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CLINICAL TRIAL REPORT

Effects of Dexmedetomidine on Minimum Alveolar Concentration of Sevoflurane for Blunting Sympathetic Response to Pneumoperitoneum: A Randomized Trial

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Purpose: Laparoscopic procedures require abdominal inflation (pneumoperitoneum), which triggers strong stress responses that typically need high concentrations of sevoflurane to manage. Despite dexmedetomidine's known anesthetic-sparing properties, its specific effects on sevoflurane minimum alveolar concentration for blunting sympathetic response (MAC_{BAR}) during pneumoperitoneum remain incompletely characterized. This study evaluates dexmedetomidine's impact on sevoflurane requirements for blocking sympathetic responses during laparoscopic pneumoperitoneum.

Patients and Methods: This prospective, randomized, double-blind, placebo-controlled trial enrolled 90 adults (aged 18–45 years) classified as American Society of Anesthesiologists physical status I–II scheduled for elective laparoscopic cholecystectomy. Participants received either saline, low-dose dexmedetomidine (target 0.3 ng/mL), or high-dose dexmedetomidine (target 0.6 ng/mL). We determined sevoflurane MAC_{BAR} using Dixon's up-and-down method, defined as the concentration preventing ≥ 20% increase in heart rate or mean arterial pressure following pneumoperitoneum. Secondary outcomes included hemodynamic responses, emergence time, adverse events, and plasma catecholamine levels.

Results: Dexmedetomidine significantly reduced sevoflurane MAC_{BAR} compared to control (4.70% ± 0.18%; 95% confidence interval [CI], 4.61–4.80): to 2.90% ± 0.19% (95% CI, 2.80–3.00) in the low-dose group and to 1.90% ± 0.16% (95% CI, 1.82–1.98) in the high-dose group (both $p < 0.001$). Patients receiving dexmedetomidine had significantly lower plasma epinephrine and norepinephrine levels following pneumoperitoneum compared to control ($p < 0.001$), with better hemodynamic stability. Emergence times and adverse event rates remained comparable between groups.

Conclusion: Dexmedetomidine produces dose-dependent reductions in sevoflurane requirements for controlling sympathetic responses during pneumoperitoneum while maintaining hemodynamic stability, making it a valuable adjunct for anesthesia in laparoscopic surgery.

Registration: The Chinese Clinical Trials Registry, ChiCTR2300071257.

Keywords: dexmedetomidine, sevoflurane, minimum alveolar concentration, pneumoperitoneum, laparoscopic cholecystectomy

Introduction

Laparoscopic procedures have transformed modern surgery by delivering substantial benefits over traditional open procedures, including reduced tissue trauma, faster recovery, and fewer postoperative complications.[1–3] However, these techniques present unique anesthetic challenges. The inflation of the abdominal cavity with carbon dioxide (pneumoperitoneum) needed

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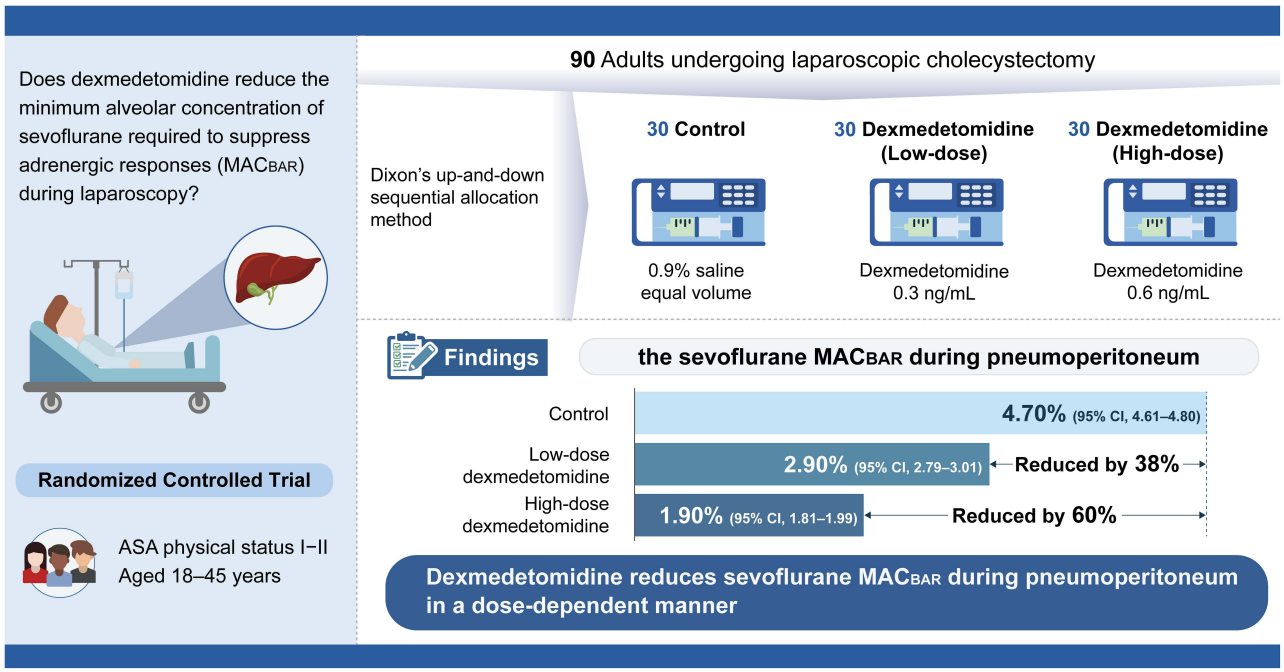
Graphical Abstract



for surgical visibility stimulates stress hormone release, resulting in significant cardiovascular responses, including hypertension and tachycardia.[4] The physiological impact of pneumoperitoneum is multifaceted. Increased intra-abdominal pressure compromises venous return and cardiac output, while CO_2 absorption leads to hypercarbia and sympathetic stimulation. Concurrently, peritoneal distension activates visceral pain pathways, contributing to both intraoperative stress responses and postoperative pain. When inadequately managed, these hemodynamic changes may progress to serious complications such as acute heart failure, myocardial ischemia, and cerebrovascular events, necessitating deeper anesthesia to maintain physiological stability.

