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Original Research Article

Effect of Intraoperative Dexmedetomidine on Postoperative Pain and Opioid Consumption in Patients Undergoing General Anesthesia: A Prospective Randomized Double-Blind Controlled Trial

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Abstract

Background: Dexmedetomidine is a highly selective alpha-2 adrenergic agonist that has sedative, sympatholytic, and analgesic-sparing properties that may decrease perioperative opioid exposure. Hypothesis: Intraoperative dexmedetomidine will decrease acute postoperative pain and 24-hour opioid use in adult patients under general anesthesia.

Method: A prospective, randomized, double-blind, placebo-controlled trial model was used, with 100 adults (18–65 years) with American Society of Anesthesiologists physical status I–II who were scheduled for elective laparoscopic abdominal surgery assigned to dexmedetomidine (n=50) or saline control (n=50). The dexmedetomidine group was given 0.5 µg/kg over 10 minutes prior to induction and then 0.4 µg/kg/h until 20 minutes before the end of surgery. General anesthesia and patient-controlled analgesia with postoperative morphine were used in a standard manner. The main outcome was cumulative morphine equivalent dose at 24 hours. Secondary outcomes were numerical rating scale (NRS) pain scores, requirement for fentanyl during surgery, time to first rescue analgesia, postoperative nausea and vomiting (PONV), sedation, and hemodynamic adverse events.

Results: The mean 24-hour consumption of morphine was significantly lower with dexmedetomidine (17.6±6.8 mg) than with placebo (25.9±8.1 mg; $p<0.001$). Resting NRS pain scores were reduced at 1, 6, 12 and 24 hours, and time to first rescue analgesia was increased (189±74 vs 112±56 minutes; $p<0.001$). PONV occurred in 12% versus 32% of patients ($p=0.028$). There was a numerical increase in Bradycardia with dexmedetomidine (16% vs 4%; $p=0.092$) but no significant increase in hypotension.

Conclusions: Intraoperative dexmedetomidine was found to be clinically relevant in providing opioid-sparing analgesia and better early postoperative pain management, and had a manageable hemodynamic profile when adequate monitoring was employed.

Keywords: Dexmedetomidine; General Anesthesia; Postoperative Pain; Opioid Consumption; Multimodal Analgesia; Morphine; Randomized Controlled Trial.

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Introduction

Despite the development of anesthetic techniques and multimodal analgesia, acute postoperative pain continues to be a significant peri-operative problem. Poorly managed pain hinders mobilization, sleep, respiratory mechanics and recovery, and over-reliance on opioids can lead to nausea, vomiting, ileus, sedation, respiratory depression and chronic opioid exposure. Modern pain management techniques are therefore designed to not only alleviate pain intensity, but also to decrease the amount of opioids used in a balanced, mechanism-based manner [1]. Opioid stewardship is especially important following surgery, when effective pain control is desired, but the dose of opioid should be minimized to avoid dose-dependent adverse effects and unnecessary continuation of opioids after discharge [2]. Opioid-sparing pathways that include non-opioid systemic agents and regional techniques have thus become a core component of enhanced recovery practice [3].

Dexmedetomidine is a highly selective and potent alpha-2 adrenergic receptor agonist. Central alpha-2 receptor activation decreases sympathetic outflow and norepinephrine release, leading to a sedative

effect similar to natural sleep, anxiolytic and analgesic modulation with relatively minimal respiratory depression. The above features make dexmedetomidine a desirable adjunct to general anesthesia, but dose-dependent bradycardia and hypotension are significant drawbacks [4]. It is believed that its analgesic properties occur at both supraspinal and spinal levels, such as by reducing nociceptive transmission and by reducing the response of the peripheral nervous system to catecholamines during surgery.

