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Analgesic Efficacy and Safety of Perineural Dexamethasone, Dexmedetomidine, and Their Combination as Adjuvants to Adductor Canal Block After Total Knee Arthroplasty: A Systematic Review and Meta-Analysis

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ABSTRACT: Total knee arthroplasty is frequently associated with clinically relevant postoperative pain that may delay mobilisation and increase analgesic requirements. This systematic review and meta-analysis evaluated the analgesic efficacy and safety of perineural dexamethasone, dexmedetomidine, and their combination as adjuvants to adductor canal block after total knee arthroplasty. PubMed, MEDLINE, Scopus, Cochrane Library were systematically searched. Eligible studies included adult patients undergoing total knee arthroplasty who received adductor canal block with dexamethasone, dexmedetomidine, or combined dexamethasone–dexmedetomidine. Primary outcomes were postoperative pain scores, analgesic consumption, time to first rescue analgesia or analgesic duration, and adverse events.

Twenty-one studies were included. Dexmedetomidine significantly prolonged time to first rescue analgesia or analgesic duration and reduced 24-hour analgesic consumption, both in the main analysis and sensitivity analysis (all $p < 0.00001$). Dexamethasone did not significantly reduce 24-hour analgesic consumption in the main analysis ($p = 0.13$) or sensitivity analysis ($p = 0.62$). For NRS pain scores, dexamethasone showed significant benefits at 6 hours at rest ($p < 0.00001$), 6 hours during movement ($p < 0.0001$), 12 hours at rest after sensitivity analysis ($p = 0.0008$), 12 hours during movement ($p = 0.01$), and 24 hours at rest after sensitivity analysis ($p = 0.007$). Dexmedetomidine significantly reduced NRS pain scores at 6, 12, and 24 hours at rest, and at 12 hours during movement. No consistent increase in serious adverse events was observed. Perineural dexmedetomidine and dexamethasone may improve early analgesia after total knee arthroplasty.

1. INTRODUCTION

Total knee arthroplasty (TKA) is commonly associated with clinically significant postoperative pain, which may delay early mobilisation, physiotherapy participation, and functional recovery. Current procedure-specific recommendations support multimodal analgesia after TKA, including non-opioid analgesics, adductor canal block (ACB), periarticular infiltration, and opioids as rescue analgesics.1 ACB has become widely used because it provides effective analgesia while better preserving quadriceps strength and ambulation compared with femoral nerve block.[2,3]

Despite these advantages, the analgesic duration of single-shot ACB may be insufficient during the early postoperative period. Perineural dexamethasone and dexmedetomidine have therefore been investigated as local anesthetic adjuvants to prolong analgesia and reduce postoperative analgesic requirements.[4-6] The combination of dexamethasone and dexmedetomidine has

also gained interest because these agents may provide complementary analgesic mechanisms, although its superiority over either adjuvant alone remains uncertain.[7] Variations in adjuvant dose, local anesthetic regimen, use of iPACK block, comparator groups, follow-up duration, and safety reporting make the relative efficacy and safety of these strategies unclear. Therefore, this systematic review and meta-analysis aimed to evaluate the analgesic efficacy and safety of perineural dexamethasone, dexmedetomidine, and their combination as adjuvants to ACB after TKA.

2. MATERIALS AND METHODS

2.1 Study design and registration

This systematic review and meta-analysis was conducted to evaluate the analgesic efficacy and safety of perineural dexamethasone, dexmedetomidine, and their combination as adjuvants to adductor canal block (ACB) after total knee arthroplasty (TKA). The review was prepared according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. The protocol was registered in PROSPERO with the registration number XX.

2.2 Search strategy

A systematic search was conducted in PubMed, MEDLINE, Scopus, and Cochrane Library from 1 January 2000 to XX Month 2026, without language restriction. Reference lists of eligible studies were also screened.

Table 1. Search strategy used for each

Database	Search string
PubMed/MEDLINE	(("Arthroplasty, Replacement, Knee"[Mesh] OR "total knee arthroplasty"[tiab] OR "total knee replacement"[tiab] OR TKA [tiab] OR TKR[tiab]) AND ("adductor canal block"[tiab] OR "saphenous nerve block"[tiab] OR "mid-thigh block"[tiab]) AND (dexamethasone[tiab] OR dexmedetomidine[tiab] OR adjuvant*[tiab] OR adjunct*[tiab]) AND (randomized controlled trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomly[tiab] OR trial[tiab]))
Scopus	TITLE-ABS-KEY (("total knee arthroplasty" OR "total knee replacement" OR TKA OR TKR) AND ("adductor canal block" OR "saphenous nerve block" OR "mid-thigh block") AND (dexamethasone OR dexmedetomidine OR adjuvant* OR adjunct*) AND (randomized OR randomised OR randomly OR trial))
Cochrane CENTRAL	("total knee arthroplasty" OR "total knee replacement" OR TKA OR TKR) AND ("adductor canal block" OR "saphenous nerve block" OR "mid-thigh block") AND (dexamethasone OR dexmedetomidine OR adjuvant* OR adjunct*)
Embase	('knee arthroplasty'/ OR 'total knee arthroplasty' OR 'total knee replacement' OR TKA OR TKR) AND ('adductor canal block' OR 'saphenous nerve block' OR 'mid-thigh block') AND ('dexamethasone' OR 'dexmedetomidine' OR dexamethasone OR dexmedetomidine OR adjuvant* OR adjunct*) AND ('randomized controlled trial' OR random* OR trial)

2.3 Eligibility criteria and study selection

Studies were included research studies involving adult patients undergoing TKA who received ACB as part of postoperative analgesia and evaluated perineural dexamethasone, dexmedetomidine, or combined dexamethasone–dexmedetomidine as local anaesthetic adjuvants. Eligible comparators included local anaesthetic alone, placebo, usual care, or another ACB-based regimen. Studies were excluded if they were non-clinical studies, animal or cadaveric studies, reviews, case reports, conference abstracts without sufficient data, or studies not involving ACB for TKA.

After duplicate removal, two reviewers independently screened titles, abstracts, and full texts. Disagreements were resolved by discussion or consultation with a third reviewer.

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2.4 Data extraction

Two reviewers independently extracted study characteristics, sample size, patient characteristics, ACB regimen, adjuvant type and dose, comparator, follow-up duration, efficacy outcomes, and safety outcomes. Authors were contacted when data were unclear or unavailable.

2.5 Outcomes

The primary outcomes were postoperative pain scores at 6, 12, 24, and 48 hours; postoperative opioid consumption within 24–48 hours; duration of analgesia or sensory block; and time to first rescue analgesia. Secondary outcomes included total rescue analgesic use, quadriceps strength or motor function, ambulation-related outcomes, length of stay, patient satisfaction, sleep quality, inflammatory markers when available, and adverse events.

2.6 Risk of bias and certainty of evidence

Risk of bias was assessed using the Cochrane Risk of Bias tool. Certainty of evidence was assessed using GRADE based on risk of bias, inconsistency, indirectness, imprecision, and publication bias.

2.7 Data synthesis and statistical analysis

Meta-analysis was performed when at least two studies reported comparable outcomes. Continuous outcomes were pooled as mean difference or standardized mean difference, while dichotomous outcomes were pooled as risk ratio or odds ratio, each with 95% confidence intervals. Heterogeneity was assessed using I^2. A random-effects model was used when heterogeneity was expected; otherwise, a fixed-effect model was considered. Non-poolable outcomes were summarized narratively.

2.8 Subgroup analysis

Subgroup analyses were planned by adjuvant type: dexamethasone, dexmedetomidine, and combined dexamethasone–dexmedetomidine. Additional subgroup analyses were considered based on iPACK use and follow-up time point when data were sufficient.