Anesthetic depth was traditionally quantified using minimum alveolar concentration (MAC), defined as the concentration preventing movement in response to surgical incision in 50% of patients.[5] With the widespread adoption of neuromuscular blocking agents, clinical focus has shifted from movement-based assessment to hemodynamic stability monitoring. This evolution led to the development of minimum alveolar concentration blocking adrenergic response (MAC_{BAR}).[6] This metric represents the concentration of inhalational anesthetics required to suppress sympathetic responses to noxious stimuli in 50% of patients, providing a valuable metric for contemporary anesthetic management.

While sevoflurane effectively suppresses surgical stress responses, it produces concentration-dependent cardiovascular effects, including reduced blood vessel tone, weakened heart muscle function, and low blood pressure. The high concentrations required to block sympathetic activation during pneumoperitoneum raise significant clinical concerns.[7] These elevated concentrations may increase the risk of renal damage and cardiovascular complications, particularly in vulnerable patients.[8–10] Therefore, research has focused on adjunctive agents that can reduce sevoflurane requirements while maintaining cardiovascular stability.[11–13] Dexmedetomidine has emerged as a promising solution for this challenge. As a highly selective α_2-adrenergic receptor agonist, it combines sedative, analgesic, and sympathetic-blocking properties.[14,15] Although dexmedetomidine reduces the anesthetic requirements of inhalational anesthetics across various surgical procedures,[16–18] its specific effect on sympathetic response suppression during pneumoperitoneum remains unexplored.

This prospective, randomized controlled trial evaluates dexmedetomidine's effect on sevoflurane MAC_{BAR} during carbon dioxide pneumoperitoneum. We hypothesize that dexmedetomidine reduces sevoflurane requirements for

suppressing sympathetic responses in a dose-dependent manner, potentially providing an evidence-based approach for optimizing anesthetic management in laparoscopic surgery.

Materials and Methods

Study Design and Ethics

This prospective, randomized, double-blind, placebo-controlled trial was conducted at Fujian Provincial Hospital, China, from May to September 2024. The Institutional Review Board of Fujian Provincial Hospital (Fuzhou, China) approved the protocol (approval number: K2022-12-004), and the study was registered with the Chinese Clinical Trial Registry (https://www.chictr.org.cn/showproj.html?proj=195010, ChiCTR2300071257) on May 9, 2023, prior to enrollment. All participants provided written informed consent. The investigation complied with Good Clinical Practice guidelines, the Declaration of Helsinki principles, and CONSORT 2010 reporting standards.[19]

Patient Selection

Adults aged 18–45 years with American Society of Anesthesiologists (ASA) physical status I–II scheduled for elective laparoscopic cholecystectomy were enrolled. Exclusion criteria comprised chronic pain syndromes, substance use disorder, pregnancy, obesity (body mass index ≥30 kg/m²), allergies to study medications, use of drugs affecting MAC_{BAR} assessment within 72 hours preoperatively, and contraindications to the planned surgical or anesthetic technique.

Randomization and Allocation

Participants were randomized in equal ratio (1:1:1) to control, low-dose dexmedetomidine, or high-dose dexmedetomidine groups using computer-generated sequences (R software, version 4.3.1). Allocation concealment was ensured through permuted block randomization (block size=6) with sequentially numbered, opaque, sealed envelopes. A designated study nurse not involved in patient care or data analysis prepared identical 50-mL syringes of study medications, maintaining double-blind conditions for all participants, healthcare providers, investigators, and outcome assessors.

Study Procedures

Patients fasted according to current ASA guidelines (6–8 hours for solids, 2 hours for clear fluids).[20] Standard monitoring included continuous electrocardiography, pulse oximetry, invasive arterial pressure measurement, and bispectral index (BIS) throughout the procedure. Core temperature was maintained at 36–37°C using a forced-air warming system (Bair Hugger 755, 3M Healthcare, USA). Following intravenous access, patients received lactated Ringer's solution at 10 mL/kg/h.

Fifteen minutes before induction, we began study drug infusions. The low-dose dexmedetomidine group received 75 μg/h for 15 minutes, then 60 μg/h maintenance to achieve plasma concentrations of 0.3 ng/mL. The high-dose group received 150 μg/h initially, then 120 μg/h, targeting 0.6 ng/mL.[17,21] Control patients received matched volumes of saline. This protocol ensured steady-state drug concentrations before pneumoperitoneum. We induced anesthesia using only sevoflurane 8% in oxygen at 6 L/min via a pre-primed circuit. After loss of consciousness, we administered rocuronium 0.6 mg/kg intravenously and intubated using video laryngoscopy one minute later. Mechanical ventilation maintained end-tidal CO_2 at 35–45 mmHg, confirmed by arterial blood gas analysis before pneumoperitoneum. No intravenous induction agents, opioids, or other adjuvants were administered during this phase.