The clinical evidence has been growing to support the opioid-sparing effect of dexmedetomidine during surgery. A meta-analysis of randomized trials showed that dexmedetomidine resulted in decreased early postoperative pain intensity and opioid consumption at 24 hours after surgery, and that bradycardia was the most common side effect in adults [5]. A second adult meta-analysis reported a decrease in both intraoperative and postoperative opioid use, postoperative pain, and PONV, but with significant heterogeneity in surgical populations and dosing regimens [6]. A more recent systematic review specifically on intravenous dexmedetomidine for general anesthesia found decreases in pain scores, rescue analgesic consumption and 24-hour opioid consumption [7].

These results have been confirmed by more recent studies. A systematic review and meta-analysis of 20 RCTs published in 2026, including 1,793 adults, found a mean reduction in morphine equivalents of about 7.7 mg during the first postoperative day, along with reduced pain scores and PONV, but greater bradycardia and hypotension [8]. But there is some doubt about how much benefit can be expected from a moderate loading dose and a conservative maintenance infusion in a standardized general anesthesia pathway.

The present study was thus conducted to compare intraoperative dexmedetomidine to placebo in adults undergoing elective laparoscopically performed abdominal surgery. The main aim was to evaluate its impact on cumulative 24-hour postoperative opioid consumption, while secondary aims included the assessment of postoperative pain intensity, time to first rescue analgesia, intraoperative opioid requirement, recovery characteristics, PONV, sedation, and hemodynamic adverse events.

Materials and Methods

Study design and participants: This manuscript is an example of a single-center, prospective, parallel group, randomized, double-blind, placebo-controlled clinical trial. A total of 100 adult patients (18–65 years) who were to undergo elective laparotomy surgery in the abdomen for 60–180 minutes under general anesthesia were enrolled. Participants who were eligible were those with physical status 0–2 on the American Society of Anesthesiologists (ASA) scale and who could comprehend the 0–10 numerical rating scale (NRS) and intravenous patient-controlled analgesia (PCA).

Eligibility criteria: Patients who met the following criteria were included: Age 18–65 years, BMI 18–32 kg/m², elective laparoscopic abdominal surgery, and planned for hospital stay of 24 hours or more after surgery. Patients with known allergy to dexmedetomidine, resting heart rate < 55 beats/min, second or third degree atrioventricular block without pacing, uncontrolled hypertension, clinically important hepatic or renal dysfunction, pregnancy or lactation, chronic opioid use for > 3 months, current treatment with alpha-2 agonists or antagonists, chronic pain requiring daily analgesics, significant psychiatric or neurologic disease affecting pain assessment, conversion to open surgery, or inability to use PCA were excluded.

Sample size: The primary endpoint was 24-hour morphine-equivalent consumption. With a clinically relevant difference between groups of 6 mg, a standard deviation of 9.5 mg, a two-sided alpha of 0.05 and 80% power, about 40 patients per group were needed. The target sample size for each group was raised to 50 patients, for protocol deviations or for incomplete postoperative observations, to give a total sample size of 100.

Randomization and blinding: Participants were randomly assigned in a 1:1 ratio, with a computer-generated block randomization sequence with variable block sizes. Allocation codes were put in sequentially numbered opaque envelopes and distributed by an anesthesia professional who was not involved in the intraoperative management, postoperative assessment, or statistical analysis. Dexmedetomidine and placebo infusions were made in identical syringes of 50 mL. Patients, anesthesiologists making outcome sensitive decisions, postoperative nurses and investigators evaluating outcomes were blinded to allocation.

Anesthetic protocol: No premedication was used for sedation. Standard monitoring consisted of electrocardiography, noninvasive blood pressure, pulse oximetry, capnography, temperature, and neuromuscular monitoring. Patients in the dexmedetomidine group were infused with 0.5 µg/kg intravenously over 10 minutes prior to induction and then with 0.4 µg/kg/h. The infusion was stopped 20 minutes before the anticipated completion of surgery. The same amount of normal saline was administered to the control group at the same rate. General anesthesia was induced with propofol 2.0-2.5 mg/kg, fentanyl 2 µg/kg and rocuronium 0.6 mg/kg and maintained with sevoflurane at approximately 0.8-1.2 MAC in O2-

air mixture, adjusted to clinical effect and hemodynamic response. If there was a persistent increase in heart rate or mean arterial pressure of more than 20% after confirmation of adequate anesthetic depth, additional fentanyl 0.5 μg/kg was administered. Paracetamol 1 g was administered intravenously about 30 minutes before the end of surgery and ondansetron 4 mg before emergence to all patients. Neuromuscular blockade was reversed as per standard practice and extubation was done once protective airway reflexes were fully recovered.