2.9 Result

Figure 1. Result

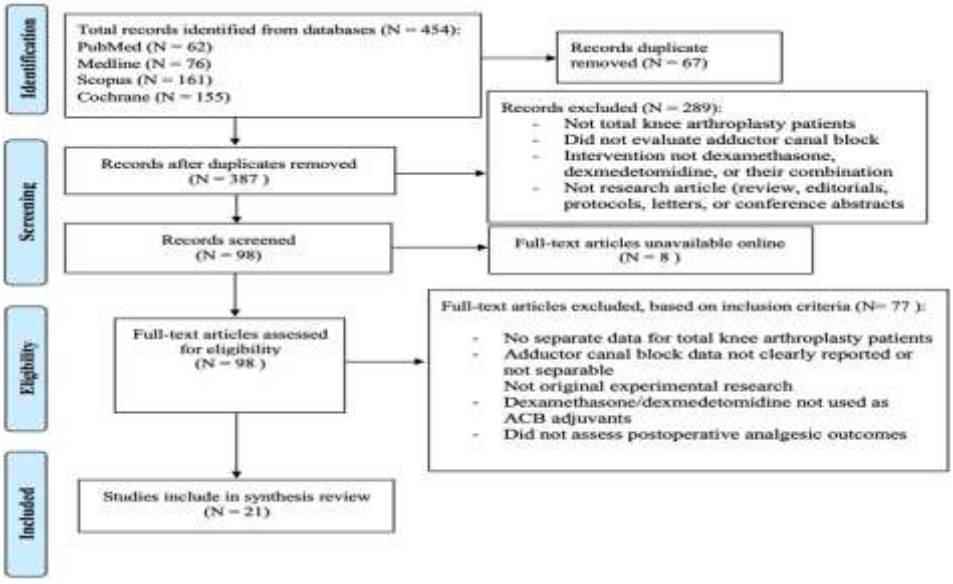


Table 2. Adjuvant Dexamethasone Studies

Author (Year)	Model/ Precondition	Main Analgesic Technique	Adjuvant & Dose	Control / Comparator	Main Outcomes	Adverse Effects
Liao et al. (2025)[8]	Adults aged 18–80 years undergoing primary unilateral TKA under general anesthesia	Single-shot distal ACB with liposomal bupivacaine 133 mg + bupivacaine HCl 0.375%, total 20 mL	No dexamethasone in intervention group	Ropivacaine 0.5% 20 mL + perineural dexamethasone 5 mg	No significant reduction in moderate-to-severe pain with movement at 48 h; lower NRS at 24–48 h; lower opioid use; better QoR-15	No significant difference in adverse events; no local anesthetic toxicity or allergic reaction
Reysner et al. (2026)[9]	Elderly patients aged ≥65 years undergoing TKA under spinal anesthesia	Combined iPACK + ACB using ropivacaine	Perineural dexamethasone 4 mg for iPACK + 4 mg for ACB, total 8 mg	iPACK + ACB with ropivacaine only	Longer time to first rescue opioid; lower 48-h opioid consumption; lower pain score at 8–12 h; no reduction in quadriceps strength	No nerve damage; no significant hyperglycemia; no difference in motor function
Sreckovic et al. (2025)[10]	Patients aged 40–90 years undergoing elective TKA under spinal anesthesia	ACB + IPACK with 0.33% levobupivacaine, 15 mL each block	Perineural dexamethasone 4 mg for ACB + 4 mg for IPACK	ACB + IPACK without dexamethasone	Lower 24-h pain score; lower opioid use, 10% vs 50%; lower rebound pain, 5% vs 30%; CPSP 1-year only 5% in control	Lower nausea, drowsiness, and rebound pain in intervention group; UTI similar between groups
Ortiz-Gómez et al. (2017)[11]	Patients undergoing elective TKA under subarachnoid anesthesia with opioids	Single-shot ACB, FNB, or epidural analgesia; ACB used 30 mL levobupivacaine 0.375%	Perineural dexamethasone 4 mg or dexmedetomidine 100 µg	Control: subarachnoid anesthesia only; other comparators: EA, FNB, ACB with/without adjuvants	Rescue analgesia lower with ACB + Dexa, 38.3%, vs ACB alone, 51.9%, and control, 72.8%; perineural dexamethasone improved postoperative analgesia	Recorded PONV, hypotension, bradycardia, arrhythmia, sedation, restlessness, sweating, and bleeding

Wang et al. (2017)[12]	Patients aged ≥18 years undergoing elective TKA under spinal anesthesia	Ultrasound-guided single-shot ACB with 10 mL ropivacaine 0.5%	Perineural dexamethasone 8 mg	ACB with ropivacaine 0.5% + normal saline	Longer sensory block, 23.42 vs 14.67 h; lower NRS at 6–24 h; lower 24-h morphine use, 4.23 vs 8.42 mg; lower CRP	Single-dose dexamethasone considered safe; adverse effects reported as rare/minor
Zeng et al. (2022)[13]	Patients aged 18–80 years undergoing unilateral TKA under general anesthesia	Ultrasound-guided ACB + IPACK; ACB 20 mL ropivacaine 0.5%, IPACK 30 mL ropivacaine 0.33%	Perineural dexamethasone 5 mg for ACB + 5 mg for IPACK, total 10 mg	ACB + IPACK with ropivacaine only	Longer time to first rescue analgesia, 18 vs 7.5 h; lower NRS; lower 72-h morphine use; higher QoR-15; earlier out-of-bed time; lower CRP and IL-6	No significant difference in nausea/vomiting, wound swelling, venous thrombosis, falls, or nerve damage
Turner et al. (2018)[14]	Patients aged 18–90 years undergoing unicompartmental knee arthroplasty	Ultrasound-guided single-shot ACB with 20 mL bupivacaine 0.25% + epinephrine	Perineural dexamethasone 1 mg or 4 mg	ACB without dexamethasone / placebo	Dexamethasone 4 mg prolonged sensory block vs placebo, 37.9 vs 29.7 h; 4 mg superior to 1 mg; no significant difference in opioid use or time to first analgesic	Adverse effects not detailed; perineural use noted as off-label with theoretical neurotoxicity concern

Table 3. Adjuvant Dexmedetomidine Studies

Author (Year)	Model / Precondition	Main Analgesic Technique	Adjuvant & Dose	Control / Comparator	Main Outcomes	Adverse Effects
Wu et al. (2026)[15]	Elderly patients aged 65–80 years undergoing unilateral TKA under	Single-shot ACB with 20 mL 0.375% ropivacaine plus multimodal postoperative analgesia	Intravenous dexmedetomidine: bolus 0.5 μg/kg over 15 min, followed by infusion 0.25–0.5 μg/kg/h until 30	No dexmedetomidine infusion and no ACB	Higher QoR-15 score at 24 h; lower 24-h oral morphine equivalent consumption;	Lower dizziness, drowsiness, nausea-vomiting, and sleep disturbance in the intervention

	general anesthesia		min before skin closure		lower adverse event incidence	group; no significant difference in
Abo-Zeid Salim et al. (2023)[16]	ASA I–II patients undergoing unilateral primary TKA under spinal anesthesia	ACB with 20 mL 0.25% levobupivacaine	Perineural dexmedetomidine 0.5 μg/kg or intravenous dexmedetomidine 0.5 μg/kg	IV dexmedetomidine + ACB levobupivacaine without perineural DEX	Perineural DEX had faster sensory block onset, longer postoperative analgesic duration, lower analgesic requirement, and lower meperidine consumption	Higher sedation scores in the IV DEX group; no intraoperative bradycardia; hypotension occurred in two patients in each group
Roy et al. (2023)[17]	Patients aged 40–85 years, ASA I–III, undergoing TKA under subarachnoid block	Modified 4-in-1 block or IPACK + ACB with 0.2% ropivacaine	Dexmedetomidine 1 μg/kg mixed with 0.2% ropivacaine 40 mL in both groups	Modified 4-in-1 block versus IPACK + ACB; no non-DEX control	VAS at 3, 6, and 24 h was comparable; VAS at 12 h was lower in the modified 4-in-1 block group	No postoperative muscle weakness; hemodynamic parameters were comparable
Krishnapriya et al. (2023)[18]	ASA I–II patients aged 18–75 years undergoing unilateral TKA under spinal anesthesia	Ultrasound-guided ACB with 20 mL 0.25% bupivacaine	Perineural dexmedetomidine 0.5 μg/kg	ACB with 20 mL 0.25% bupivacaine alone	Longer time to rescue analgesia: 18.34 ± 8.41 h vs 12.91 ± 4.57 h; lower 24-h tramadol consumption: 33.23 ± 11.95 mg vs 62.22 ± 19.80 mg; lower VAS at 6 and 12 h	No adverse events reported; RSS, HR, MAP, and SpO_2 were comparable
Krishnamurthy et al. (2021/2022)[19]	ASA I–III patients undergoing unilateral TKR under spinal anesthesia	Ultrasound-guided ACB with 30 mL 0.2% ropivacaine	Perineural dexmedetomidine 100 μg	ACB with 30 mL 0.2% ropivacaine + clonidine 150 μg	Longer analgesia duration: 16.01 ± 0.545 h vs 13.021 ± 0.543 h; lower rescue analgesic requirement; lower NRS at several postoperative time points; better sedation score	Two patients in the DEX group had transient bradycardia treated with IV glycopyrrolate; no other significant adverse effects
Khan et al. (2024)[20]	ASA I–II patients aged 18–75 years undergoing	Ultrasound-guided ACB with 20 mL	Dexmedetomidine 0.5 μg/kg in ACB; note: abstract mentions 1 μg/kg,	Local infiltration analgesia with 0.125% bupivacaine +	Longer time to first rescue analgesia in ACB: 11.30 ± 0.8 h vs	Minimal and comparable complications; no hypotension,