Initial target end-tidal sevoflurane concentrations were set at 4.6% (control group), 2.8% (low-dose dexmedetomidine), and 1.8% (high-dose dexmedetomidine).[22] Following intubation, sevoflurane concentrations were adjusted to these targets and maintained for ≥15 minutes to ensure alveolar-cerebral equilibration.[23] End-tidal sevoflurane was monitored continuously (CARESCAPE Monitor B650, GE Healthcare, Helsinki, Finland; accuracy ± 0.1%). Pneumoperitoneum was established via Veress needle with intra-abdominal pressure maintained at 12 mmHg. Hemodynamic assessment included heart rate (HR) and mean arterial pressure (MAP), with baseline values derived from measurements at 3 and 1 minutes pre-pneumoperitoneum. Sympathetic response was classified as positive with ≥20% increase in either HR or MAP, while a negative response required both parameters to remain below this threshold. Sevoflurane concentrations for subsequent patients were adjusted by ± 0.2% according to the previous patient's response.

No opioids were administered before or during MAC_{BAR} determination. After determining the primary outcome, we discontinued dexmedetomidine and maintained anesthesia with sevoflurane 2.0% plus remifentanil, titrating to maintain BIS values of 40–60 and hemodynamic parameters within 20% of baseline. For postoperative nausea and vomiting prophylaxis, we administered dexamethasone 8 mg and tropisetron 5 mg intravenously. Analgesia consisted of flurbiprofen axetil 50 mg intravenously plus ropivacaine infiltration at surgical port sites. We administered sufentanil 0.1 μg/kg during the final 5 minutes of surgery. Following sugammadex 2 mg/kg for neuromuscular blockade reversal, we extubated patients after confirming adequate recovery (train-of-four ratio ≥0.95).

Study Outcomes

The primary outcome was sevoflurane MAC_{BAR} during pneumoperitoneum, determined using Dixon's up-and-down sequential allocation method.[24] For each crossover pair (consecutive patients with positive and negative sympathetic responses), MAC_{BAR} was calculated as the midpoint between the respective end-tidal sevoflurane concentrations. The group MAC_{BAR} was defined as the mean of all crossover midpoints within each treatment arm.

Secondary outcomes comprised hemodynamic changes following pneumoperitoneum, emergence time, adverse events (bradycardia, hypotension, nausea and vomiting, hypoxemia), and plasma catecholamine concentrations. For catecholamine analysis, blood samples (3 mL) were collected 3 minutes before and 3 minutes after pneumoperitoneum, immediately centrifuged, and stored at −80°C until analysis by ELISA (Nanjing Jiancheng Bioengineering Institute, China).

Sample Size Calculation

Sample size was calculated using PASS Software 2021 (NCSS LLC, USA). Based on pilot data (control group sevoflurane MAC_{BAR}: 4.6% ± 0.2%), 29 patients per group were required to detect a 0.2% difference in MAC_{BAR} with 90% power at a significance level of 0.017 (Bonferroni-adjusted for three-group comparisons). To compensate for potential dropouts, 30 patients were enrolled in each group.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 27 (IBM Corp., Armonk, NY, USA). We tested all continuous variables for normal distribution using the Shapiro–Wilk test and for equal variances using Levene's test or Bartlett's test, as appropriate. Continuous variables with normal distributions were expressed as mean ± standard deviation (SD), while non-normally distributed variables were presented as median (interquartile range, IQR). Categorical variables were reported as frequencies (percentages).

For between-group comparisons of normally distributed continuous variables, one-way analysis of variance (ANOVA) was performed with Bonferroni correction for multiple post-hoc comparisons. Non-normally distributed continuous variables were analyzed using the Kruskal–Wallis test followed by Dunn's test with Bonferroni adjustment. Categorical variables were compared using the chi-square test or Fisher's exact test as appropriate. Sevoflurane MAC_{BAR} was determined using Dixon's up-and-down method and verified through probit regression analysis. All statistical tests were two-tailed, with $p < 0.05$ considered statistically significant.

Results

Between May 13 and September 10, 2024, we screened 97 patients for eligibility, with 90 meeting inclusion criteria and undergoing randomization to receive saline, low-dose dexmedetomidine, or high-dose dexmedetomidine (Figure 1). One patient in the low-dose group was withdrawn due to rocuronium-induced allergic shock, resulting in 89 patients completing the protocol. Baseline demographic and clinical characteristics were comparable across treatment groups (Table 1).

Individual responses to pneumoperitoneum were determined using Dixon's up-and-down method (Figure 2). Dexmedetomidine significantly reduced sevoflurane MAC_{BAR} compared to control (4.70% ± 0.18%; 95% CI, 4.61–4.80): to 2.90% ± 0.19% (95% CI, 2.79–3.01) in the low-dose group and to 1.90% ± 0.16% (95% CI, 1.81–1.99) in the high-dose group (both $p < 0.001$), representing reductions of 38% and 60%, respectively. Probit regression analysis confirmed these findings, yielding MAC_{BAR} values of 4.59% (95% CI, 4.32–4.79) for the control group, 2.79% (95% CI, 2.53–3.00) for the low-dose group, and 1.81% (95% CI, 1.61–2.01) for the high-dose group (Figure 3).

