0.8) vs. 4.8 (0.8), P = 0.010], 6 hours [3.2 (0.6) vs. 3.4 (0.7), P = 0.028], and 12 hours [2.2 (0.5) vs. 2.7 (0.6), P = 0.001]. At 24 hours, the difference between TIVA and IA was not statistically significant [1.5 (0.3) vs. 1.7 (0.4), P = 0.063]. With a Bonferroni-adjusted threshold of $P < 0.0125$ for four time-point comparisons, the 2-hour and 12-hour differences remained statistically significant, whereas the 6-hour and 24-hour differences did not (Table 3, Figure 2).

Table 3. Postoperative pain scores (NRS 0-10) by time point

Time point	TIVA group (n = 29) mean (SD)	IA group (n = 30) mean (SD)	Total (n = 59) mean (SD)	Mean difference (95% CI)	P-value
2 hours	4.3 (0.8)	4.8 (0.8)	4.6 (0.8)	-0.50 (-0.92 to -0.08)	0.010
6 hours	3.2 (0.6)	3.4 (0.7)	3.3 (0.7)	-0.20 (-0.54 to 0.14)	0.023
12 hours	2.2 (0.5)	2.7 (0.6)	2.5 (0.6)	-0.50 (-0.79 to -0.21)	0.001
24 hours	1.5 (0.3)	1.7 (0.4)	1.6 (0.4)	-0.20 (-0.38 to -0.02)	0.063

CI: confidence interval, IA: inhalation anesthesia, NRS: Numerical Rating Scale, SD: standard deviation, TIVA: total intravenous anesthesia. A Bonferroni-adjusted threshold of $P < 0.0125$ applies to the four time-point comparisons; unadjusted P-values are shown as reported.

Figure 2. Mean pain scores by anesthetic group over time



Rescue analgesia and postoperative nausea and vomiting

Secondary postoperative outcomes are summarized in Table 4. Patients in the TIVA group requested rescue analgesia significantly later than those in the IA group, with a mean difference of 1.3 hours (95% CI: 0.45 to 2.15; P = 0.004). Total tramadol consumption during the first 24 postoperative hours was significantly lower in the TIVA group, with a mean difference of -16.7 mg (95% CI: -29.9 to -3.5; P = 0.016). The incidence of postoperative nausea and vomiting was numerically lower in the TIVA group (17.2% vs. 23.3%), although the difference was not statistically significant (risk difference: -6.1%, 95% CI: -26.6% to 14.4%; P = 0.560).

Table 4. Secondary postoperative outcomes

Outcome	TIVA (n = 29)	IA (n = 30)	Mean Difference (95% CI)	P-value
Time to first rescue analgesia (hours), mean (SD)	4.2 (1.8)	2.9 (1.5)	+1.3 hours (0.45 to 2.15)	0.004
Total tramadol consumption in 24 hours (mg), mean (SD)	48.3 (22.5)	65.0 (28.1)	-16.7 mg (-29.9 to -3.5)	0.016
PONV, n (%)	5 (17.2)	7 (23.3)	-6.1% (-26.6% to 14.4%)	0.560

IA: inhalation anaesthesia, PONV: postoperative nausea and vomiting, SD: standard deviation; TIVA: total intravenous anaesthesia, CI: confidence interval

Discussion

This RCT evaluated the effect of propofol-based TIVA on early POP among Libyan patients undergoing LC. The findings suggest that TIVA was associated with lower early pain scores and reduced rescue opioid consumption compared with isoflurane-based IA; however, the between-group difference was not sustained at 24 hours.

Previous studies have reported inconsistent findings regarding differences in postoperative pain between TIVA and IA [9, 12]. In the present study, propofol-based TIVA was associated with modestly lower pain scores during the early postoperative period. The absence of a significant difference at 24 hours suggests that any analgesic benefit of propofol-based TIVA may be time-limited and most relevant during the immediate recovery phase.

Pain scores decreased over time in both groups, which is consistent with the expected postoperative recovery trajectory after LC under standardized multimodal analgesia. Adequate early POP control remains clinically important because poorly controlled pain can impair mobilization, reduce patient satisfaction, and delay recovery [16].