	TKA under spinal anesthesia	0.125% bupivacaine	but methods state 0.5 μg/kg	dexmedetomidine 0.5 μg/kg, total 40 mL	9.40 ± 1.1 h; fewer 24-h rescue analgesic doses: 1.47 ± 0.4 vs 1.77 ± 0.7	bradycardia, local anesthetic toxicity, or distal neurovascular deficit
Karthik et al. (2022)[21]	ASA I–III patients aged 18–85 years undergoing unilateral TKR with continuous postoperative ACB	Continuous ACB: 20 mL 0.2% ropivacaine bolus followed by 0.2% ropivacaine infusion via perineural catheter at 8 mL/h	Group A: dexmedetomidine 0.5 μg/kg; Group B: dexmedetomidine 1 μg/kg	Lower-dose DEX 0.5 μg/kg; no non-DEX control	DEX 1 μg/kg produced lower pain scores from 2 to 24 h; lower rescue fentanyl use: 60 μg vs 330 μg; lower rescue analgesia requirement: 6% vs 23%	No significant difference in motor block, sedation, or hemodynamics; no bradycardia, hypotension, dry mouth, nausea, or vomiting
Goyal et al. (2017)[22]	ASA I–II patients aged 18–75 years undergoing simultaneous bilateral TKR	Bilateral ultrasound-guided ACB with ropivacaine 7.5 mg/mL, total volume 20 mL per side	DEX 0.25 μg/kg or DEX 0.50 μg/kg added to ropivacaine	ACB with ropivacaine + saline	Longest analgesia duration in DEX 0.50 μg/kg: 18.4 ± 7.4 h; DEX 0.25 μg/kg: 14.6 ± 7.1 h; control: 10.8 ± 7 h. Lower 24-h tramadol consumption, lower movement pain, and higher satisfaction in DEX groups	HR, BP, SpO_2, and postoperative adverse effects were comparable; no local anesthetic systemic toxicity; no paresthesia or thigh pain within 72 h
Ortiz-Gómez et al. (2017)[11]	Patients undergoing elective TKA under subarachnoid anesthesia with intrathecal opioids	Multiple analgesic techniques: control, epidural analgesia, FNB, and single-shot ACB	For ACB: perineural dexamethasone 4 mg or dexmedetomidine 100 μg; ACB used 30 mL 0.375% levobupivacaine	Control without additional block; ACB without adjuvant; FNB ± adjuvant; epidural analgesia	Rescue analgesia: control 72.8%, ACB 51.9%, ACB + dexamethasone 38.3%, ACB + dexmedetomidine 61.5%; dexamethasone appeared more favorable than dexmedetomidine for ACB	Adverse outcomes included nausea-vomiting, hypotension, and block-related complications; some discontinuations occurred due to hematoma, disorientation, cardiac event, and neurologic event
George et al. (2022)[23]	ASA I–II patients aged	Ultrasound-guided ACB or	Dexmedetomidine 50 μg added to	FNB + dexmedetomidine;	VAS scores were comparable	No major adverse effect

	≥18 years undergoing TKA under spinal anesthesia	FNB with 20 mL 0.25% bupivacaine	both ACB and FNB	no non-DEX control	between groups; time to analgesic request was longer in ACB: 8.14 ± 0.92 h vs 6.49 ± 1.32 h; ambulation was earlier in ACB: 4.23 ± 0.90 h vs 7.06 ± 7.04 h	was clearly reported; HR and MAP were compared across several time points
AbdelRady et al. (2021)[24]	ASA I–II patients aged 18–60 years undergoing unilateral TKA under spinal anesthesia	Single-shot ACB with 20 mL 0.25% levobupivacaine	Perineural dexmedetomidine 0.5 μg/kg	ACB with 20 mL 0.25% levobupivacaine + normal saline	Longer time to first analgesic request: 515.10 ± 27.98 min vs 406.77 ± 10.64 min; lower 24-h morphine consumption: 6.47 ± 2.01 mg vs 10.93 ± 2.35 mg; lower VAS at rest and movement; better ROM, 100-foot walking test, and satisfaction	No major adverse effects in both groups; adverse event rate was low
Chattopadhyay et al. (2022)[25]	ASA I–II patients aged 18–75 years undergoing unilateral TKR under spinal anesthesia	Ultrasound-guided ACB with 20 mL 0.375% ropivacaine	DEX 0.25 μg/kg or DEX 0.50 μg/kg added to ropivacaine	ACB with 20 mL 0.375% ropivacaine alone	Longer rescue analgesia duration in DEX 0.50 μg/kg: 19.78 ± 5.57 h; DEX 0.25 μg/kg: 16.44 ± 6.21 h; control: 15.71 ± 4.87 h. Lower 24-h tramadol consumption in DEX 0.50 μg/kg: 33.33 ± 13.95 mg; lower NRS at selected time points; higher satisfaction	No adverse event reported; RSS, HR, MAP, and SpO_2 were comparable

Table 4. Combination Adjuvant Dexmedetomidine and Dexamethasone Studies

Author (Year)	Model / Precondition	Main Analgesic Technique	Adjuvant & Dose	Control / Comparator	Main Outcomes	Adverse Effects
Herman et al. (2020)[26]	Case series; 3 TKA patients	ACB + IPACK	ACB: dexmedetomidine 25 mcg + dexamethasone 5 mg; IPACK: dexamethasone 5 mg	No control group	Analgesia lasted 4–5 days; 2 patients required no postoperative opioids	No serious adverse effects reported
Shoni et al. (2024)[27]	Retrospective propensity-matched cohort; unilateral TKA	Single-shot ACB + IPACK	IPACK: dexmedetomidine 1 μg/kg + dexamethasone 4 mg + bupivacaine 0.25%	ACB alone	Lower opioid consumption: total MME during stay 160.11 vs 268.77; lower early VAS at 0–8 h and 8–16 h; no difference in LOS, ambulation, ED visit, or readmission.	No significant difference in complications
Swain et al. (2025/2026)[28]	Double-blind RCT; 58 TKA patients	Single-shot ACB	Dexamethasone 4 mg + dexmedetomidine 50 mcg + ropivacaine 0.5%	Dexamethasone 4 mg + ropivacaine 0.5%	Lower morphine use at 24 h and 48 h; lower early NRS pain scores; no meaningful difference in quadriceps strength, TUG time, sedation, or complication rate.	No serious adverse events reported

3. RESULTS AND DISCUSSION

3.1 Study Selection

A total of 454 records were identified from PubMed, MEDLINE, Scopus, and the Cochrane Library. After removing duplicates, screened, eligibility, excluding studies with non-separable TKA data, unclear ACB reporting, irrelevant adjuvant use, or no postoperative analgesic outcomes, 21 studies were included in the final synthesis (Tables 2–4). The study selection process is presented in Figure 1. The included studies evaluated dexamethasone, dexmedetomidine, or combined dexamethasone–dexmedetomidine as adjuvants to adductor canal block in patients undergoing total knee arthroplasty or total knee replacement. Seven studies assessed dexamethasone-based regimens, twelve assessed dexmedetomidine-based regimens, and three evaluated

combined dexamethasone–dexmedetomidine regimens. Most studies were randomized controlled trials, although evidence for the combined regimen also included non-randomized designs. Block techniques varied across studies and included single-shot ACB, continuous ACB, and ACB combined with iPACK block. The main outcomes were postoperative pain scores, analgesic consumption, time to first rescue analgesia or duration of analgesia, rescue analgesic requirement, functional recovery, and adverse events.

3.2 Meta-analysis Results

Meta-analysis was performed when at least two studies reported comparable numerical outcomes. Continuous outcomes were pooled as mean differences with 95% confidence intervals.

Time to First Rescue Analgesia / Duration of Analgesia

Figure 2. Time to First Rescue Analgesia / Duration of Analgesia

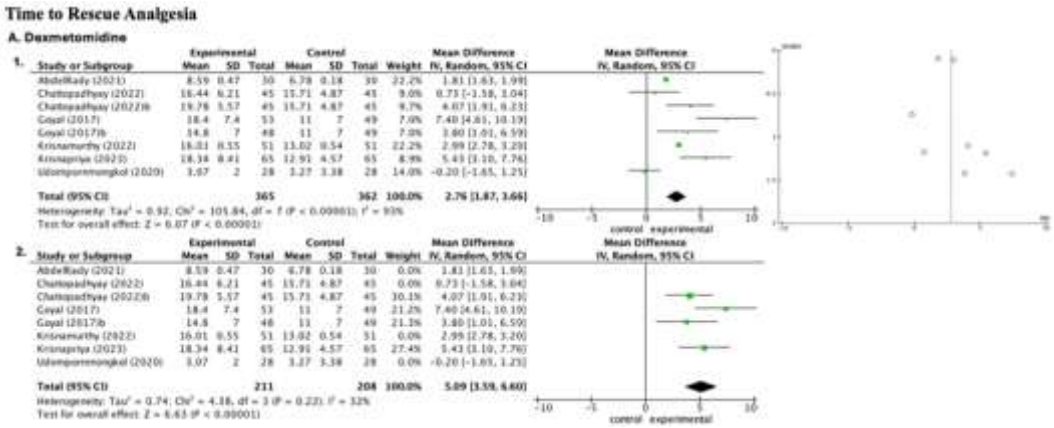


Figure 2. Time to rescue analgesia for dexmedetomidine. (A1.) All eligible studies included in the meta-analysis , (A2.) presents the leave-one-out sensitivity analysis after excluding the most influential study.