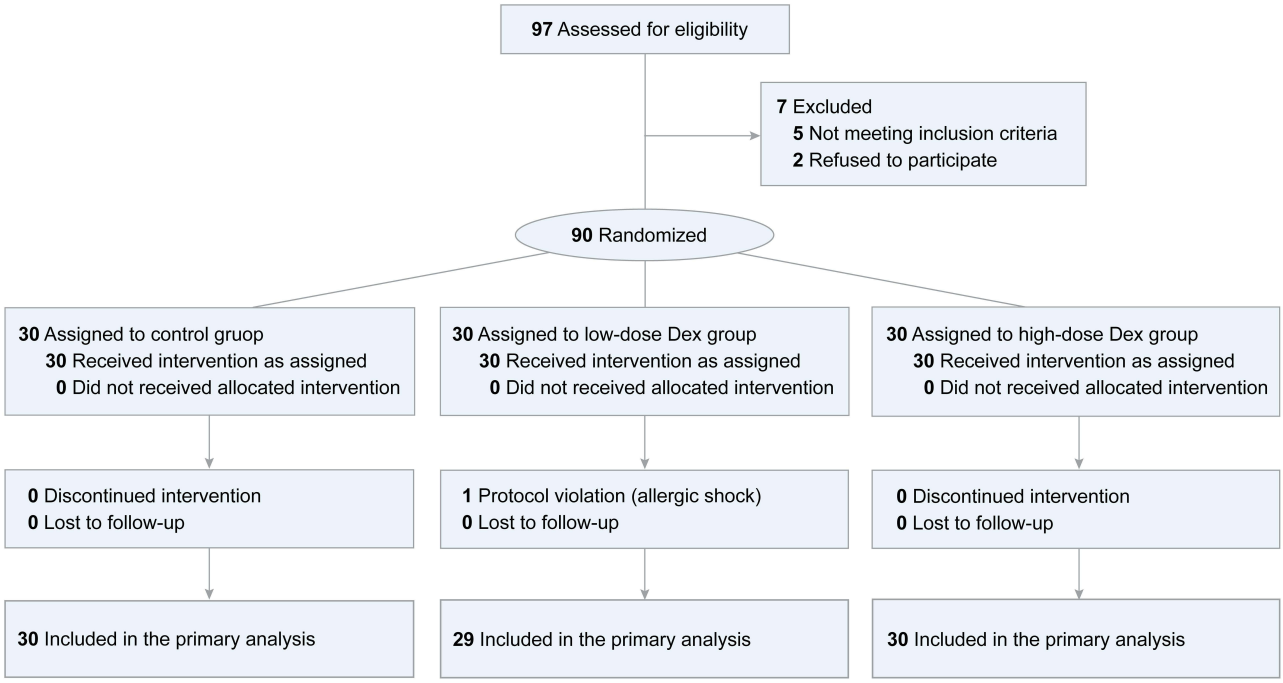


Figure 1 CONSORT flow diagram of patient enrollment, allocation, follow-up, and analysis.
Abbreviation: Dex, dexmedetomidine.

Dexmedetomidine was administered approximately 35 minutes before MAC_{BAR} determination. Initial cardiovascular effects were minimal, with MAP maintained within 30% of baseline and HR above 45 beats/minute, requiring no intervention. Hemodynamic responses to pneumoperitoneum differed significantly between groups (Table 2). Both dexmedetomidine groups demonstrated superior cardiovascular stability, with significantly smaller increases in MAP (low-dose: 15.9% ± 2.8%, high-dose: 12.3% ± 2.3% vs control: 25.4% ± 2.6%, $p < 0.001$) and HR (low-dose: 16.6% ± 4.0%, high-dose: 14.2% ± 4.4% vs

Table 1 Baseline Characteristics

	Control (n=30)	Low-Dose Dexmedetomidine (n=29)	High-Dose Dexmedetomidine (n=30)	p value
Age, yr	41.0 [39.0–43.0]	42 [38.0–43.5]	41.0 [38.8–42.0]	0.395
Sex, n (%)				0.799
Female	16 (53.3)	17 (58.6)	15 (50.0)	
Male	14 (46.7)	12 (41.4)	15 (50.0)	
Weight, kg	66.0 (6.3)	66.1 (6.4)	67.4 (6.6)	0.640
Height, cm	164 [159–174]	165 [160–174]	167 [161–173]	0.543
BMI, kg/m^2	23.8 (1.4)	23.8 (1.4)	24.1 (1.3)	0.469
ASA physical status, n (%)				0.458
I	23 (76.7)	25 (86.2)	22 (73.3)	
II	7 (23.3)	4 (13.8)	8 (26.7)	

(*Continued*)

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Table 1 (Continued).

	Control (n=30)	Low-Dose Dexmedetomidine (n=29)	High-Dose Dexmedetomidine (n=30)	p value
Body temperature, °C	36.6 [36.4–36.8]	36.7 [36.3–36.8]	36.5 [36.3–36.8]	0.395
Hemoglobin, g/L	126 [119–132]	124 [119–130]	129 [117–138]	0.266
$PaCO_2$, mmHg	40 [38–41]	40 [39–43]	40 [39–42]	0.237
PH value	7.41 [7.38–7.43]	7.41 [7.40–7.42]	7.40 [7.38–7.42]	0.587
Duration of surgery, min	48 (11)	51 (12)	54 (13)	0.214
Duration of anesthesia, min	68 (12)	72 (14)	74 (14)	0.171

Notes: Data are presented as mean (SD), median [IQR], or n (%).
Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index.

control: 21.4% ± 4.8%, $p < 0.001$). This attenuated response corresponded with significantly lower plasma catecholamine elevations in both dexmedetomidine groups compared to control ($p < 0.001$, Table 2).

We systematically documented all adverse events throughout the study period. Bradycardia demonstrated a dose-dependent pattern, occurring in 6.7% of control patients, 13.8% of low-dose dexmedetomidine patients, and 20.0% of high-dose dexmedetomidine patients. Similarly, hypotension rates increased with dexmedetomidine dose (3.3%, 10.3%, and 13.3%, respectively). Despite these dose-related increases, all hemodynamic changes were mild and resolved spontaneously without requiring intervention or vasopressor support. No patient experienced major complications, including severe hemodynamic instability, myocardial ischemia, anaphylaxis, or hypoxemia. Postoperative nausea and vomiting occurred less frequently in patients receiving dexmedetomidine compared to control subjects. Emergence times remained comparable across all three groups ($p = 0.428$, Table 2).