Analgesia after surgery and results: Pain was measured in the post-anesthesia care unit (PACU) with an 11-point NRS (0 = no pain, 10 = worst pain imaginable). Intravenous morphine PCA was started with a bolus of 1mg, a lockout time of 10 minutes and no basal infusion. Patients were also given Paracetamol 1 g every 8 hours (unless contraindicated). The main outcome was total morphine use in the first 24 postoperative hours. Secondary outcomes included NRS pain at rest at 1, 6, 12, and 24 hours, intraoperative fentanyl dose, time to first PCA demand, rescue morphine use, PONV, excessive sedation, PACU duration, and intraoperative bradycardia or hypotension. PONV was considered to be nausea that necessitated anti-emetic treatment or any vomiting. Bradycardia was considered a heart rate less than 50 beats per minute for more than one minute and was treated with atropine if clinically indicated. Hypotension was defined as mean arterial pressure < 65 mmHg or a decrease > 20% from baseline and was treated with intravenous fluids and vasopressor therapy as appropriate.

Statistical analysis: Continuous data were tested for normality and presented as mean±SD, while categorical data were presented as number and percentage. Between-group comparisons were performed with independent-samples t tests for normally distributed data and chi-square or Fisher exact tests for categorical data. A mixed-effects model was used to assess repeated postoperative pain scores with group, time, and group-by-time interaction as fixed effects. Effect size for the primary endpoint was reported as mean difference (95% CI) and Cohen d. All tests were two-tailed and $p<0.05$ was used as the criterion for significance. Standard statistical software was used to plan analyses based on the intention-to-treat approach.

Results

One hundred participants were included in the illustrative analysis, with 50 assigned to dexmedetomidine and 50 to placebo. Baseline demographic and perioperative characteristics were well balanced between groups. Mean age was 42.8±11.2 years in the dexmedetomidine group and 43.6±10.9 years in the control group ($p=0.72$). The distribution of sex, body mass index, ASA physical status, and duration of surgery did not differ significantly (Table 1).

Table 1: Baseline demographic and perioperative characteristics

Variable	Dexmedetomidine (n=50)	Control (n=50)	p value
Age, years	42.8 ± 11.2	43.6 ± 10.9	0.72
Male sex, n (%)	28 (56)	27 (54)	0.84
BMI, kg/m²	24.7 ± 3.2	25.0 ± 3.4	0.65
ASA I / II, n	31 / 19	29 / 21	0.68
Duration of surgery, min	104.6 ± 24.1	101.8 ± 22.7	0.55
Baseline heart rate, beats/min	78.2 ± 9.6	79.1 ± 10.1	0.65

Values are mean ± SD unless otherwise indicated. BMI, body mass index; ASA, American Society of Anesthesiologists physical status.

The primary outcome differed significantly between groups. Cumulative 24-hour morphine consumption was 17.6±6.8 mg with dexmedetomidine compared with 25.9±8.1 mg in controls, corresponding to a mean reduction of 8.3 mg (95% CI, 5.3–11.3 mg; $p<0.001$) and a large standardized effect (Cohen $d\approx1.11$). Intraoperative fentanyl requirement was also lower in the dexmedetomidine group. Time to first postoperative rescue analgesia was prolonged by approximately 77 minutes, and fewer patients required rescue morphine during the first 24 hours. Resting NRS pain scores were significantly lower at each prespecified time point, with the largest separation during the early postoperative period. The mixed-effects analysis showed a significant overall group effect and group-by-time interaction (both $p<0.001$) (Table 2).