Dexmedetomidine significantly prolonged time to first rescue analgesia or duration of analgesia compared with control, with a pooled mean difference of 2.76 hours (95% CI 1.87 to 3.66; $p < 0.00001$) (Figure 2). However, heterogeneity was substantial ($I^2 = 93\%$). Sensitivity analysis restricted to more comparable studies showed a stronger and more consistent effect, with a mean difference of 5.09 hours (95% CI 3.59 to 6.60; $p < 0.00001$) and reduced heterogeneity ($I^2 = 32\%$). These findings suggest that dexmedetomidine provides more consistent prolongation of analgesia. The combined dexamethasone–dexmedetomidine regimen was not pooled for this outcome because the available studies did not provide sufficiently comparable data.

24-Hours Analgesic Consumption

Figure 3. 24-Hours Analgesic Consumption

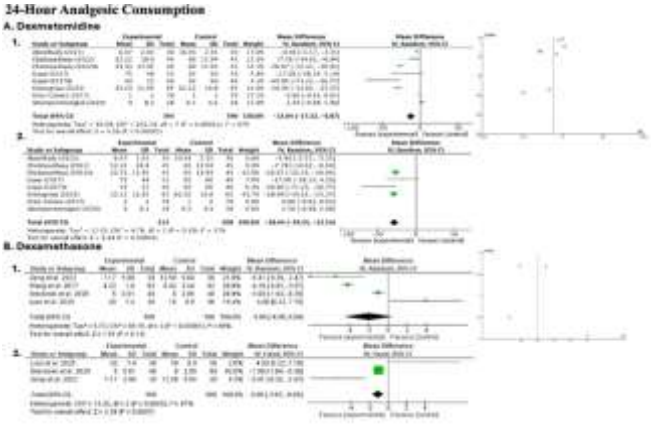


Figure 3. 24-hour analgesic consumption. (A1.) Dexmedetomidine: all eligible studies included in the meta-analysis. (A2.) Dexmedetomidine: leave-one-out sensitivity analysis after excluding the most influential study. (B1.) Dexamethasone: all eligible studies included in the meta-analysis. (B2.) Dexamethasone: leave-one-out sensitivity analysis after excluding the most influential study.

Pooled analysis showed that dexmedetomidine significantly reduced 24-hour analgesic consumption compared with control (MD −12.04; 95% CI −17.22 to −6.87; $p < 0.00001$), although heterogeneity was substantial ($I^2 = 97\%$). Sensitivity analysis restricted to more comparable studies (Figure 3A.2) showed a consistent reduction with lower heterogeneity (MD −28.44; 95% CI −34.35 to −22.54; $p < 0.00001$; $I^2 = 37\%$).

For dexamethasone, four studies were pooled, including Liao et al. The overall effect favored dexamethasone but was not statistically significant (MD −1.99; 95% CI −4.58 to 0.59; $p = 0.13$), with high heterogeneity ($I^2 = 95\%$). After sensitivity analysis, the effect remained non-significant (MD −0.98; 95% CI −4.85 to 2.89; $p = 0.62$), although heterogeneity decreased slightly ($I^2 = 87\%$). Therefore, dexmedetomidine showed a more consistent analgesic-sparing effect, whereas dexamethasone showed a favorable but less stable effect for 24-hour analgesic consumption. The combined dexamethasone–dexmedetomidine regimen was not pooled because comparable numerical data were limited.

Postoperative Pain Scores (NRS)

6-Hours NRS Pain Score

Figure 4. 6-Hours NRS Pain Score

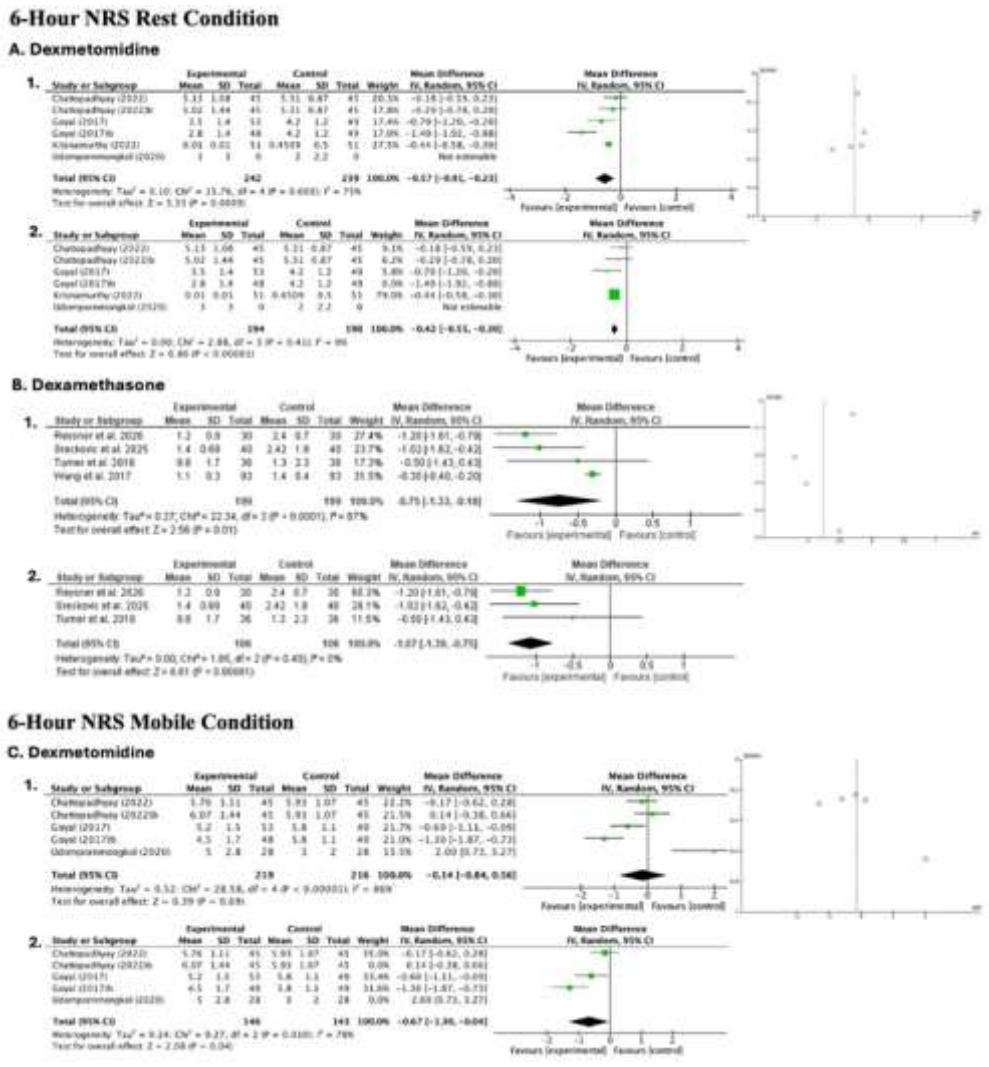


Figure 4. 6-hour NRS pain score. (A1.) Dexmedetomidine at rest: all eligible studies included in the meta-analysis. (A2.) Dexmedetomidine at rest: leave-one-out sensitivity analysis. (B1.) Dexamethasone at rest: all eligible studies included in the meta-analysis. (B2.) Dexamethasone at rest: leave-one-out sensitivity analysis. (C1.) Dexmedetomidine during movement: all eligible studies included in the meta-analysis. (C2.) Dexmedetomidine during movement: leave-one-out sensitivity analysis.

Figure 4 showed NRS score at 6 hours postoperatively, dexamethasone significantly reduced NRS pain scores at rest compared with control (MD −1.14; 95% CI −1.48 to −0.80; $p < 0.00001$), with no observed heterogeneity ($I^2 = 0\%$). A similar benefit was observed for NRS pain scores during movement, although the effect size was smaller (MD −0.31; 95% CI −0.45 to −0.17; $p < 0.0001$; $I^2 = 0\%$).