Discussion

This randomized controlled trial advances our understanding of dexmedetomidine's anesthetic-sparing effects by quantitatively demonstrating its impact on MAC_{BAR} during laparoscopic procedures. Our findings show that dexmedetomidine significantly reduces sevoflurane requirements during laparoscopic cholecystectomy in a dose-dependent manner, decreasing sevoflurane MAC_{BAR} by 38% and 60% in the low-dose and high-dose groups, respectively, compared with control. Importantly, these substantial reductions were achieved without increasing adverse events or prolonging emergence time, establishing a favorable clinical profile for this intervention.

In our control group, the sevoflurane MAC_{BAR} during pneumoperitoneum (4.7%) significantly exceeded previously reported values for surgical incisions (2.8–2.9%).[6,7] This difference stems from the distinct physiological responses elicited by these stimuli. While surgical incision generates an acute, localized nociceptive response that rapidly resolves, carbon dioxide insufflation during laparoscopy produces sustained, intense sympathetic activation. Despite the minimally invasive nature of laparoscopic surgery, pneumoperitoneum induces substantial catecholamine release, causing pronounced elevations in heart rate and blood pressure. This robust sympathetic response necessitates higher sevoflurane concentrations for adequate suppression, explaining the elevated MAC_{BAR} observed in our investigation.

Sedative and analgesic agents reduce volatile anesthetic MAC to varying degrees, depending on both drug selection and dosage.[25–27] Clinical investigations have consistently demonstrated dexmedetomidine's efficacy in reducing opioid requirements, enhancing postoperative analgesia, and improving recovery profiles.[28,29] Our investigation reveals substantially greater anesthetic-sparing effects than previously documented. While Fragen et al[16] reported only a 17% reduction in sevoflurane MAC with dexmedetomidine 0.7 ng/mL during surgical incision, we observed markedly larger reductions in MAC_{BAR} during pneumoperitoneum—38% and 60% in the low-dose and high-dose groups, respectively—using identical infusion methodology. This enhanced effect appears attributable to two key mechanisms: first,

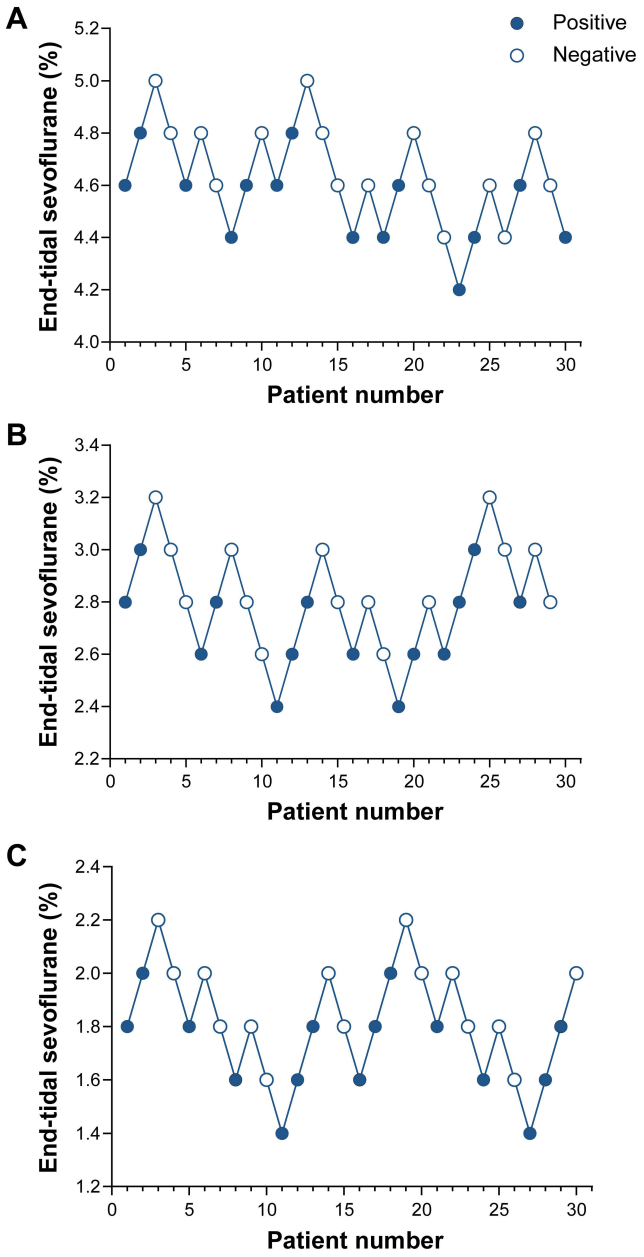

Figure 2 Individual responses to pneumoperitoneum determined by Dixon's up-and-down method.
Notes: Sequential up-and-down plots showing individual patient responses to pneumoperitoneum in three treatment groups: (**A**) control, (**B**) low-dose dexmedetomidine (target 0.3 ng/mL), and (**C**) high-dose dexmedetomidine (target 0.6 ng/mL). Hollow circles represent negative responses (stable hemodynamics), while solid circles indicate positive responses (≥20% increase in heart rate or blood pressure). The calculated minimum alveolar concentration of sevoflurane blocking adrenergic response (MAC_{BAR}) values were 4.70% ± 0.18% in the control group, 2.90% ± 0.19% in the low-dose dexmedetomidine group, and 1.90% ± 0.16% in the high-dose dexmedetomidine group, demonstrating dose-dependent reduction with dexmedetomidine administration.

pneumoperitoneum generates more intense and sustained nociceptive input compared with surgical incision, highlighting dexmedetomidine's particular efficacy against prolonged sympathetic activation; second, dexmedetomidine's selective α_2 -adrenergic receptor agonism attenuates central sympathetic outflow,[15] synergistically complementing sevoflurane's effects. Our laboratory findings support this mechanistic explanation, demonstrating significantly reduced plasma catecholamine concentrations in dexmedetomidine-treated subjects.

