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Original Contribution

Dexmedetomidine in oxycodone patient-controlled analgesia after lumbar spinal fusion: A randomized, double-blind, placebo-controlled trial

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HIGHLIGHTS

- First randomized, double-blind trial of dexmedetomidine added to oxycodone PCA after lumbar fusion.
- Dexmedetomidine reduced opioid use during early postoperative period but not more at 24 h.
- Improved tolerability (lower PONV and pruritus at 24 h), supporting use as an adjuvant in spine surgery analgesia.

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ABSTRACT

Background: Spinal fusion surgery causes severe postoperative pain often managed with strong opioids, which may lead to adverse effects. Dexmedetomidine is a potential adjuvant in opioid patient-controlled analgesia (PCA), but the optimal dose remains unclear.

Methods: In this double-blind, placebo-controlled trial, adult patients undergoing major lumbar spinal fusion were randomized to receive placebo (D0) or dexmedetomidine at 2.5 (D2), 5 (D5), or 10 μg/ml (D10) combined with oxycodone (1 mg/ml) PCA for 24 h, followed by oxycodone alone for 48 h. The primary outcome was cumulative oxycodone consumption at 24 h.

Results: Ninety-eight patients were included in the final analysis. Unadjusted postoperative opioid consumption was lower in D10 at 1 h (mean difference 3.1 mg, 95% CI 0.6–5.9, $p = 0.011$) and at 2 h (3.7 mg, 95% CI 0.5–6.9 mg, $p = 0.019$) and in D5 at 2 h (3.5 mg, 0.3–6.9 mg, $p = 0.027$) compared with control group D0. No differences were found in cumulative consumption at 24 or 72 h. When 24-h postoperative opioid consumption was adjusted with age and weight, the results remained unchanged. Compared with D0, patients receiving dexmedetomidine had less postoperative nausea and vomiting ($p = 0.04$) and itching ($p = 0.024$) at 24 h. Adverse events and patient satisfaction were otherwise comparable.

Conclusions: Adding dexmedetomidine to oxycodone PCA provided modest early opioid-sparing effects without reducing 72-h opioid consumption. The main benefit was improved 24-h tolerability, with fewer opioid-related side effects. Dexmedetomidine may therefore serve as a useful adjunct in patients at risk of opioid-induced adverse events after lumbar fusion surgery.

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1. Introduction

Severe postoperative pain is common after major spinal fusion surgery [1] and is associated with adverse clinical outcomes and increased health-care costs [2]. Although opioids remain the cornerstone of postoperative analgesia, concerns regarding opioid-related adverse effects and the ongoing opioid crisis have driven the development of opioid-sparing strategies.

Multimodal analgesia targets different pain pathways by combining two or more analgesic modalities to achieve additive or synergistic effects [3]. In major spinal fusion surgery, multimodal analgesia has proven feasible and effective in optimizing pain relief while minimizing opioid-related adverse effects [4,5].

Patient-controlled analgesia (PCA) is associated with lower pain intensity and greater patient satisfaction compared with conventional analgesic administration routes [6]. PCA enhances patient autonomy by providing rapid access to analgesia. Morphine remains the most commonly used opioid in PCA, whereas oxycodone has been associated with higher patient satisfaction scores [6,7].

Dexmedetomidine is a highly selective alpha-2 adrenoceptor agonist with sedative, anxiolytic, and analgesic properties [8]. Earlier meta-analyses concluded that combining dexmedetomidine with an opioid in intravenous PCA during the postoperative period improves analgesia and reduces opioid consumption [9,10]. A randomized controlled trial further demonstrated reduced postoperative opioid consumption during the first 12 h when dexmedetomidine was added to opioid PCA [11]. More recent evidence has clarified dexmedetomidine's clinical role: a 2024 Bayesian meta-analysis demonstrated improved quality of recovery and reduced risk of chronic postsurgical pain, albeit with increased risks of bradycardia and hypotension [12,13]. Additional systematic reviews published in 2024 confirmed improved gastrointestinal recovery [14] and showed that adding dexmedetomidine to opioid-based intravenous PCA reduces early opioid use and postoperative nausea and vomiting, consistent with earlier findings [10,15].

However, these benefits are not uniform across surgical populations, and the optimal dexmedetomidine-to-opioid ratio in intravenous PCA remains unclear, particularly in patients undergoing lumbar spinal fusion surgery, for whom high-quality randomized data are still limited.

To address this knowledge gap, we conducted a randomized, double-blind, placebo-controlled trial comparing three different doses of dexmedetomidine versus placebo as an adjuvant to oxycodone IV-PCA administered for 24 h after lumbar spinal fusion surgery. After the study intervention, IV oxycodone-PCA without dexmedetomidine was continued for further 48 h. We hypothesized that adjunct dexmedetomidine would reduce opioid consumption and opioid-related adverse events. The primary outcome was cumulative oxycodone consumption at 24 h, with secondary outcomes including postoperative pain intensity, cumulative oxycodone consumption, and adverse events up to 72 h after surgery.

2. Methods

2.1. Ethics and registration

This study (DoseRespDex) was approved by the Institutional Review Board of the Hospital District of Southwest Finland (number: 110/1800/2014) and the Finnish Medicines Agency (FIMEA, KL 28/2015). The trial was registered before patient enrollment at clinicaltrials.gov (NCT02454881) and in the EudraCT database (2014–003252-31). No changes to methods were made after trial commencement. The detailed study protocol is available upon request from the authors. Written informed consent was obtained from the participants before inclusion to the study. This manuscript complies with the Consolidated Standards of Reporting Trials guidelines (CONSORT).

2.2. Patient population

This single center study was carried out at the TYKS ORTO Surgical hospital at Turku University Hospital in Turku, Southwest Finland. Adult patients scheduled for elective posterolateral lumbar spine fusion with bilateral transpedicular screw instrumentation under general anesthesia were recruited between 23 June 2015 and 2 Mar 2021 (Fig. 1).

Patients with a history of intolerance to the study drug; concomitant treatment with strong opioids or potent CYP3A4 or CYP2B6 inducers or inhibitors within two weeks prior to the study; age under 20 or over 80 years; BMI >35; sleep apnea or other sleep disorders; significant hepatic or renal disease; history of alcoholism or drug abuse; or psychological or emotional conditions likely to invalidate informed consent were excluded. Intraoperative blood loss exceeding 1500 ml was also an exclusion criterion. Patients were pre-screened by a preoperative care nurse. Potentially eligible subjects were directed to investigators for further screening and information.