Dexmedetomidine also reduced 6-hour NRS pain scores at rest (MD −0.57; 95% CI −0.91 to −0.23; $p = 0.0009$), but heterogeneity was substantial ($I^2 = 75\%$). Sensitivity analysis showed a more consistent effect with no heterogeneity (MD −0.42; 95% CI −0.55 to −0.30; $p < 0.00001$; $I^2 = 0\%$). In contrast, dexmedetomidine did not significantly reduce 6-hour NRS pain scores during movement (MD −0.14; 95% CI −0.84 to 0.56; $p = 0.69$), with high heterogeneity ($I^2 = 86\%$). Overall, both adjuvants improved early pain at rest, while the effect on movement-related pain was more consistent for dexamethasone than dexmedetomidine.

12-Hours NRS Pain Score

Figure 5. 12-Hours NRS Pain Score

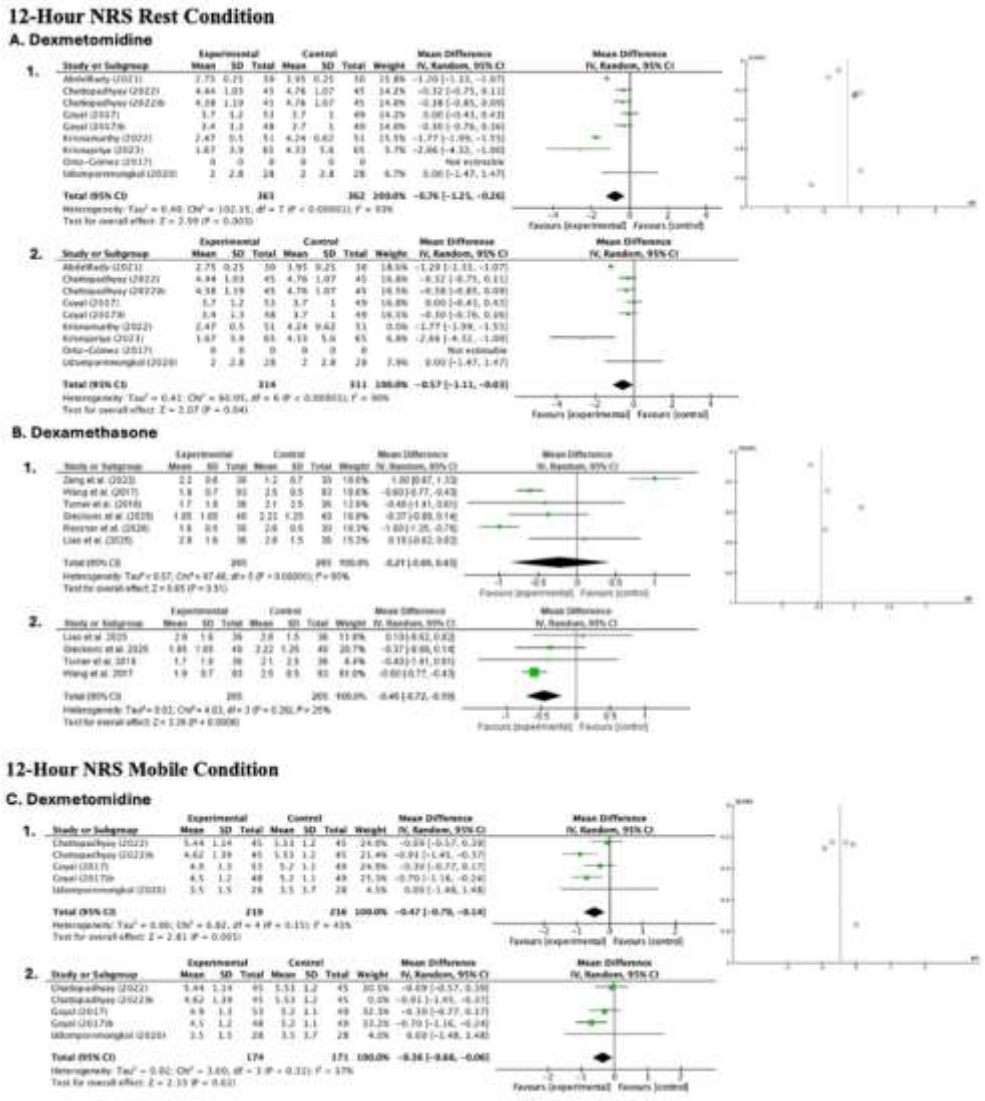


Figure 5. 12-hour NRS pain score. (A1.) Dexmedetomidine at rest: all eligible studies included in the meta-analysis. (A2.) Dexmedetomidine at rest: leave-one-out sensitivity analysis. (B1.) Dexamethasone at rest: all eligible studies included in the meta-analysis. (B2.) Dexamethasone at rest: leave-one-out sensitivity analysis. (C1.) Dexmedetomidine during movement: all eligible studies included in the meta-analysis. (C2.) Dexmedetomidine during movement: leave-one-out sensitivity analysis.

At 12 hours, dexamethasone showed an inconsistent effect on NRS pain scores at rest in the complete analysis (MD −0.21; 95% CI −0.86 to 0.43; p = 0.51; I^2 = 95%). After sensitivity analysis, the effect became statistically significant with lower heterogeneity (MD −0.46; 95% CI −0.72 to −0.19; p = 0.0008; I^2 = 25%). Dexamethasone also significantly reduced 12-hour movement-related pain scores (MD −0.47; 95% CI −0.85 to −0.10; p = 0.01), with low heterogeneity (I^2 = 21%) (Figure 5).

Dexmedetomidine significantly reduced 12-hour NRS at rest in the complete analysis (MD −0.76; 95% CI −1.25 to −0.26; p = 0.003; I^2 = 93%) and remained significant after sensitivity analysis (MD −0.57; 95% CI −1.11 to −0.03; p = 0.04; I^2 = 90%). For 12-hour movement pain, dexmedetomidine also showed a significant reduction (MD −0.47; 95% CI −0.79 to −0.14; p = 0.005; I^2 = 41%), with a consistent effect after sensitivity analysis (MD −0.36; 95% CI −0.66 to −0.06; p = 0.02; I^2 = 17%). Overall, dexmedetomidine improved 12-hour pain scores, particularly during movement, although rest-pain findings remained heterogeneous.

24-Hour NRS Pain Score

Figure 6. 24-Hour NRS Pain Score

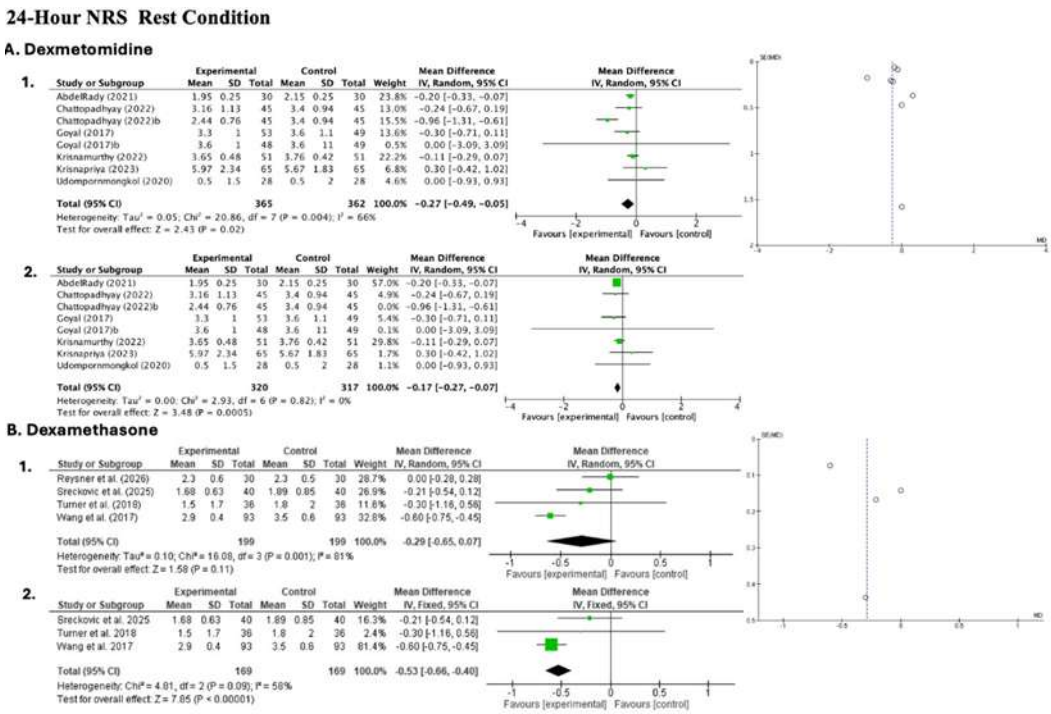


Figure 6. 24-hour NRS pain score. (A1.) Dexmedetomidine at rest: all eligible studies included in the meta-analysis. (A2.) Dexmedetomidine at rest: leave-one-out sensitivity analysis. (B1.) Dexamethasone at rest: all eligible studies included in the meta-analysis. (B2.) Dexamethasone at rest: leave-one-out sensitivity analysis.