The sevoflurane-sparing effect achieved through dexmedetomidine administration may reduce sevoflurane-associated adverse effects.[30,31] However, these benefits must be weighed against potential cardiovascular complications. While previous investigations reported significant concerns regarding dexmedetomidine-induced bradycardia and hypotension,[32–34] our

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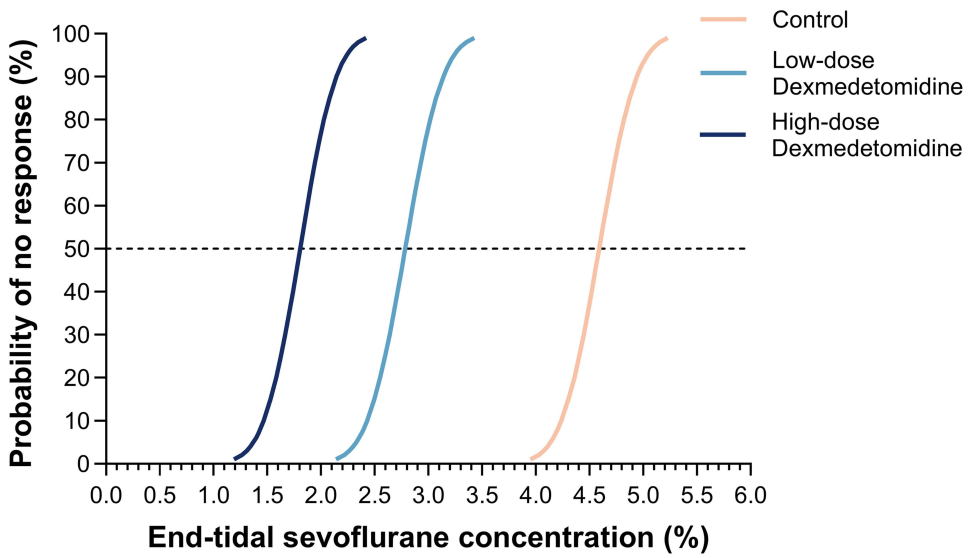

Figure 3 Probability curves for inhibition of sympathetic response during pneumoperitoneum.
Notes: Probit regression analysis showing probability of no sympathetic response at different end-tidal sevoflurane concentrations. Control group (light line), low-dose dexmedetomidine group (0.3 ng/mL, medium line), and high-dose dexmedetomidine group (0.6 ng/mL, dark line) are displayed. The horizontal dashed line at 50% probability indicates sevoflurane MAC_{BAR} values: 4.59% (control), 2.79% (low-dose), and 1.81% (high-dose). Leftward shift of the curves demonstrates dose-dependent reduction in sevoflurane requirements with increasing dexmedetomidine concentration.
Abbreviation: MAC_{BAR}, minimum alveolar concentration blocking adrenergic response.

findings demonstrate an enhanced safety profile attributable to three key factors: an optimized two-step infusion protocol (initial loading followed by maintenance), selective patient enrollment (ASA I–II, aged 18–45), and appropriate hemodynamic monitoring parameters. Additionally, the sympathetic stimulation elicited by pneumoperitoneum appears to provide a physiological counterbalance to dexmedetomidine's sympatholytic properties.

Table 2 Secondary Outcomes

	Control (n=30)	**Low-Dose Dexmedetomidine (n=29)**	**High-Dose Dexmedetomidine (n=30)**	**p value**
HR, bpm				
Pre-pneumoperitoneum	68 (4)	67 (4)	66 (4)	0.245
Delta HR, %	21.4 (4.8)	16.6 (4.0)*	14.2 (4.4)*	<0.001
MAP, mmHg				
Pre-pneumoperitoneum	77 [75–78]	76 [75–77]	75 [75–77]	0.175
Delta MAP, %	25.4 (2.6)	15.9 (2.8)*	12.3 (2.3)*	<0.001
Norepinephrine, pg mL^{-1}				
Pre-pneumoperitoneum	377.5 (47.2)	370.0 (40.7)	365.4 (38.5)	0.471
Delta norepinephrine, %	17.6 (1.7)	12.2 (1.6)*	9.5 (1.5)*	<0.001
Epinephrine, pg mL^{-1}				
Pre-pneumoperitoneum	66.3 (12.0)	64.7 (11.7)	63.5 (12.8)	0.337
Delta epinephrine, %	15.4 (1.9)	10.9 (1.1)*	8.6 (0.9)*	<0.001

(*Continued*)

Table 2 (Continued).

	Control (n=30)	Low-Dose Dexmedetomidine (n=29)	High-Dose Dexmedetomidine (n=30)	p value
Emergence time, min	12 [10–13]	12 [10–14]	13 [11–15]	0.428
Adverse events, n (%)				
Bradycardia	2 (6.7)	4 (13.8)	6 (20.0)	0.317
Hypotension	1 (3.3)	3 (10.3)	4 (13.3)	0.432
PONV	5 (16.7)	3 (10.9)	2 (6.7)	0.498
Hypoxemia	0 (0)	0 (0)	0 (0)	NA

Notes: Data are presented as mean (SD), median [IQR] or n (%). * $p < 0.001$ vs control.
Abbreviations: HR, heart rate; MAP, mean arterial pressure; PONV, postoperative nausea and vomiting; NA, not applicable.