2.3. Sex and gender reporting

Both women and men were eligible. Biological sex was recorded from hospital records; gender identity was not collected. No prespecified subgroup analyses were planned, and the study was not powered to detect sex-based differences (noted as a limitation, per SAGER guidance).

2.4. Study design, randomization, and blinding

A randomized, double-blind, controlled dose-response study design was used (Fig. 1). The allocation ratio was 1:1:1:1. Subjects were randomly assigned to one of four dosing groups (G) for intravenous PCA:

D0, oxycodone 1 mg ml-1 alone.

D2, oxycodone 1 mg ml-1 + Dexmedetomidine 2.5 μg ml-1 (ratio 400:1).

D5, oxycodone 1 mg ml-1 + Dexmedetomidine 5 μg ml-1 (ratio 200:1),

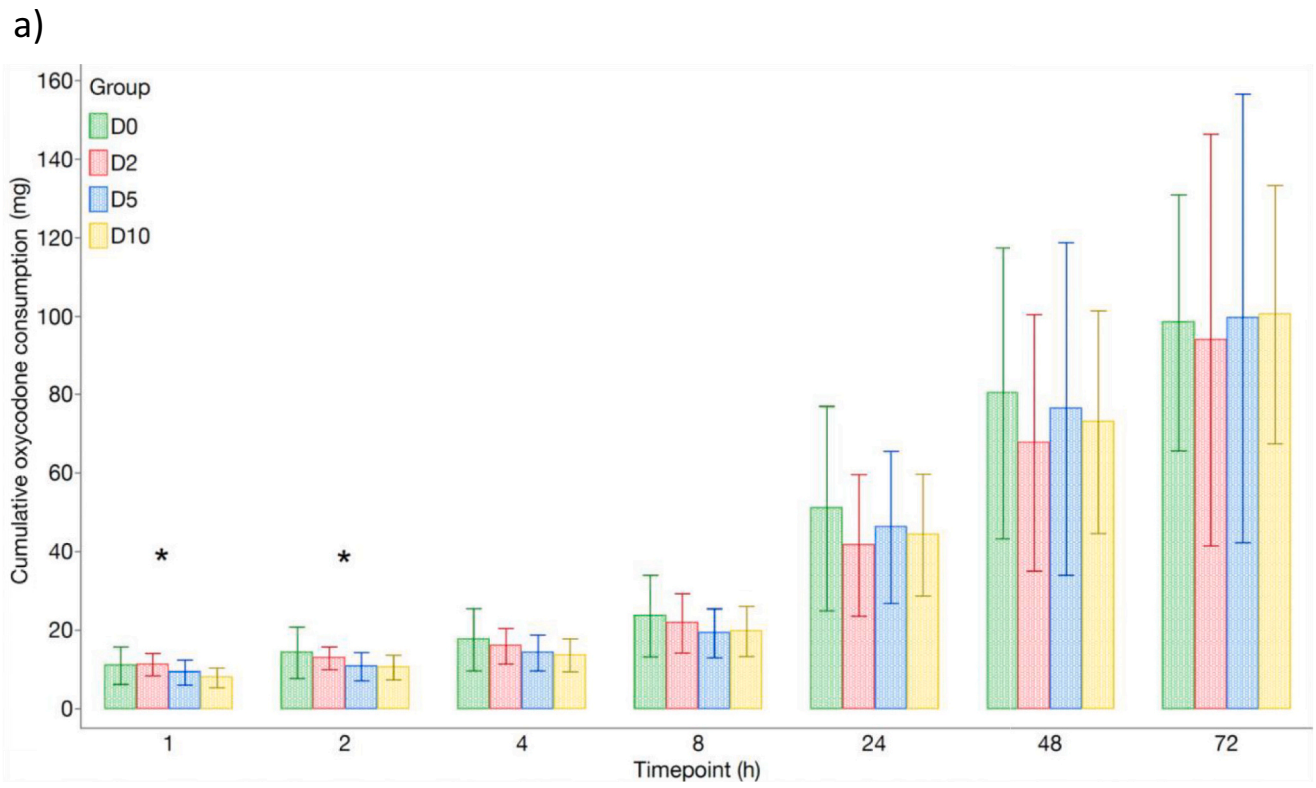
D10, oxycodone 1 mg ml-1 + Dexmedetomidine 10 μg ml-1 (ratio 100:1).

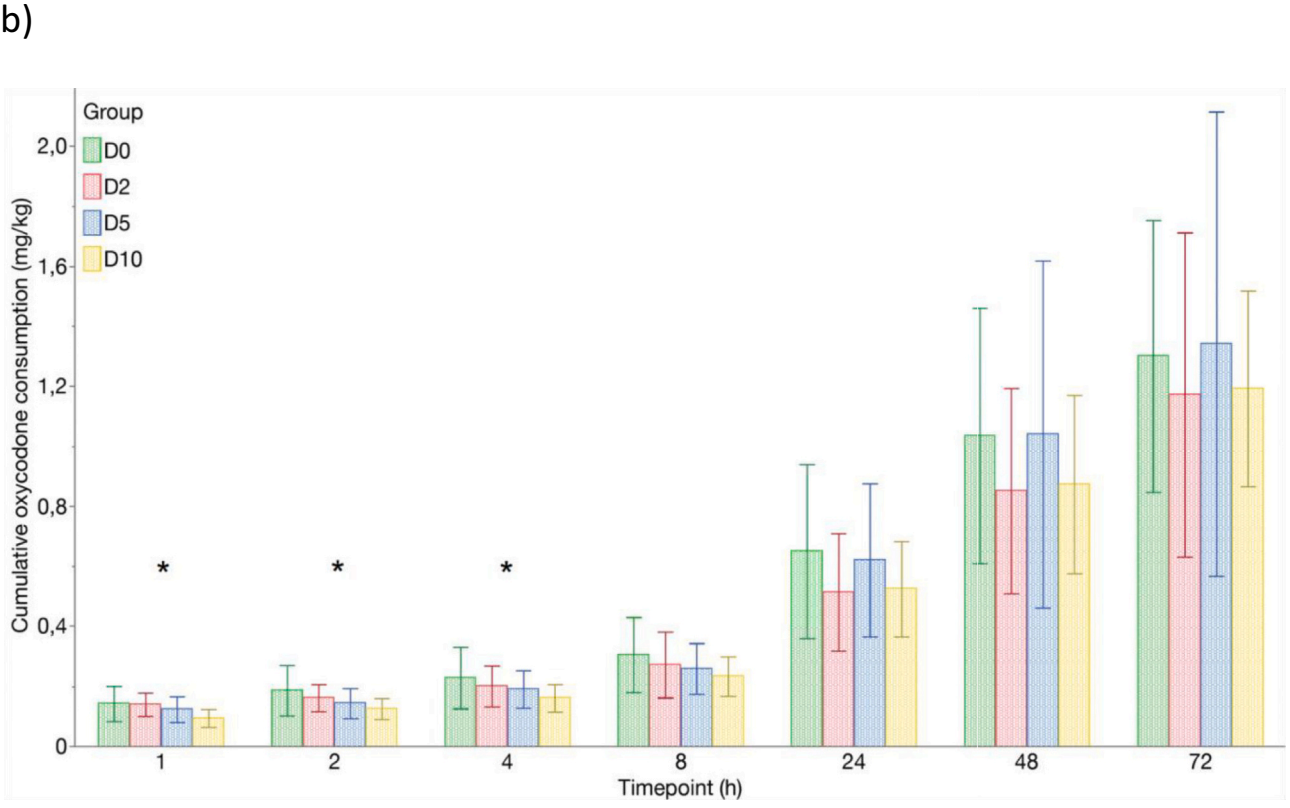
PCA reservoirs were prepared under aseptic conditions in the hospital pharmacy on the day of surgery. Oxycodone (10 mg/ml) and dexmedetomidine (100 μg/ml) were diluted with 0.9% NaCl to reach final concentrations of 1 mg/ml oxycodone and 2.5, 5.0, or 10 μg/ml dexmedetomidine. The 24-h stability and compatibility of these mixtures had been verified in advance in our laboratory, and their physical and chemical compatibility was confirmed in a separate dedicated stability study (https://www.doria.fi/handle/10024/181535).