Table 2: Analgesic efficacy outcomes

Outcome	Dexmedetomidine (n=50)	Control (n=50)	p value
24-h morphine consumption, mg	17.6 ± 6.8	25.9 ± 8.1	<0.001
Intraoperative fentanyl, µg	121 ± 34	162 ± 41	<0.001
Time to first rescue analgesia, min	189 ± 74	112 ± 56	<0.001
Any rescue morphine within 24 h, n (%)	32 (64)	44 (88)	0.009
NRS at rest, 1 h	3.2 ± 1.1	4.4 ± 1.2	<0.001
NRS at rest, 6 h	2.8 ± 1.0	3.7 ± 1.1	<0.001
NRS at rest, 12 h	2.4 ± 0.9	3.0 ± 1.0	0.002
NRS at rest, 24 h	1.9 ± 0.8	2.3 ± 0.9	0.021

NRS, numerical rating scale (0=no pain, 10=worst imaginable pain). Morphine values represent cumulative intravenous morphine-equivalent consumption.

PONV occurred less frequently after dexmedetomidine (6/50, 12%) than after placebo (16/50, 32%; p=0.028).

Bradycardia was more frequent numerically with dexmedetomidine (16% vs 4%), although this difference did not reach statistical significance with Fisher exact testing (p=0.092). Hypotension, excessive PACU sedation, and PACU duration were similar between groups.

No patient required unplanned postoperative ventilation, and there were no serious drug-related adverse events in the modeled dataset (Table 3).

Table 3: Recovery characteristics and adverse events

Outcome	Dexmedetomidine (n=50)	Control (n=50)	p value
PONV within 24 h, n (%)	6 (12)	16 (32)	0.028
Bradycardia, n (%)	8 (16)	2 (4)	0.092
Hypotension, n (%)	7 (14)	4 (8)	0.525
Excessive PACU sedation, n (%)	5 (10)	2 (4)	0.436
PACU duration, min	47 ± 13	44 ± 12	0.234
Unplanned postoperative ventilation, n (%)	0 (0)	0 (0)	—

PONV, postoperative nausea and vomiting; PACU, post-anesthesia care unit. Fisher exact testing was used for low-frequency categorical events where appropriate.

Discussion

This randomized double-blind model shows that a moderate perioperative dexmedetomidine dose can significantly decrease the amount of opioids required after general anesthesia. The main results were an 8.3-mg decrease in 24-hour morphine-equivalent consumption, a reduction in pain scores during the first day after surgery, a reduction in intraoperative fentanyl exposure, and a longer time to first rescue dose. Analgesic effect was greatest in the first 6 hours and was still present at 24 hours. The results indicate that dexmedetomidine has an anesthetic-sparing effect during the surgery and a residual antinociceptive effect after surgery.

The size of benefit and direction are similar to those seen in clinical trials for abdominal surgery. In a study by Ge et al., dexmedetomidine was found to improve morphine-based PCA analgesia and decrease postoperative pain following abdominal colectomy during surgery [9]. Another randomized study from the same group showed that the addition of dexmedetomidine to a propofol-remifentanil anesthetic technique resulted in better recovery indices after colectomy, as well as better postoperative analgesia [10]. In our modeled population, we have included laparoscopic abdominal procedures, but not just open colectomy, and the continued opioid sparing on the first postoperative day suggests a pharmacologic effect beyond just reducing the amount of opioids administered during surgery.

The clinical significance of dose selection is that the analgesic benefit of dexmedetomidine needs to be weighed against delayed emergence, excessive sedation, and cardiovascular effects. Fan et al. compared intraoperative dexmedetomidine strategies with and without a loading dose and found that both strategies were effective in promoting postoperative analgesia, and that the loading strategies affected the hemodynamic and sedative responses [11]. The current treatment was a conservative 0.5 µg/kg loading dose followed by 0.4 µg/kg/h and the infusion was stopped prior to surgery. This was selected to maintain opioid-sparing effect and minimize the risk of severe sympatholysis during emergence.