Our investigation offers several methodological strengths, including its randomized controlled design, standardized protocols, and comprehensive physiological monitoring. Nevertheless, several limitations warrant acknowledgment. The primary methodological constraint was our inability to directly measure plasma dexmedetomidine concentrations. Although we utilized a validated two-step infusion protocol to achieve target concentrations, direct plasma measurements would have provided critical pharmacokinetic data, allowing more precise correlation between drug concentrations and observed clinical effects. Our study population—limited to ASA I–II patients undergoing elective laparoscopic cholecystectomy—restricts generalizability of findings to broader clinical contexts. Additionally, while we demonstrated significant reductions in anesthetic requirements, our sample size (n=89) lacked sufficient statistical power to detect differences in low-frequency safety outcomes.

Future research should address these limitations through: (1) incorporation of plasma dexmedetomidine monitoring to establish definitive pharmacokinetic-pharmacodynamic relationships; (2) extension of investigations to diverse surgical procedures and broader patient populations, including those with higher ASA classifications; and (3) implementation of adequately powered multicenter trials examining both safety outcomes and cost-effectiveness to develop evidence-based clinical protocols.

Conclusion

Dexmedetomidine produces dose-dependent reductions in sevoflurane MAC_{BAR} during carbon dioxide pneumoperitoneum in patients undergoing laparoscopic cholecystectomy. Administration of low-dose (0.3 ng/mL) and high-dose (0.6 ng/mL) dexmedetomidine decreased sevoflurane requirements by 38% and 60%, respectively. These clinically significant reductions occurred without compromising hemodynamic stability, prolonging recovery, or increasing adverse event incidence. Our findings demonstrate that dexmedetomidine represents an effective adjunctive agent for optimizing anesthetic management during laparoscopic procedures, particularly when dosing is individualized according to patient characteristics.

Data Sharing Statement

The de-identified participant data, study protocol, and complete statistical analysis plan from this research will be made available upon reasonable request to the corresponding author. Available data includes individual participant records that support the published findings, with appropriate measures in place to maintain participant confidentiality according to established research ethics guidelines.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

References

1. Fichtinger RS, Aldrighetti LA, Abu Hilal M, et al. Laparoscopic versus open hemihepatectomy: the Orange II PLUS multicenter randomized controlled trial. *J Clin Oncol*. 2024;42:1799–1809. doi:10.1200/JCO.23.01019
2. Hakkenbrak NAG, Jansma EP, van der Wielen N, et al. Laparoscopic versus open distal gastrectomy for gastric cancer: a systematic review and meta-analysis. *Surgery*. 2022;171:1552–1561. doi:10.1016/j.surg.2021.11.035
3. Coccolini F, Catena F, Pisano M, et al. Open versus laparoscopic cholecystectomy in acute cholecystitis. Systematic review and meta-analysis. *Int J Surg*. 2015;18:196–204. doi:10.1016/j.ijsu.2015.04.083
4. Joris JL, Chiche JD, Canivet JL, et al. Hemodynamic changes induced by laparoscopy and their endocrine correlates: effects of clonidine. *J Am Coll Cardiol*. 1998;32:1389–1396. doi:10.1016/s0735-1097(98)00406-9
5. Aranake A, Mashour GA, Avidan MS. Minimum alveolar concentration: ongoing relevance and clinical utility. *Anaesthesia*. 2013;68:512–522. doi:10.1111/anae.12168
6. Wu Z, Yu J, Zhang T, et al. Effects of $etco_2$ on the minimum alveolar concentration of sevoflurane that blunts the adrenergic response to surgical incision: a prospective, randomized, double-blinded trial. *Anesth Analg*. 2022;135:62–70. doi:10.1213/ANE.0000000000005784
7. Ura T, Higuchi H, Taoda M, et al. Minimum alveolar concentration of sevoflurane that blocks the adrenergic response to surgical incision in women: MACBAR. *Eur J Anaesthesiol*. 1999;16:176–181. doi:10.1046/j.1365-2346.1999.00446.x
8. Gentz BA, Malan TP Jr. Renal toxicity with sevoflurane: a storm in a teacup? *Drugs*. 2001;61:2155–2162. doi:10.2165/00003495-200161150-00001
9. Jacob AT, Kumar AH, Halivana G, et al. Bioinformatics-guided disproportionality analysis of sevoflurane-induced nephrogenic diabetes insipidus using the FDA Adverse Event Reporting System database. *Br J Clin Pharmacol*. 2024;90(8):1804–1810. doi:10.1111/bcp.15869
10. Miao M, Han Y, Zhang Y, et al. Epileptiform EEG discharges during sevoflurane anesthesia in children: a meta-analysis. *Clin Neurophysiol*. 2022;143:48–55. doi:10.1016/j.clinph.2022.08.019
11. Albertin A, Casati A, Bergonzi P, et al. Effects of two target-controlled concentrations (1 and 3 ng/mL) of remifentanil on $MAC_{BAR}$of sevoflurane. *Anesthesiology*. 2004;100:255–259. doi:10.1097/00000542-200402000-00012
12. Chen C, Pang Q, Tu A, et al. Effect of low-dose ketamine on MAC_{BAR} of sevoflurane in laparoscopic cholecystectomy: a randomized controlled trial. *J Clin Pharm Ther*. 2021;46:121–127. doi:10.1111/jcpt.13263
13. Guo Y, Wang D, Yang X, et al. Effects of different sufentanil target concentrations on the MACBAR of sevoflurane in patients with carbon dioxide pneumoperitoneum stimulus. *BMC Anesthesiol*. 2020;20:239. doi:10.1186/s12871-020-01160-1
14. Weerink MAS, Struys MMRF, Hannivoort LN, et al. Clinical pharmacokinetics and pharmacodynamics of dexmedetomidine. *Clin Pharmacokinet*. 2017;56:893–913. doi:10.1007/s40262-017-0507-7
15. Mantz J, Josserand J, Hamada S. Dexmedetomidine: new insights. *Eur J Anaesthesiol*. 2011;28:3–6. doi:10.1097/EJA.0b013e32833e266d
16. Fragen RJ, Fitzgerald PC. Effect of dexmedetomidine on the minimum alveolar concentration (MAC) of sevoflurane in adults age 55 to 70 years. *J Clin Anesth*. 1999;11:466–470. doi:10.1016/s0952-8180(99)00081-1
17. Aantaa R, Jaakola ML, Kallio A, et al. Reduction of the minimum alveolar concentration of isoflurane by dexmedetomidine. *Anesthesiology*. 1997;86:1055–1060. doi:10.1097/00000542-199705000-00008
18. Yao Y, Qian B, Chen Y, et al. Intranasal dexmedetomidine premedication reduces the minimum alveolar concentration of sevoflurane for tracheal intubation in children: a randomized trial. *J Clin Anesth*. 2014;26(4):309–314. doi:10.1016/j.jclinane.2013.12.012
19. Juszczak E, Altman DG, Hopewell S, et al. Reporting of multi-arm parallel-group randomized trials: extension of the CONSORT 2010 Statement. *JAMA*. 2019;321(16):1610–1620. doi:10.1001/jama.2019.3087
20. Joshi GP, Abdelmalak BB, Weigel WA, et al. 2023 American society of anesthesiologists practice guidelines for preoperative fasting: carbohydrate-containing clear liquids with or without protein, chewing gum, and pediatric fasting duration-a modular update of the 2017 American society of anesthesiologists practice guidelines for preoperative fasting. *Anesthesiology*. 2023;138:132–151. doi:10.1097/ALN.0000000000004381
21. Dyck JB, Maze M, Haack C, et al. The pharmacokinetics and hemodynamic effects of intravenous and intramuscular dexmedetomidine hydrochloride in adult human volunteers. *Anesthesiology*. 1993;78(5):813–820. doi:10.1097/00000542-199305000-00002
22. Zou ZY, Zhao YL, Yang XL, et al. Effects of different remifentanil target concentrations on MAC BAR of sevoflurane in gynaecological patients with CO_2 pneumoperitoneum stimulus. *Br J Anaesth*. 2015;114:634–639. doi:10.1093/bja/aeu400