A relatively small proportion of patients in this Libyan cohort used opioid rescue analgesia, which is consistent with previous Libyan reports [3, 17]. The present findings are also broadly consistent with studies by Ortiz et al. [10] and Wong et al. [9], which did not demonstrate a sustained overall pain advantage for propofol-based anesthesia. Conversely, the early reduction in pain scores observed here aligns with reports suggesting an early analgesic benefit of propofol-based TIVA [12, 18].

Compared with an Iranian RCT [19] and an Indian observational study [20], patients in the present cohort appeared to report relatively higher postoperative pain levels. These differences may reflect variation in analgesic protocols, healthcare system resources, pain assessment practices, and cultural factors influencing pain reporting. Previous studies have reported broad ranges of acute POP prevalence across settings [21, 22], underscoring the importance of context-specific pain management research.

Limitations

Several limitations should be acknowledged. First, the final sample size of 59 patients was below the planned target, which may have limited the statistical power to detect smaller or sustained between-group differences. Second, recruitment from two centers in Eastern Libya may limit the generalizability of the findings to other regions and healthcare systems. Third, although the postoperative analgesic regimen was standardized, individual variation in pain perception and use of non-pharmacological pain-relief measures could not be fully controlled. Fourth, the study did not evaluate longer-term outcomes, such as chronic postsurgical pain, which may also be influenced by anesthetic technique.

Conclusion

Propofol-based TIVA was associated with lower early postoperative pain scores, delayed rescue analgesic request, and reduced 24-hour tramadol consumption after LC compared with isoflurane-based IA. However, the analgesic advantage was not sustained at 24 hours. These findings support selective use of propofol-based TIVA when early POP control is a priority, particularly within enhanced recovery or early-discharge pathways.

Acknowledgments

The authors thank the surgical and nursing staff at Derna and Shahat Hospitals for their cooperation and Dr. Emman Al Salheen for statistical guidance. The authors are especially grateful to the patients who participated in this study.