An independent statistician created a computer-generated randomization list using permutated block randomization. The list was sent to the local hospital pharmacy, which took care of assignment. Coded PCA reservoirs with no other markings were delivered to the operation room by the pharmacy on the day of surgery to ensure double blinding. Patients, researchers, and clinical staff were blinded to group allocation.

2.5. Conduct of the study and anesthesia

After providing written informed consent, patients learned to use the PCA system (CADD®-Solis VIP and CADD-Legacy® PCA Pump Model 6300, Smiths Medical, Minneapolis, MN, USA) and numerical rating scale (NRS; 0 denotes no pain, and 10 indicates the worst imaginable pain). Preoperatively, all patients received 1000 mg of paracetamol orally. Routine anesthetic monitoring included pulse oximetry, electrocardiography, invasive blood pressure via radial artery cannulation, and body temperature measurement. General anesthesia was induced and maintained with propofol (Propofol-Lipuro 20 mg ml-1; B. Braun Melsungen AG, Melsungen, Germany) and remifentanil (Remifentanil B.





*Analysis of variance p<0.05

Fig. 1. Mean (SD) cumulative postoperative oxycodone consumption (a) and mean (SD) weight based cumulative postoperative oxycodone consumption (b).

Braun 1 mg ml-1; B. Braun Melsungen AG, Melsungen, Germany) target-controlled infusions. Schnider- and Minto-effect-site models were used for propofol and remifentanil, respectively [16,17]. No opioids other than remifentanil were used before or during anesthesia. Rocuronium bromide (Esmeron 10 mg ml.-1; Merck Sharp & Dohme B.V., BN Haarlem, The Netherlands) 0.4–0.6 mg kg-1 facilitated endotracheal intubation. The depth of anesthesia (bispectral index BIS or entropy index) was targeted from 45 to 55 with entropy (GE B850 Monitor Entropy Module, GE, Helsinki, Finland) or BIS monitor (The Philips BIS module, Philips Medical Systems, Eindhoven, The Netherlands). Mean arterial pressure (MAP) was maintained at 65–75 mmHg. Intravenous bolus doses of ephedrine and/or noradrenaline infusion were administered if necessary. Local anesthetic was injected to the skin incision area before incision (lidocaine 5 mg kg-1 c. adrenaline 5 μg kg-1; Orion Pharma, Espoo, Finland) and after wound closure (levobupivacaine 2.5 mg kg-1; Chirocaine 2.5 mg ml.1, AbbVie S.r.l., Campoverde di Aprilia, Italy) as per hospital routines.

At the end of surgery, the PCA pump was attached to the intravenous line and activated. The first dose of PCA solution was given just after entering the PACU. As soon as the patient awoke, they were encouraged to use PCA to treat postoperative pain if necessary. The starting dose of oxycodone (Oxycodone Orion 10 mg ml-1; Orion Pharma, Espoo, Finland) in the PCA solution was 2 mg with a lockout interval of 5 min. When NRS was 4 or lower, the PCA oxycodone dose was decreased to 1 mg (D0–D10). The study PCA dosing continued for 24 h from the end of surgery, after which the PCA cassettes were changed in all study groups and contained only 1 mg/ml oxycodone thereafter in all study groups.

The total duration of PCA treatment was three days. Postoperative nausea and vomiting (PONV) were treated with intravenous ondansetron and dehydrobenzperidol if necessary. All the study patients spent the first postoperative night in the intermediate surgical ward, as per hospital routines for multilevel spine surgery with instrumentation procedure.

2.6. Surgical technique

All patients underwent elective posterolateral lumbar spine fusion with bilateral transpedicular screw instrumentation performed by experienced spine surgeons. After standard sterile preparation and prone positioning, a midline incision and subperiosteal exposure were performed. Decompression and fusion with autologous bone grafts, with or without cages, were carried out as indicated. Hemostasis was secured, drains were placed, and the wound was closed in layers. Local anesthetic infiltration was administered before incision and after wound closure according to institutional protocol.

2.7. Measurements and data handling

Heart rate, blood pressure, NRS (0−10) for pain intensity at rest and upon movement, level of sedation with the Richmond Agitation-Sedation scale (RASS), nausea, vomiting, pruritus were registered immediately after arrival in the recovery room and at the following time points: 60, 120, and 240 min and eight, 24, 48, and 72 h later. Patients evaluated their pain relief satisfaction (yes/no) at 72 h.

All clinical patient data were collected on individual case report forms. All data were subsequently transferred to electronic format for exploratory data analysis. All outcome assessments were performed by research anesthesiologists trained in standardized data collection and blinded to group allocation.