23. Merkel G, Eger EI. A comparative study of halothane and halopropane anesthesia including method for determining equipotency. *Anesthesiology*. 1963;24:346–357. doi:10.1097/00000542-196305000-00016
24. Oron AP, Souter MJ, Flournoy N. Understanding research methods: up-and-down designs for dose-finding. *Anesthesiology*. 2022;137:137–150. doi:10.1097/ALN.0000000000004282
25. Müller J, Plöchl W, Reiter B, et al. The effect of oral Δ-9-tetrahydrocannabinol on the minimal alveolar concentration of sevoflurane: a randomized, controlled, observer-blinded experimental study. *Eur J Anaesthesiol*. 2021;38:58–63. doi:10.1097/EJA.0000000000001295
26. Chen BZ, Chu QJ, Yu JR, et al. The effect of remifentanil on the minimum alveolar concentration of isoflurane in children. *J Clin Anesth*. 2015;27:504–507. doi:10.1016/j.jclinane.2015.03.026
27. Luo LL, Zhou LX, Wang J, et al. Effects of propofol on the minimum alveolar concentration of sevoflurane for immobility at skin incision in adult patients. *J Clin Anesth*. 2010;22:527–532. doi:10.1016/j.jclinane.2010.02.006
28. Grape S, Kirkham KR, Frauenknecht J, et al. Intra-operative analgesia with remifentanil vs. dexmedetomidine: a systematic review and meta-analysis with trial sequential analysis. *Anaesthesia*. 2019;74(6):793–800. doi:10.1111/anae.14657
29. Verret M, Jbp L, Lalu MM, et al. Effectiveness of dexmedetomidine on patient-centered outcomes in surgical patients: a systematic review and Bayesian meta-analysis. *Br J Anaesth*. 2024;133:615–627. doi:10.1016/j.bja.2024.06.007
30. Karam C, Zeeni C, Yazbeck-Karam V, et al. Respiratory adverse events after LMA® mask removal in children: a randomized trial comparing propofol to sevoflurane. *Anesth Analg*. 2023;136:25–33. doi:10.1213/ANE.0000000000005945
31. Cao SJ, Zhang Y, Zhang YX, et al. Delirium in older patients given propofol or sevoflurane anesthesia for major cancer surgery: a multicenter randomized trial. *Br J Anaesth*. 2023;131:253–265. doi:10.1016/j.bja.2023.04.024
32. Beloeil H, Garot M, Lebuffe G, et al. Balanced opioid-free anesthesia with dexmedetomidine versus balanced anesthesia with remifentanil for major or intermediate noncardiac surgery. *Anesthesiology*. 2021;134:541–551. doi:10.1097/ALN.0000000000003725
33. De Cassai A, Boscolo A, Geraldini F, et al. Effect of dexmedetomidine on hemodynamic responses to tracheal intubation: a meta-analysis with meta-regression and trial sequential analysis. *J Clin Anesth*. 2021;72:110287. doi:10.1016/j.jclinane.2021.110287
34. De Cassai A, Sella N, Geraldini F, et al. Preoperative dexmedetomidine and intraoperative bradycardia in laparoscopic cholecystectomy: a meta-analysis with trial sequential analysis. *Korean J Anesthesiol*. 2022;75:245–254. doi:10.4097/kja.21359

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