Pooled data from NRS at 24 hours, Dexamethasone showed no significant reduction in the complete analysis (MD −0.29; 95% CI −0.65 to 0.07; p = 0.11; I^2 = 81%). However, after sensitivity analysis, dexamethasone significantly reduced 24-hour resting pain scores (MD −0.43; 95% CI −0.74 to −0.12; p = 0.007; I^2 = 58%).

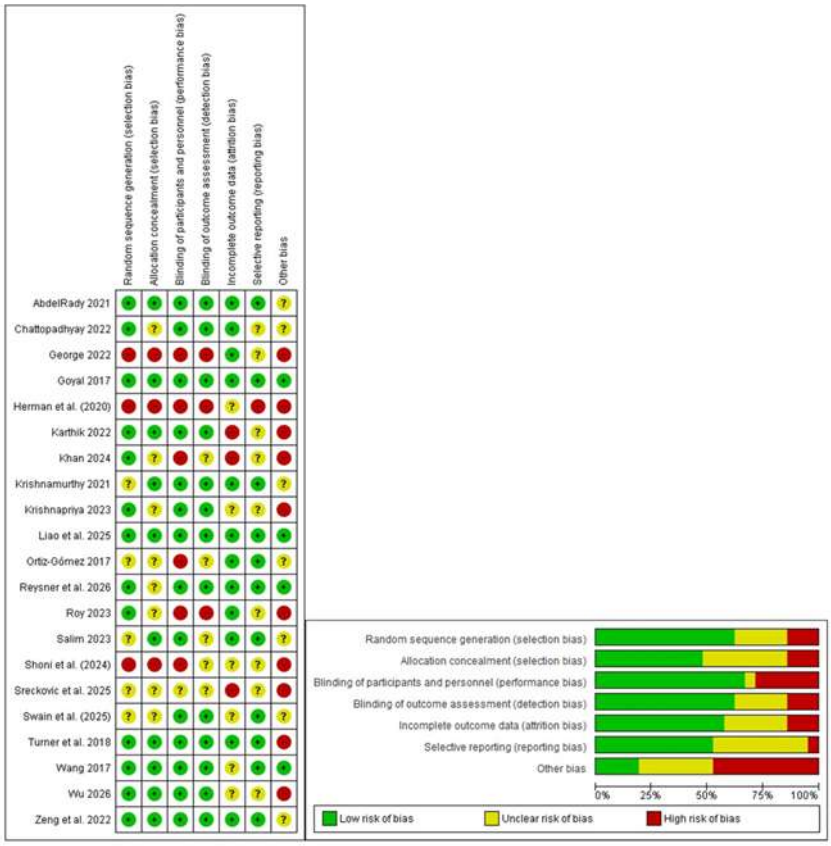
Dexmedetomidine significantly reduced NRS pain scores at rest compared with control (MD −0.27; 95% CI −0.49 to −0.05; p = 0.02; I^2 = 66%) (Figure 6B). After sensitivity analysis, the effect remained significant with no heterogeneity (MD −0.17; 95% CI −0.27 to −0.07; p = 0.0005; I^2 = 0%).

3.3 Adverse Events

Adverse events were inconsistently reported and could not be reliably pooled. Overall, dexamethasone and dexmedetomidine did not show a consistent increase in serious adverse events compared with control. Isolated bradycardia, hypotension, or sedation were reported with dexmedetomidine, whereas dexamethasone was not clearly associated with increased hyperglycemia, nerve injury, infection, or motor impairment. Evidence for the combined regimen remained limited, but no clear safety signal was observed.

Risk of Bias Assessment

Figure 7. Risk of Bias from 21 studies with ROBIN-2



Risk of bias assessment showed that most domains were judged as low risk (Figure 7). Across 147 domain-level judgments from 21 studies, 77 judgments were low risk of bias (52.4%), 41 were unclear risk of bias (27.9%), and 29 were high risk of bias (19.7%). The main concerns were related to allocation concealment, blinding, selective reporting, and other potential sources of bias, while several randomized trials showed generally acceptable methodological quality.

3.4 Discussion

Principal Findings and Clinical Relevance

This systematic review and meta-analysis showed that perineural dexamethasone and dexmedetomidine as adjuvants to adductor canal block improved postoperative analgesia after total knee arthroplasty, mainly by reducing early pain scores, prolonging analgesic duration, and decreasing analgesic consumption. These findings are clinically relevant because inadequate pain control after TKA may delay mobilisation, physiotherapy, and functional recovery. Tan et al. reported that perineural dexamethasone prolonged analgesic duration and reduced 24-hour postoperative pain scores compared with intravenous dexamethasone, while Abdallah and Brull showed that dexmedetomidine could prolong sensory block duration and time to first analgesic request when used as a local anesthetic adjuvant. Further found that dexamethasone and dexmedetomidine

produced comparable analgesic effects as peripheral local anesthetic adjuvants, although optimal dosing and safety remain uncertain.[29,30]

Mechanistic Basis of Perineural Adjuvant Effects

The analgesic benefit observed in this review is biologically plausible. Dexamethasone is thought to enhance peripheral nerve block by suppressing local inflammatory responses, reducing perineural edema, and decreasing nociceptive sensitization after surgical tissue injury.[31] Its glucocorticoid activity may reduce the release of inflammatory mediators around injured tissues and peripheral nerves, thereby limiting C-fiber–mediated nociceptive transmission and postoperative hyperalgesia[32]. In addition, perineural dexamethasone may prolong local anesthetic action through local vasoconstrictive effects that slow vascular uptake of the anesthetic, although systemic absorption may also contribute to its clinical effect.[30,32] Recent dose–response evidence suggests that perineural dexamethasone may achieve block-prolonging effects at lower doses than intravenous dexamethasone, supporting a potential local pharmacodynamic contribution while also emphasizing the need for cautious dose selection.[33]

Dexmedetomidine provides analgesic modulation mainly through α2-adrenergic activity and direct effects on peripheral nerve excitability. Experimental evidence suggests that perineural dexmedetomidine can prolong local anesthetic analgesia by inhibiting hyperpolarization-activated cation currents, which delays neuronal recovery from hyperpolarization and reduces repetitive firing of nociceptive fibers.[34] This mechanism may explain the longer time to first rescue analgesia and reduced analgesic consumption observed in the dexmedetomidine group. Dexmedetomidine may also produce local vasoconstriction and systemic analgesic-sedative effects after absorption, which can further contribute to postoperative opioid sparing.[30,35–37] The combination of dexamethasone and dexmedetomidine is therefore mechanistically attractive because dexamethasone primarily targets inflammation-related nociceptive sensitization, while dexmedetomidine modulates neuronal excitability and adrenergic analgesia. However, current clinical evidence has not yet confirmed that the combined regimen is consistently superior to dexamethasone alone, so its use should still be interpreted as promising but not definitive[38].

Potential Role of Combined Dexamethasone–Dexmedetomidine

The combined dexamethasone–dexmedetomidine regimen represents the key focus of this review because both adjuvants may provide complementary analgesic effects.[7] Dexamethasone mainly contributes through anti-inflammatory activity, reduction of perineural edema, and prolongation of local anesthetic action.[4] Dexmedetomidine adds α2-adrenergic analgesic modulation and reduced neuronal excitability.[6] This dual mechanism may be clinically relevant in TKA, where postoperative pain is driven by inflammatory tissue injury, nociceptive transmission, and early mobilisation-related pain.[7]

TKA-specific studies support this potential benefit, although the evidence remains limited. Herman et al. reported prolonged analgesia lasting several days after combined ACB and IPACK using dexamethasone and dexmedetomidine.[26] Shoni et al. found lower opioid consumption and lower early pain scores with combined ACB/IPACK using bupivacaine, dexmedetomidine, and dexamethasone compared with ACB alone.[27] Swain et al. provided more direct randomized evidence, showing that adding dexmedetomidine to dexamethasone in ACB reduced morphine consumption and early NRS pain scores without meaningful impairment in quadriceps strength, TUG time, sedation, or complication rates.[28]

Opioid-Sparing Effect and Enhanced Recovery Implications

The opioid-sparing effect is clinically relevant because reduced opioid exposure may support enhanced recovery after TKA by decreasing nausea, vomiting, dizziness, sedation, constipation, and delayed mobilisation. Dexmedetomidine showed a more consistent reduction in 24-hour analgesic consumption, whereas dexamethasone showed a favorable but less stable effect. Similar findings were reported by Wang et al. and Zeng et al., who found lower morphine consumption after dexamethasone-enhanced ACB or ACB/IPACK. Heterogeneity in analgesic protocols, opioid conversion, and block techniques reduces certainty in the estimated magnitude of benefit. This finding is consistent with previous reviews showing that regional and multimodal analgesic strategies reduce perioperative opioid exposure while maintaining postoperative pain control after total joint arthroplasty.[30]