2.8. Primary and secondary outcomes

The primary endpoint was cumulative oxycodone consumption at 24 h after surgery, the end of period when three different ratios of dexmedetomidine were added to oxycodone PCA solution.

Secondary outcomes included cumulative postoperative opioid consumption at 1, 2, 4, 8, 24, 48 and 72 h and postoperative NRS at rest at 1, 2, 4, 8, 24, 48 and 72 h, NRS at movement at 4, 8, 24, 48 and 72 h and cumulative number of participants with adverse events at 72 h after surgery.

2.9. Sample size calculation

Sample size was calculated (80% power) for the primary endpoint to demonstrate a clinically significant 25% reduction in oxycodone consumption at 24 h postoperatively. Based on a previous study [18], where mean total consumption of morphine in placebo group was 42.8 (SD 10.9) we calculated sample size based on mean difference of 10.7 mg. We used Dunnett's correction in alpha level (alpha 0.017) and 80% power. With these assumptions 22 patients per group would be needed. To include possibility of some drop outs, twenty-five (25) patients per group and total of 100 patients was deemed to be necessary.

2.10. Adverse effects

Bradycardia was defined as heart rate lower than 40/min and tachycardia as heart rate over 100/min. Hypotension was defined as systolic blood pressure lower than 90 mmHg. Hypertension was defined as systolic blood pressure over 150 mmHg. Excessive sedation was defined as RASS < -1 within 4 postoperative hours and as RASS <0 between 4 and 72 postoperative hours. Other adverse events included incidence of postoperative nausea and vomiting (PONV), severe PONV, and pruritus. Severe adverse events were defined as hemodynamic adverse effects requiring treatment or respiratory insufficiency requiring invasive or non-invasive ventilation during the 72 h study period.

2.11. Statistical analyses

The primary outcome measure, cumulative opioid consumption during the first 24 h is presented as mean and standard deviation (SD). Cumulative opioid consumption at 1, 2, 4, 8, 24, 48, and 72 h was analyzed by using a analysis of covariance including group and adjusted with age and weight. Also, weight based cumulative opioid consumption (mg/kg) was compared between the group with one-way analysis of variance. Multiple comparisons between the groups were adjusted with Tukey's method. Studentized residuals were used to check assumptions.

To study pain burden, we analyzed if the NRS differed between the groups separately at 1, 2, 4, 8, 24, 48 or 72 postoperative hours using analysis of covariance (adjusted with group, age, weight).

Differences in the amounts of adverse events among groups at 24, 48, and 72 h postoperatively were evaluated with Fisher's exact test. Differences in the amounts of adverse events among groups (D0 versus DEX groups combined) at 24, 48, and 72 h postoperatively were evaluated with Fisher's exact test, continued with calculating odds ratios (ORs) with 95% confidence intervals.

Descriptive statistics are shown as means and SD when variables are normally distributed and otherwise as medians and IQRs. Categorical variables are summarized as counts and percentages. The statistical significance level was set to $P < 0.05$ (two-tailed). Statistical analyses were performed with 2025 JMP® (Version 17 for Windows (JMP Statistical Discovery LLC, Cary, NC) and SAS software, Version 9.4 for Windows (SAS Institute Inc., Cary, NC, USA).

3. Results

A total of 121 patients were assessed for eligibility. 101 patients were recruited in the study (Fig. 1B) between June 2015 and March 2021. Two patients were excluded due to PCA administration error and one patient due to missing local wound infiltration. Thus, 98 patients were included in the final analysis; 25 in groups D0 and D10, and 24 in groups D2 and D5. Median (range) age of the patients was 60 (28–78) years and

57% were women. No significant differences in baselines characteristics were present among the groups (Table 1). Cumulative mean (SD) dexmedetomidine doses were 1.28 (0.49) mcg/kg, 3.10 (1.28) mcg/kg and 5.24 (1.59) mcg/kg for groups D2, D5 and D10, respectively.

3.1. Postoperative opioid consumption

There was no difference in the 24-h opioid consumption between the groups ($p = 0.44$) (Table 2, Fig. 1). When 24-h postoperative opioid consumption was adjusted with age and weight, the results remained unchanged.

At 60 min patients in group D10 had lower unadjusted cumulative opioid consumption compared with patients in group D0 (mean difference 3.1 mg; 95% CI 0.5–5.6 mg, $p = 0.011$) and compared with patients in group D2 (mean difference 3.3 mg; 95% CI 0.7–5.9 mg, $p = 0.006$). Weight based cumulative opioid consumption was lower in group D10 (mean difference 0.05 mg/kg; 95% CI 0.02–0.08 mg/kg; $p = 0.001$) and in group D2 (mean difference 0.05 mg/kg; 95% CI 0.01–0.08 mg/kg; $p = 0.003$) (Table 2, Fig. 1).

At 120 min patients in group D10 had lower unadjusted cumulative opioid consumption compared with patients in group D0 (mean difference 3.7 mg; 95% CI 0.5–6.9 mg), p = 0.011) and patients in group D5 compared with patients in group D0 (mean difference 3.5 mg; 95% CI 0.3–6.8 mg), $p = 0.019$). Weight based cumulative opioid consumption was lower in group D10 (mean difference 0.05 mg/kg; 95% CI 0.02–0.08 mg/kg; p = 0.001) and in group D2 (mean difference 0.05 mg/kg; 95% CI 0.01–0.08 mg/kg; $p = 0.002$) (Table 2, Fig. 1).

At 240 min, patients in group D10 had lower weight based cumulative opioid consumption compared with patients in group D0 (mean difference 0.07 mg/kg; 95% CI 0.01–0.12 mg; $p = 0.008$) (Fig. 1).

3.2. Acute pain measurements during postoperative care

There was no differences in postoperative NRS measured at rest or movement at any postoperative timepoints. There were also no differences in postoperative NRS measured at movement at any postoperative timepoints. When postoperative NRS was adjusted with age and weight, the results remained unchanged at all timepoints for both NRS rest and NRS movement (Table 3 and Fig. 2).

3.3. Adverse effects

There was no difference in the total amount of adverse effects during 48 h or 72 h follow-up. Patients in group D0 had higher cumulative amount of PONV (OR 3.7, 95% CI 1.1–10.0, $p = 0.04$) and itching (OR 8.9, 95% CI 1.6–49.0) at 24 h ($p = 0.024$) compared to all groups receiving dexmedetomidine. Cumulative amount of adverse events at 72 h are summarized in Table 4. There were no severe adverse effects. None of the patients developed respiratory insufficiency requiring invasive or non-invasive ventilation during the 72-h study period. No rescue medications were required during the study.