References

1. Zhao HX, Han L, Wang D, Jin J, Ji FH, Guo W, et al. Impact of opioid-free anesthesia on the overall benefit of analgesia score after laparoscopic cholecystectomy: protocol and statistical analysis plan for a multicenter, randomized, controlled trial. Ann Med. 2025 Dec;57(1):2589570. doi: 10.1080/07853890.2025.2589570.
2. Bisgaard T, Klarskov B, Rosenberg J, Kehlet H. Characteristics and prediction of early pain after laparoscopic cholecystectomy. Pain. 2001;90(3):261-9. doi: 10.1016/S0304-3959(00)00406-1.
3. Makhlouf SM, Algabaily AK, Hawil MR, Albkouri FO. Prevalence of acute postoperative pain with risk factors following appendectomy and cholecystectomy in tertiary hospitals in Eastern Libya. Indian J Pain. 2025;39(1):29-35.
4. Jones C, Harris J. Total intravenous anaesthesia. Br J Hosp Med (Lond). 2021;82(6):1-2. doi: 10.12968/hmed.2021.0190.
5. Richebé P, Brulotte V. Anaesthesia maintenance with propofol versus sevoflurane to reduce postoperative pain: Still too early for recommendations? Eur J Pain. 2019;23(5):847-8. doi: 10.1002/ejp.1385.
6. Lin WL, Lee MS, Wong CS, Chan SM, Lai HC, Wu ZF, et al. Effects of intraoperative propofol-based total intravenous anesthesia on postoperative pain in spine surgery: Comparison with desflurane anesthesia - a randomised trial. Medicine (Baltimore). 2019;98(13):e15074. doi: 10.1097/MD.0000000000015074.
7. Matta JA, Cornett PM, Miyares RL, Abe K, Sahibzada N, Ahern GP. General anesthetics activate a nociceptive ion channel to enhance pain and inflammation. Proc Natl Acad Sci U S A. 2008;105(25):8784-9. doi: 10.1073/pnas.0711038105.
8. Cheng SS, Yeh J, Flood P. Anesthesia matters: Patients anesthetized with propofol have less postoperative pain than those anesthetized with isoflurane. Anesth Analg. 2008;106(1):264-9.
9. Wong SSC, Choi EKY, Chan WS, Cheung CW. Propofol total intravenous anaesthesia versus inhalational anaesthesia for acute postoperative pain in patients with morphine patient-controlled analgesia: A large-scale retrospective study with covariate adjustment. BMC Anesthesiol. 2022;22(1):140. doi: 10.1186/s12871-022-01683-9.
10. Ortiz J, Chang LC, Tolpin DA, Minard CG, Scott BG, Rivers JM. Randomized, controlled trial comparing the effects of anesthesia with propofol, isoflurane, desflurane, and sevoflurane on pain after laparoscopic cholecystectomy. Braz J Anesthesiol. 2014;64(3):145-51. doi: 10.1016/j.bjane.2013.03.011.
11. Peng K, Liu HY, Wu SR, Liu H, Zhang ZC, Ji FH. Does propofol anesthesia lead to less postoperative pain compared with inhalational anesthesia? A systematic review and meta-analysis. Anesth Analg. 2016;123(4):846-58. doi: 10.1213/ANE.0000000000001504.
12. Wong SSC, Leung MYY, Cheung CW. The effect of total intravenous anaesthesia with propofol on postoperative pain after third molar surgery: A double-blind randomized controlled trial. Eur J Pain. 2019;23(5):884-93. doi: 10.1002/ejp.1354.
13. Raeder JC, Mjåland O, Aasbø V, Grøgaard B, Buanes T. Desflurane versus propofol maintenance for outpatient laparoscopic cholecystectomy. Acta Anaesthesiol Scand. 1998;42(1):106-10. doi: 10.1111/j.1399-6576.1998.tb05089.x.
14. Tan T, Bhinder R, Carey M, Briggs L. Day-surgery patients anesthetized with propofol have less postoperative pain than those anesthetized with sevoflurane. Anesth Analg. 2010;111(1):83-5. doi: 10.1213/ANE.0b013e3181c0ee9e.
15. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: Updated guidelines for reporting parallel group randomized trials. BMJ. 2010;340:c332. doi: 10.1136/bmj.c332.
16. Gan TJ. Poorly controlled postoperative pain: Prevalence, consequences, and prevention. J Pain Res. 2017;10:2287-98. doi: 10.2147/JPR.S144066.
17. Makhlouf SM. Postoperative pain management outcomes at a Libyan hospital: A cross-sectional survey. Int J Pain. 2024;15(2):88-97. doi: 10.56718/ijp.24-020.
18. Wong SSC, Chan WS, Irwin MG, Cheung CW. Total intravenous anesthesia (TIVA) with propofol for acute postoperative pain: A scoping review of randomized controlled trials. Asian J Anesthesiol. 2020;58(3):79-93. doi: 10.6859/aja.202009_58(3).0001.
19. Amiri AA, Karvandian K, Rahimi M, Ashouri M, Amiri AA. Postoperative nausea and vomiting and postoperative pain in patients undergoing elective laparoscopy; comparison of total intravenous anesthesia versus inhalational anesthesia: A randomized clinical trial. Arch Anesthesiol Crit Care. 2020;6(2):71-7. doi: 10.18502/aacc.v6i2.2759.
20. Sharma SK, Thakur K, Mudgal SK, Payal YS. Acute postoperative pain experiences and satisfaction with its management among patients with elective surgery: An observational study. Indian J Anaesth. 2020;64(5):403-8. doi: 10.4103/ija.IJA_33_20.
21. Bimrew D, Misganaw A, Samuel H, Desta TD, Bayable SD. Incidence and associated factors of acute postoperative pain within the first 24 h in women undergoing cesarean delivery at a resource-limited setting in Addis Ababa, Ethiopia: A prospective observational study. SAGE Open Med. 2022;10:20503121221133190. doi: 10.1177/20503121221133190.
22. van Boekel RLM, Steegers MAH, van Noord I, van de Sande R, Vissers KCP. Acute pain services and postsurgical pain management in the Netherlands: A survey. Pain Pract. 2015;15(5):447-54. doi: 10.1111/papr.12192.