Table 5. GRADE Outcome

Outcome	Effect	Main concern	Certainty
Analgesic duration / time to rescue	Dexmedetomidine significantly prolonged analgesia; dexamethasone favored longer duration	Initial heterogeneity, improved after sensitivity analysis	Moderate for dexmedetomidine; Low for dexamethasone
24-hour analgesic consumption	Dexmedetomidine consistently reduced analgesic use; dexamethasone showed less stable benefit	Different analgesic protocols and opioid units	Moderate for dexmedetomidine; Low for dexamethasone
Early NRS pain scores	Both adjuvants reduced early pain scores, especially at rest	Variable time points and heterogeneity	Moderate
Quadriceps strength / functional recovery	No relevant motor impairment; some studies showed better ROM or ambulation	Limited and inconsistent reporting	Low to Moderate
Adverse events	No consistent increase in serious adverse events; mostly mild or absent events	Incomplete safety reporting	Low
Combined dexamethasone–dexmedetomidine	Promising for early analgesia and opioid sparing	Few studies; meta-analysis not feasible	Low

The overall certainty of evidence ranged from low to moderate. Although some outcomes initially showed high heterogeneity, sensitivity or leave-one-out analysis improved consistency for key dexmedetomidine outcomes, especially analgesic duration and 24-hour analgesic consumption. Functional recovery and safety findings were generally supportive, but certainty remained limited because quadriceps strength, ROM, ambulation, and adverse events were not uniformly reported across studies.

Motor-Sparing Analgesia and Functional Recovery

ACB remains valuable after TKA because it provides predominantly sensory analgesia with better preservation of quadriceps function than more motor-impairing blocks such as femoral nerve block.[39,40] This motor-sparing profile may support early ambulation, rehabilitation, and fall-risk reduction. Dexmedetomidine-containing ACB regimens improved analgesic outcomes without consistent evidence of clinically relevant quadriceps impairment.[22,25] The combined dexamethasone–dexmedetomidine regimen also reduced analgesic requirements and early pain scores without meaningful impairment in quadriceps strength, TUG time, sedation, or complication rates.[27,28] However, functional outcomes should be interpreted cautiously because quadriceps strength, motor block, ambulation, TUG test, and mobilisation were not uniformly reported, and block techniques varied across studies.[22,25,28] Recent network meta-analysis evidence also supports the role of motor-sparing nerve blocks in TKA, although the incremental clinical benefit of adding single-shot ACB or iPACK to local infiltration analgesia may be modest and protocol-dependent.[41]

Safety and Practical Considerations

Most included studies did not show a consistent increase in serious adverse events after adding dexmedetomidine, dexamethasone, or their combination to ACB.[22,25,27,28] Dexmedetomidine still requires monitoring because bradycardia, hypotension, sedation, and desaturation remain clinically plausible adverse effects, although Swain et al. found no significant difference in sedation, hypotension, bradycardia, desaturation, or complication rates after adding dexmedetomidine to

dexamethasone in ACB.[28] Dexamethasone requires caution in patients with diabetes or hyperglycemia risk, and perineural use should be interpreted carefully because it remains off-label in many settings.[4,42]

Figure 8. Graphical Abstract

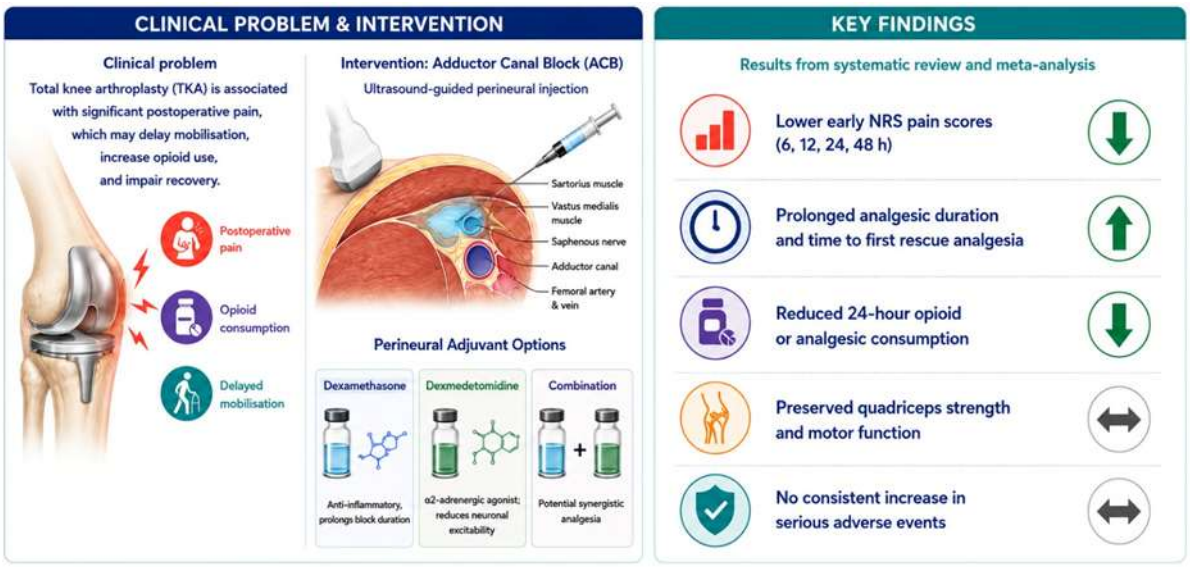


Figure 8 summarizes the clinical rationale, intervention, and main findings of this review. Total knee arthroplasty is frequently associated with significant postoperative pain, increased analgesic requirements, and delayed mobilisation. Adductor canal block was evaluated as a motor-sparing regional analgesic technique, with perineural dexamethasone, dexmedetomidine, or their combination used as adjuvants. Overall, these adjuvant strategies were associated with lower early NRS pain scores, prolonged analgesic duration, longer time to first rescue analgesia, and reduced 24-hour opioid or analgesic consumption. Quadriceps strength and motor function were generally preserved, and no consistent increase in serious adverse events was observed.

The strength of this review is its specific focus on dexamethasone, dexmedetomidine, and their combination as ACB adjuvants after TKA, with evaluation of both analgesic and safety outcomes. The main limitations were variability in adjuvant dose, local anesthetic type and volume, single-shot versus continuous ACB, use of IPACK block, comparator groups, opioid-conversion methods, and follow-up duration. Evidence for the combined dexamethasone–dexmedetomidine regimen remains limited because only a few studies directly evaluated this strategy, including Herman et al., Shoni et al., and Swain et al.[26–28] A meta-analysis of the combined regimen could not be performed because the available studies were few, used different study designs, applied different block combinations, and reported non-uniform analgesic and functional outcomes.[26–28] Future multicenter RCTs should use standardized ACB/IPACK protocols, 48–72-hour follow-up, systematic adverse-event reporting, and consistent functional outcomes.

4. CONCLUSION

Perineural dexamethasone and dexmedetomidine as adjuvants to ACB may improve postoperative analgesia after TKA by reducing early pain scores, prolonging analgesic duration, and decreasing analgesic consumption. Dexmedetomidine showed a more consistent analgesic-sparing effect, while dexamethasone demonstrated favorable effects on early pain control. The combined dexamethasone–dexmedetomidine regimen appears promising, but current evidence remains limited and is insufficient for definitive recommendation. Further well-designed RCTs with standardized protocols and systematic safety reporting are needed.

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AUTHOR CONTRIBUTIONS

Danang Kuntoadi: Conceptualization, Data Curation, Formal Analysis, Writing—Original Draft.

Alamsyah Ambo Ala Husain: Methodology, Data Curation, Formal Analysis.

Madonna Damayanthie Datu: Data Curation, Formal Analysis, Supervision.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICS STATEMENT

Ethical approval was not required for this study, as it is a systematic review and meta-analysis of previously published data.