Table 1
Demographic data.

	All (n = 98)	D0 (n = 25)	D2 (n = 24)	D5 (n = 24)	D10 (n = 25)	p-value
Age (years)[1]	58 (51–67)	56 (45–63)	57 (53–64)	65 (53–70)	58 (50–70)	0.27
Female (n; %)	56 (57%)	15 (60%)	12 (50%)	16 (67%)	13 (52%)	0.65
Body weight (kg)[2]	79.9 (14.0)	77.3 (11.7)	82.4 (16.6)	75.4 (12.1)	84.2 (14.2)	0.09
BMI (kg/m^{-2})[2]	28.0 (3.6)	27.4 (3.0)	28.7 (4.1)	27.5 (3.7)	28.4 (3.6)	0.46

D0, Patient controlled intravenous oxycodone 1 mg/ml (n = 25); D2, Patient controlled intravenous oxycodone 1 mg/ml + dexmedetomidine 2.5 μg/ml (n = 25); D5, Patient controlled intravenous oxycodone 1 mg/ml + dexmedetomidine 5.0 μg/ml (n = 25); D10, Patient controlled intravenous oxycodone 1 mg/ml + dexmedetomidine 10 μg/ml (n = 25).; n, number of non-missing value; BMI, body-mass index; ASA, American Society of Anesthesiologists.
[1] Median and interquartile range
[2] Mean and standard deviation

Table 2
Mean (SD) cumulative postoperative oxycodone consumption as milligrams.

Timepoint	All (n = 98)	D0 (n = 25)	D2 (n = 24)	D5 (n = 24)	D10 (n = 25)	p-value
60 min	9.8 (3.7)	10.9 (4.8)	11.3 (2.9)	9.2 (3.0)	8.0 (2.9)	*0.003*
120 min	12.2 (4.6)	14.2 (6.6)	13.0 (3.0)	10.6 (3.4)	11.0 (4.0)	*0.009*
240 min	15.5 (5.9)	17.5 (7.9)	16.2 (4.7)	14.1 (4.3)	14.2 (5.6)	0.06
480 min	21.4 (8.3)	23.6 (10.4)	22.0 (7.5)	19.2 (6.0)	20.7 (8.5)	0.18
24 h	46.8 (20.9)	51.0 (26.1)	43.3 (18.1)	45.8 (18.8)	46.9 (20.1)	0.44
48 h	77.3 (36.3)	80.4 (37.1)	72.6 (34.9)	77.6 (38.3)	78.6 (37.0)	0.70
72 h	100.4 (45.9)	98.4 (32.6)	96.1 (52.2)	101.6 (53.2)	106.0 (45.7)	0.97

PACU, postoperative care unit, D0, Patient controlled intravenous oxycodone 1 mg/ml (n = 25); D2, Patient controlled intravenous oxycodone 1 mg/ml + dexmedetomidine 2.5 μg/ml (n = 24); D5, Patient controlled intravenous oxycodone 1 mg/ml + dexmedetomidine 5.0 μg/ml (n = 24); D10, Patient controlled intravenous oxycodone 1 mg/ml + dexmedetomide 10.0 μg/ml (n = 25).

Table 3
Median (IQR) postoperative NRS.

NRS at rest

Timepoint	All (n = 98)	D0 (n = 25)	D2 (n = 24)	D5 (n = 24)	D10 (n = 25)	p-value
60 min	5 (4–7)	5 (3–7)	4 (3–6)	5 (3–6)	6 (3–7)	0.07
120 min	4 (3–5)	3 (2–5)	4 (3–4)	4 (2–5)	5 (3–6)	0.22
240 min	4 (2–5)	3 (2–5)	4 (2–5)	4 (2–5)	4 (3–5)	0.93
480 min	3 (2–4)	3 (2–5)	3 (1–4)	3 (1–4)	3 (2–5)	0.70
24 h	3 (2–4)	3 (2–4)	3 (1–4)	2 (1–4)	3 (2–5)	0.87
48 h	2 (1–3)	2 (1–3)	2 (0–3)	2 (1–3)	2 (1–3)	0.99
72 h	1 (0–2)	1 (0–2)	1 (0–2)	1 (1–2)	1 (0–2)	0.80

NRS at movement

Timepoint	All (n = 98)	D0 (n = 25)	D2 (n = 24)	D5 (n = 24)	D10 (n = 25)	p-value
240 min	6 (4–7)	5 (3–7)	6 (4–7)	5 (4–8)	6 (4–8)	0.67
480 min	5 (4–7)	5 (4–8)	6 (3–7)	5 (4–8)	7 (4–8)	0.60
24 h	7 (5–8)	7 (5–8)	7 (5–8)	5 (5–8)	8 (5–8)	0.61
48 h	5 (3–7)	5 (3–6)	4 (3–7)	6 (4–7)	5 (3–7)	0.58
72 h	4 (3–5)	3 (2–4)	4 (2–5)	4 (3–5)	5 (3–6)	0.14

NRS, numerical rating scale; D0, Patient controlled intravenous oxycodone 1 mg/ml (n = 25); D2, Patient controlled intravenous oxycodone 1 mg/ml + dexmedetomidine 2.5 μg/ml (n = 24); D5, Patient controlled intravenous oxycodone 1 mg/ml + dexmedetomidine 5.0 μg/ml (n = 24); D10, Patient controlled intravenous oxycodone 1 mg/ml + dexmedetomide 10.0 μg/ml (n = 25); IQR, interquartile range.

3.4. Patient satisfaction

There was no difference in patient satisfaction between the groups.