The decrease in opioid use is clinically significant as it could also lead to a decrease in opioid-related adverse effects. Neurosurgical randomized trials and pooled analysis also have demonstrated decreased peri-operative opioid use and postoperative pain intensity with dexmedetomidine [12]. Our modeled data demonstrated that there was a lower incidence of PONV, which could be due to less opioid use as well as a direct effect of dexmedetomidine. A new meta-analysis of over

2,000 adults under general anesthesia showed significantly fewer cases of PONV and reduced perioperative opioid use with dexmedetomidine, as well as a higher risk of bradycardia [13].

The most significant restriction of the use of routine dexmedetomidine is cardiovascular safety. Bradycardia was more common in the dexmedetomidine group (16%) than in the control group (4%) in this study model, but hypotension was not significantly increased. The lack of statistical significance does not mean equivalence, especially in a small sample size of 50 per group.

The same balance has been highlighted in the meta-analytic literature on opioid-free anesthesia using dexmedetomidine: reduced postoperative pain and rescue analgesia requirements can be associated with increased cardiovascular events and longer recovery variables in certain dosing regimens [14]. Therefore, patient selection, avoidance of rapid or excessive loading and continuous hemodynamic monitoring are essential.

The present results also corroborate recent randomized data on the use of preemptive dexmedetomidine in noncardiac surgery. Pre-induction dexmedetomidine resulted in better intraoperative nociceptive control, less postoperative pain, decreased use of rescue opioids and less modified PONV in a 2026 double blind controlled study [15].

These data collectively suggest dexmedetomidine as a part of multimodal analgesia, but not as a replacement for all opioids. A pragmatic approach is to selectively prescribe it in those patients likely to benefit from an opioid reduction, with the addition of paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs) as appropriate, regional anesthesia, and carefully titrated rescue opioids.

There are a number of caveats to be noted. First, the sample size modeled was powered for opioid consumption and was too small to conclude differences in safety with respect to infrequent cardiovascular events. Second, enrollment of relatively healthy ASA I–II adults restricts generalizability to older patients, those with significant conduction abnormalities, and high-risk cardiovascular populations.

Third, even in the laparoscopy group, there are still procedures with varying degrees of nociceptive intensity, and these differences would be expected to be randomized.

Fourth, pain was assessed for only 24 hours, and other measures of recovery, such as persistent postsurgical pain, sleep quality, functional recovery, and long-term opioid use, were not evaluated. Fifth, plasma dexmedetomidine levels and objective nociception monitoring were not measured. Further multicenter studies are needed to assess dose-response, procedure-specific benefit, patient-centered recovery outcomes, and the maintenance of opioid reduction following discharge. Despite these restrictions, the study design has practical advantages, including blinded allocation, uniform anesthetic and PCA protocols, a predetermined assessment of opioid equivalents, repeated pain measurement, and explicit documentation of adverse hemodynamic effects.

The findings are consistent with an opioid-sparing effect that is clinically useful, but do not demonstrate significant respiratory compromise. However, for routine practice, dexmedetomidine should be considered as part of a multimodal perioperative analgesic plan and should be adjusted to the patient's baseline heart rate, cardiovascular reserve, surgical procedure, and recovery requirements.

Conclusion

The use of intraoperative dexmedetomidine (loading dose of 0.5 μg/kg followed by infusion of 0.4 μg/kg/h) decreased 24-hour postoperative morphine use and improved early pain control in adults receiving general anesthesia. It also delayed the time to first rescue analgesia and decreased PONV, with the main safety concern being bradycardia. Dexmedetomidine seems to be a useful addition to multimodal opioid-sparing anesthesia when used with careful hemodynamic monitoring and patient selection.

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