4. Discussion

This randomized, double-blind, placebo-controlled study evaluated

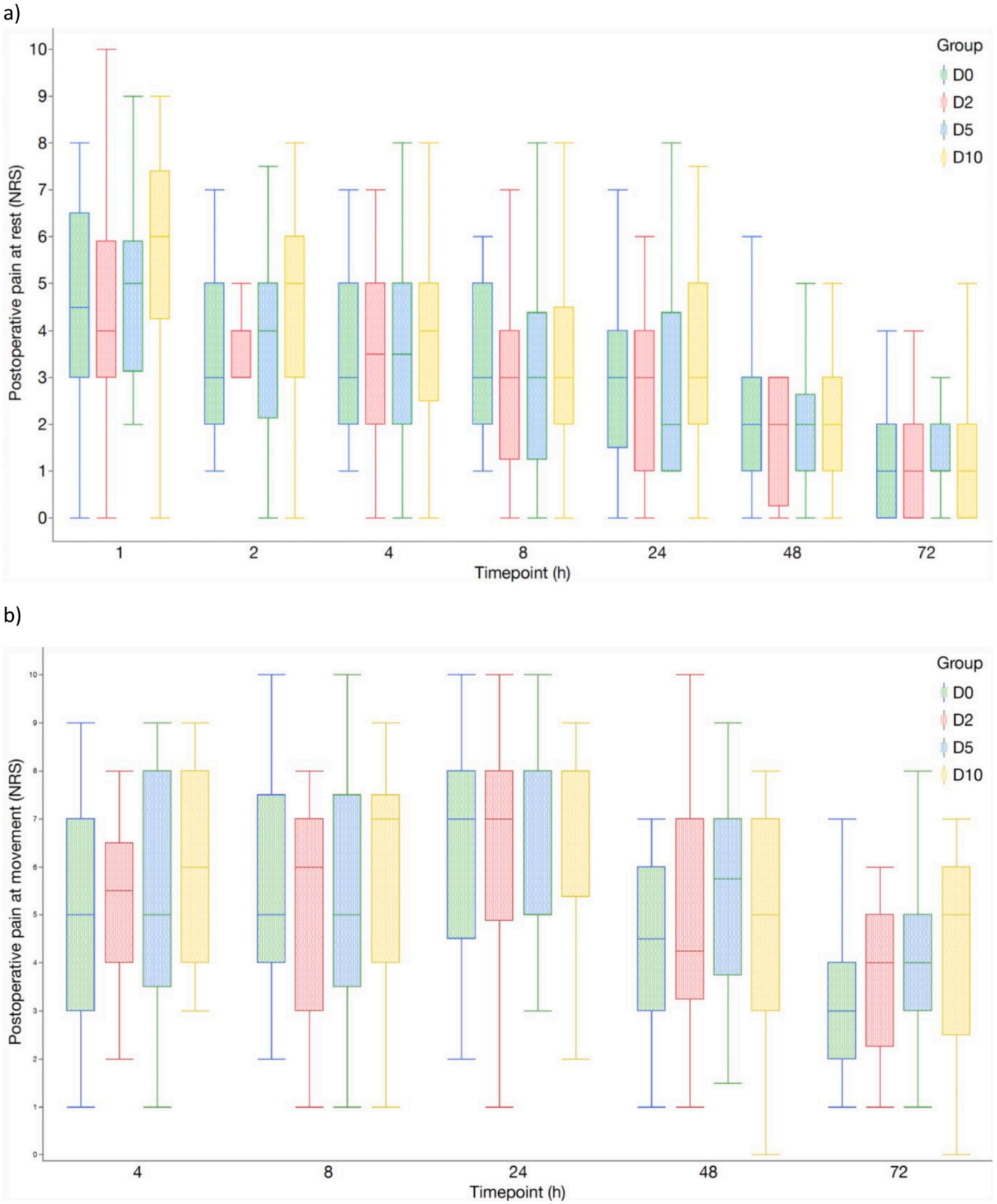


Fig. 2. Median (IQR and range) numerical rating scale for postoperative pain at rest (a) and movement (b).

Table 4
Amount of study drug related adverse effects at postoperative 72 h.

Adverse effect	All (*n* = 98)	D0 (n = 25)	D2 (n = 24)	D5 (n = 24)	D10 (n = 25)	p-value
Sedation 0–4 h	3 (3.1)	0 (0.0)	1 (4.2)	1 (4.2)	1 (4.0)	0.72
Sedation 0–72 h	11 (11.2)	2 (8.0)	3 (12.5)	3 (12.5)	3 (12.0)	0.95
PONV	17 (17.3)	7 (28.0)	5 (20.8)	4 (16.7)	1 (4.0)	0.12
Pruritus	7 (7.1)	4 (16.0)	2 (8.3)	1 (4.2)	0 (0.0)	0.15
Bradycardia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1.00
Tachycardia	4 (4.1)	1 (4.0)	0 (0.0)	1 (4.2)	2 (8.0)	0.90
Hypotension	10 (10.2)	1 (4.0)	2 (8.3)	3 (12.5)	4 (16.0)	0.58
Hypertension	24 (24.5)	6 (24.0)	7 (29.2)	5 (20.8)	6 (24.0)	0.93

D0, Patient controlled intravenous oxycodone 1 mg/ml (n = 25); D2, Patient controlled intravenous oxycodone 1 mg/ml + dexmedetomidine 2.5 μg/ml (n = 24); D5, Patient controlled intravenous oxycodone 1 mg/ml + dexmedetomidine 5.0 μg/ml (n = 24); D10, Patient controlled intravenous oxycodone 1 mg/ml + dexmedetomide 10.0 μg/ml (n = 25); PONV, postoperative nausea and vomiting.

the effect of adding incremental doses of dexmedetomidine to oxycodone PCA in patients who underwent major lumbar spinal fusion surgery. Although earlier timepoint comparisons indicated lower oxycodone consumption in the dexmedetomidine groups (D5 and D10) groups compared to placebo, no statistically significant differences were found at 24 h or at later timepoints. This suggests that the initially observed opioid-sparing effect may not persist beyond the early postoperative period, or that between-subject variability in opioid use was too high to detect robust group differences using a distribution-free method.

Patient-controlled analgesia (PCA) remains a valuable method in major spinal fusion surgery, as it enables individualized pain control and improves patient satisfaction compared to conventional opioid administration. Opioid-sparing strategies - such as adding dexmedetomidine to opioid-based PCA—have been evaluated in multiple randomized trials and meta-analyses. The systematic review by Peng et al. [10] first demonstrated early opioid-sparing and reduced postoperative nausea and vomiting (PONV), but highlighted heterogeneous dosing and variable quality across studies.

Recent meta-analyses have provided a broader perspective on dexmedetomidine in this context. Xu et al. [15] and Liu et al. [14] confirmed consistent reductions in early opioid use and improved side effect profiles when dexmedetomidine was added to opioid PCA, but did not demonstrate sustained 24-h opioid sparing. Verret et al. [12,13] further reported likely improvements in quality of recovery and possible reductions in chronic postsurgical pain, albeit with higher risks of bradycardia and hypotension. In parallel, Dinges et al. [7] demonstrated that equianalgesic opioid PCA regimens are associated with high rates of nausea, vomiting, and pruritus, emphasizing the importance of tolerability outcomes. The link between postoperative opioid exposure and development of chronic postsurgical pain [2] highlights why reducing both opioid consumption and side effects remains clinically relevant.

Earlier individual trials, such as Dexter et al. (2009) in pediatric spinal fusion and Song et al. (2016) in adult surgery, reported transient opioid-sparing or early antiemetic benefits of dexmedetomidine. Our findings differ, as we did not observe sustained differences in cumulative opioid consumption at 24 h. These discrepancies likely reflect differences in patient populations, surgical techniques, timing and duration of dexmedetomidine administration, and type of opioid used.

Other opioid-sparing strategies have shown more pronounced benefits in lumbar spine surgery. Ketamine appears to reduce postoperative opioid consumption in a dose-dependent manner when used as a PCA adjunct after lumbar fusion [19]. Intravenous lidocaine has been reported to lower pain scores, decrease opioid use, and shorten hospital stay in spine surgery [20]. NSAIDs likewise provide effective non-opioid analgesia. In a recent randomized trial, intravenous ketorolac substantially reduced opioid use and improved early postoperative pain without increasing complications or compromising fusion outcomes [21]. These findings indicate that ketamine, lidocaine, and NSAIDs may offer more robust or sustained opioid-sparing effects than postoperative dexmedetomidine alone.

Previous studies have reported moderate to severe postoperative pain following lumbar spinal fusion surgery [1,21,22]. In the present study, postoperative pain intensity was comparable to or lower than that reported in earlier studies. Perioperative pain management followed a multimodal analgesic approach, including paracetamol, local anesthetic wound infiltration, and an oxycodone bolus administered after discontinuation of remifentanil. This analgesic strategy may have contributed to the observed pain outcomes. However, differences in perioperative analgesic practices across institutions should be considered when comparing results between studies.

In the current study, the opioid-sparing effect of dexmedetomidine was likely short-lived because administration was restricted to the first 24 postoperative hours, delivered only through PCA oxycodone and without a continuous background infusion, leading to relatively low total exposure. In addition, dexmedetomidine was not given intraoperatively, in contrast to many studies reporting more prolonged analgesic effects. As the influence of this brief postoperative regimen diminished over time, opioid requirements between groups converged during the 72-h follow-up period.

A major strength of this study is its randomized, double-blind, placebo-controlled design, with clearly defined dosing groups and consistent surgical technique and anesthesia protocols. The use of both parametric and non-parametric analyses enhances the robustness. Despite the absence of sustained analgesic or opioid sparing effects, the observed improvement in tolerability support dexmedetomidine's role as a side effect-reducing rather than opioid-sparing adjuvant.

Future studies should aim to refine the optimal dexmedetomidine-to-opioid ratio in intravenous PCA using pharmacokinetic and pharmacodynamic modeling, particularly within multimodal analgesia strategies. Because dexmedetomidine appears to enhance analgesic tolerability more than provide sustained opioid sparing, its role should be examined in a broader perioperative frameworks, possibly in combination with other non-opioid adjuncts such as ketamine, lidocaine, or NSAIDs. Personalized approaches that incorporate patient-specific factors — such as baseline opioid tolerance, body weight, and genetic polymorphisms in opioid metabolism, may further optimize outcomes. Larger trials with extended follow-up periods and stratified dosing protocols are needed to identify subgroups, including opioid-naïve and high-risk patients, who may derive the greatest benefits.

In conclusion, our results demonstrate that adding 5 or 10 μg ml-1 of dexmedetomidine to 1 mg/ml oxycodone PCA may decrease short term opioid consumption, but it does not appear to have clinically meaningful effect on postoperative opioid consumption or postoperative pain score compared patients who received only oxycodone after major lumbar fusion. These findings imply that adjunct dexmedetomidine may offer early but not sustained opioid-sparing benefits. The observed reduction in opioid-related side effects (PONV and pruritus) in the dexmedetomidine groups suggests that its perioperative utility may lie more in improving tolerability of analgesia than in reducing total opioid exposure. Future studies could help define optimal dosing strategies and patient populations that may benefit most from this adjuvant.

AI declaration

During the preparation of this manuscript, the authors used ChatGPT to improve grammar and clarity. The authors reviewed and edited all content and are responsible for the final manuscript.

CRediT authorship contributions

Sanna Mäkelä: Conceptualization, Data curation, Patient recruitment and Data collection, Investigation, Visualization, Writing – original draft, Writing – review & editing. **Janne Gröhn**: Writing – original draft, Writing – review & editing. **Juho Rantakokko**: Conceptualization, Patient recruitment. **Eliisa Löyttyniemi**: Formal analysis, Investigation, Writing – review & editing. **Marko Peltoniemi**: Patient recruitment and Data collection, Writing – review & editing. **Antti Liukas**: Conceptualization, Patient recruitment and Data collection, Writing – original draft, Writing – review & editing, Supervision. **Riku Aantaa**: Conceptualization, Funding acquisition, Supervision. **Teijo I. Saari**: Conceptualization, Methodology, Formal analysis, Funding acquisition, Data curation, Supervision, Writing – original draft, Writing – review & editing. **Panu Uusalo**: Conceptualization, Methodology, Formal analysis, Data curation, Visualization, Funding acquisition, Supervision, Writing – original draft, Writing – review & editing.

CRediT authorship contribution statement

Sanna Mäkelä: Writing – review & editing, Writing – original draft, Visualization, Investigation, Data curation, Conceptualization. **Janne Gröhn:** Writing – review & editing, Writing – original draft. **Juho Rantakokko:** Data curation. **Eliisa Löyttyniemi:** Writing – review & editing, Investigation, Formal analysis. **Marko Peltoniemi:** Writing – review & editing, Data curation. **Riku Aantaa:** Funding acquisition, Conceptualization. **Antti Liukas:** Writing – review & editing, Data curation, Conceptualization. **Teijo Saari:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Methodology, Funding acquisition, Formal analysis, Data curation. **Panu Uusalo:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Methodology, Funding acquisition, Formal analysis.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jclinane.2026.112191.

References

[1] Geisler A, Zachodnik J, Køppen K, Chakari R, Bech-Azeddine R. Postoperative pain treatment after spinal fusion surgery: a systematic review with meta-analyses and trial sequential analyses. Pain Rep 2022;7:e1005. https://doi.org/10.1097/PR9.0000000000001005.

[2] Sluka KA, Wager TD, Sutherland SP, et al. Predicting chronic postsurgical pain: current evidence and a novel program to develop predictive biomarker signatures. Pain 2023;164:1912–26. https://doi.org/10.1097/j.pain.0000000000002938.

[3] Carron M, Tamburini E, Linassi F, et al. Efficacy of nonopioid analgesics and adjuvants in multimodal analgesia for reducing postoperative opioid consumption and complications in obesity: a systematic review and network meta-analysis. Br J Anaesth 2024;133:1234–49. https://doi.org/10.1016/j.bja.2024.08.009.

[4] Rajan S, Rishi G, Ibrahim M. Opioid alternatives in spine surgeries. Curr Opin Anaesthesiol 2024;37:470–7. https://doi.org/10.1097/ACO.0000000000001423.

[5] Bullock WM, Kumar AH, Manning E, Jones J. Perioperative analgesia in spine surgery: a review of current data supporting future direction. Orthop Clin North Am 2023;54:495–506. https://doi.org/10.1016/j.ocl.2023.05.007.

[6] McNicol ED, Ferguson MC, Hudcova J. Patient controlled opioid analgesia versus non-patient controlled opioid analgesia for postoperative pain. Cochrane Database Syst Rev 2015 Jun 2;2015(6):CD003348. https://doi.org/10.1002/14651858.CD003348.pub3.

[7] Dinges HC, Otto S, Stay DK, et al. Side effect rates of opioids in equianalgesic doses via intravenous patient-controlled analgesia: a systematic review and network meta-analysis. Anesth Analg 2019;129:1153–62. https://doi.org/10.1213/ANE.0000000000003887.

[8] Weerink MAS, Struys MMRF, Hannivoort LN, et al. Clinical pharmacokinetics and pharmacodynamics of Dexmedetomidine. Clin Pharmacokinet 2017 Aug;56(8):893–913. https://doi.org/10.1007/s40262-017-0507-7. PMID: 28105598; PMCID: PMC5511603.

[9] Feng M, Chen X, Liu T, et al. Dexmedetomidine and sufentanil combination versus sufentanil alone for postoperative intravenous patient-controlled analgesia: a systematic review and meta-analysis of randomized controlled trials. BMC Anesthesiol 2019;19:81. https://doi.org/10.1186/s12871-019-0756-0.

[10] Peng K, Liu HY, Wu SR, Cheng H, Ji FH. Effects of combining dexmedetomidine and opioids for postoperative intravenous patient-controlled analgesia: a systematic review and meta-analysis. Clin J Pain 2015;31:1097–104. https://doi.org/10.1097/AJP.0000000000000219.

[11] Song Y, Shim JK, Song JW, Kim EK, Kwak YL. Dexmedetomidine added to an opioid-based analgesic regimen for the prevention of postoperative nausea and vomiting in highly susceptible patients: a randomised controlled trial. Eur J Anaesthesiol 2016 Feb;33(2):75–83. https://doi.org/10.1097/EJA.0000000000000327 [PMID: 26258655].

[12] Verret M, Le JBP, Lalu MM, et al. Effectiveness of dexmedetomidine on patient-centred outcomes in surgical patients: a systematic review and Bayesian meta-analysis. Br J Anaesth 2024;133:615–27. https://doi.org/10.1016/j.bja.2024.06.007.

[13] Verret M, Turgeon AF, McIsaac DI, et al. Effectiveness of dexmedetomidine during surgery under general anaesthesia on patient-centred outcomes: protocol for a systematic review and Bayesian meta-analysis. BMJ Open 2024;14:e080012. https://doi.org/10.1136/bmjopen-2023-080012.

[14] Liu Y, Li X, Zhang H, et al. Effect of perioperative dexmedetomidine on recovery of gastrointestinal function after general anaesthesia: a meta-analysis. BMC Anesthesiol 2024;24:288. https://doi.org/10.1186/s12871-024-02868-0.

[15] Xu W, Zheng Y, Wang Q, et al. Impact of the addition of dexmedetomidine to patient-controlled intravenous analgesia on postoperative pain-sleep interaction cycle and delirium: a systematic review and meta-analysis of randomized controlled trials. Heliyon 2024 Mar 11;10(6):e27623. https://doi.org/10.1016/j.heliyon.2024.e27623.

[16] Schnider TW, Minto CF, Shafer SL, Gambus PL, Andresen C, Goodale DB, et al. The influence of age on propofol pharmacodynamics. Anesthesiology 1999;90:1502–16. https://doi.org/10.1097/00000542-199906000-00003.

[17] Minto CF, Schnider TW, Egan TD, Youngs E, Lemmens HJ, Billard V, et al. Influence of age and gender on the pharmacokinetics and pharmacodynamics of remifentanil. I model development. Anesthesiology 1997;86:10–23. https://doi.org/10.1097/00000542-199701000-00004.

[18] Turan A, Karamanlioğlu B, Memiş D, Hamamcioglu MK, Tükenmez B, Pamukçu Z, et al. Analgesic effects of gabapentin after spinal surgery. Anesthesiology 2004 Apr;100(4):935–8. https://doi.org/10.1097/00000542-200404000-00025.

[19] Brinck ECV, Virtanen T, Mäkelä S, Soini V, Hynninen VV, Mulo J, et al. S-ketamine in patient-controlled analgesia reduces opioid consumption in a dose-dependent manner after major lumbar fusion surgery: a randomized, double-blind, placebo-controlled clinical trial. PloS One 2021 Jun 7;16(6):e0252626. https://doi.org/10.1371/journal.pone.0252626.

[20] Iyer S, Steinhaus ME, Kazarian GS, Zgonis EM, Cunningham ME, Farmer JC, et al. Intravenous ketorolac substantially reduces opioid use and length of Stay after lumbar fusion: a randomized controlled trial. Spine (Phila Pa 1976) 2024 Jan 15;49(2):73–80. https://doi.org/10.1097/BRS.0000000000004831.

[21] Kim KT, Cho DC, Sung JK, Kim YB, Kang H, Song KS, et al. Intraoperative systemic infusion of lidocaine reduces postoperative pain after lumbar surgery: a double-blinded, randomized, placebo-controlled clinical trial. Spine J 2014 Aug 1;14(8):1559–66. https://doi.org/10.1016/j.spinee.2013.09.031.

[22] Gerbershagen HJ, Aduckathil S, van Wijck AJ, Peelen LM, Kalkman CJ, Meissner W. Pain intensity on the first day after surgery: a prospective cohort study comparing 179 surgical procedures. Anesthesiology 2013 Apr;118(4):934–44. https://doi.org/10.1097/ALN.0b013e31828866b3 [PMID: 23392233].