DATA AVAILABILITY STATEMENT

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

REFERENCES

[1] Lavand'homme PM, Kehlet H, Rawal N, Joshi GP. Pain management after total knee arthroplasty. Eur J Anaesthesiol. 2022 Sep;39(9):743–57. doi:10.1097/EJA.0000000000001691

[2] Jiang X, Wang Q, Wu C, Tian W. Analgesic Efficacy of Adductor Canal Block in Total Knee Arthroplasty: A Meta-analysis and Systematic Review. Orthop Surg. 2016 Aug 14;8(3):294–300. doi:10.1111/os.12268

[3] Wang D, Yang Y, Li Q, Tang SL, Zeng WN, Xu J, et al. Adductor canal block versus femoral nerve block for total knee arthroplasty: a meta-analysis of randomized controlled trials. Sci Rep. 2017 Jan 12;7(1):40721. doi:10.1038/srep40721

[4] Baeriswyl M, Kirkham KR, Jacot-Guillarmod A, Albrecht E. Efficacy of perineural vs systemic dexamethasone to prolong analgesia after peripheral nerve block: a systematic review and meta-analysis. Br J Anaesth. 2017 Aug;119(2):183–91. doi:10.1093/bja/aex191

[5] Tan ESJ, Tan YR, Liu CWY. Efficacy of perineural versus intravenous dexamethasone in prolonging the duration of analgesia when administered with peripheral nerve blocks: a systematic review and meta-analysis. Korean J Anesthesiol. 2022 Jun 1;75(3):255–65. doi:10.4097/kja.21390

[6] Abdallah FW, Brull R. Facilitatory effects of perineural dexmedetomidine on neuraxial and peripheral nerve block: a systematic review and meta-analysis. Br J Anaesth. 2013 Jun;110(6):915–25. doi:10.1093/bja/aet066

[7] Maagaard M, Andersen JH, Jaeger P, Mathiesen O. Effects of combined dexamethasone and dexmedetomidine as adjuncts to peripheral nerve blocks: a systematic review with meta-analysis and trial sequential analysis. Reg Anesth Pain Med. 2025 Apr;50(4):311–20. doi:10.1136/rapm-2023-105098

[8] Liao C, Li J, Hu X, Sun Y, Zheng K, Pan X, et al. Liposomal Bupivacaine Versus Ropivacaine With Perineural Dexamethasone in Adductor Canal Block for Total Knee Arthroplasty: A Randomized Clinical Trial. J Arthroplasty. 2025 Nov. doi:10.1016/j.arth.2025.11.015

[9] Reysner T, Kowalski G, Mularski A, Perek A, Daroszewski P, Reysner M. Optimizing Postoperative Analgesia in Total Knee Arthroplasty. Clin J Pain. 2026 Feb;42(2). doi:10.1097/AJP.0000000000001344

[10] Sreckovic S, Milovanovic D, Vukman P, Djukanovic M, Simic M, Vesic J, et al. The effect of adding dexamethasone to adductor block and IPACK block on acute postoperative, rebound, and chronic pain following knee arthroplasty—1-year follow-up. Front Med (Lausanne). 2025 Apr 29;12. doi:10.3389/fmed.2025.1570795

[11] Ortiz-Gómez JR, Perepérez-Candel M, Vázquez-Torres JM, Rodriguez-Del RÍO JM, Torrón-Abad B, Fornet-Ruiz I, et al. Postoperative analgesia for elective total knee arthroplasty under subarachnoid anesthesia with opioids: comparison between epidural, femoral block and adductor canal block techniques (with and without perineural adjuvants). A prospective, randomized, clinical trial. Minerva Anestesiol. 2017 Jan;83(1). doi:10.23736/S0375-9393.16.11646-3

[12] Wang CJ, Long FY, Yang LQ, Shen YJ, Guo F, Huang TF, et al. Efficacy of perineural dexamethasone with ropivacaine in adductor canal block for post operative analgesia in patients undergoing total knee arthroplasty: A randomized controlled trial. Exp Ther Med. 2017 Oct 1;14(4):3942–6. doi:10.3892/etm.2017.4974

[13] Zeng Y, Wang Q, Hu J, Yang J. Adding Dexamethasone to Adductor Canal Block Combined With iPACK Block Improve Postoperative Analgesia of Total Knee Arthroplasty. Clinical Journal of Pain. 2022 Sep 12;38(9):575–81. doi:10.1097/AJP.0000000000001056 PubMed PMID: 35819163.

[14] Turner JD, Dobson SW, Henshaw DS, Edwards CJ, Weller RS, Reynolds JW, et al. Single-Injection Adductor Canal Block With Multiple Adjuvants Provides Equivalent Analgesia When Compared With Continuous Adductor Canal Blockade for Primary Total Knee Arthroplasty: A Double-Blinded, Randomized, Controlled, Equivalency Trial. J Arthroplasty. 2018 Oct;33(10):3160-3166.e1. doi:10.1016/j.arth.2018.05.026

[15] Wu M, Wu M, Hao S, Wang G, Li C, Li X, et al. Effect of infusion of low-dose dexmedetomidine combined with adductor canal block on quality of recovery after unilateral total knee arthroplasty in elderly patients: a prospective randomized controlled trial. Eur J Med Res. 2026 Apr 8. doi:10.1186/s40001-026-04217-y

[16] Abo-Zeid Salim MA, Bakrey S, Elbadrawy RE. Intravenous versus perineural dexmedetomidine as adjuvant in adductor canal block for total knee arthroplasty. Korean J Anesthesiol. 2023 Aug 1;76(4):307–16. doi:10.4097/kja.22579

[17] Roy R, Agarwal G, Latwal BS, Patel A, Mohta A. A comparative randomized controlled study of modified 4 in 1 block versus IPACK plus adductor canal block for post-operative analgesia in total knee arthroplasty. Indian J Anaesth. 2023 Mar;67(3):296–301. doi:10.4103/ija.ija_530_22

[18] Krishnapriya K, Suchitra M, Kumar KP, Ashalatha P. EVALUATION OF POSTOPERATIVE ANALGESIC EFFICACY OF BUPIVACAINE WITH DEXMEDETOMIDINE AS ADJUVANT IN ULTRASOUND GUIDED ADDUCTOR CANAL BLOCK IN PATIENTS UNDERGOING TOTAL KNEE ARTHROPLASTY. Int J Sci Res. 2023 Dec 1;31–3. doi:10.36106/ijsr/3007132

[19] Krishnamurthy BK, Aparna B, Chikkegowda S, Kumar KSL. Comparison between Dexmedetomidine and Clonidine as an Adjuvant to Ropivacaine in Ultrasound-Guided Adductor Canal Block for Postoperative Analgesia in Total Knee Replacement. Anesth Essays Res. 2021 Apr;15(2):245–9. doi:10.4103/aer.aer_143_21

[20] Khan MJ, Tauheed N, Siddiqui AH, Sabir AB, Haleem S. Adductor Canal Block Versus Local Infiltration Analgesia for Postoperative Pain Management in Total Knee Arthroplasty. Cureus. 2024 Apr 1. doi:10.7759/cureus.57408

[21] Karthik NM, Das SG, Johney J, George M, Issac E, Vasudevan A. Comparison of postoperative analgesia with two different doses of dexmedetomidine as an adjuvant to ropivacaine in adductor canal block for unilateral total knee replacement surgery: A randomized double-blinded study. J Anaesthesiol Clin Pharmacol. 2022 Jul;38(3):428–33. doi:10.4103/joacp.JOACP_493_20

[22] Goyal R, Mittal G, Yadav A, Sethi R, Chattopadhyay A. Adductor canal block for post-operative analgesia after simultaneous bilateral total knee replacement: A randomised controlled trial to study the effect of addition of dexmedetomidine to ropivacaine. Indian J Anaesth. 2017;61(11):903. doi:10.4103/ija.IJA_277_17

[23] George ND, Bhat S, B. V S. Comparison of Femoral Nerve Block with Dexmedetomidine and Adductor Canal Block with Dexmedetomidine for Postoperative Analgesia for Total Knee Arthroplasty. Biomedical and Pharmacology Journal. 2022 Sep 29;15(3):1519–27. doi:10.13005/bpj/2490

[24] AbdelRady MM, Ali WN, Younes KT, Talaat EA, AboElfadl GM. Analgesic efficacy of single- shot adductor canal block with levobupivacaine and dexmedetomidine in total knee arthroplasty: A randomized clinical trial. Egypt J Anaesth. 2021 Jan 23;37(1):386–93. doi:10.1080/11101849.2021.1968713

[25] Kumar A, Chattopadhyay A, Parashar P, Kohli A, Teckchandani C, Gupta L. Evaluation of postoperative analgesic efficacy of dexmedetomidine as adjuvant with ropivacaine in ultrasound guided adductor canal block in patients undergoing unilateral Total Knee Replacement. Indian Journal of Clinical Anaesthesia. 2022 Feb 28;9(1):105–11. doi:10.18231/j.ijca.2022.020

[26] Herman J, Urits I, Eskander J, Kaye A, Viswanath O. Adductor Canal Block Duration of Analgesia Successfully Prolonged With Perineural Dexmedetomidine and Dexamethasone in Addition to IPACK Block for Total Knee Arthroplasty. Cureus. 2020 Sep 21. doi:10.7759/cureus.10566

[27] Shoni M, Samineni A V., Salavati S, Mikkilineni N, Wang A, Abdeen A, et al. Combined Single-Shot Infiltration Between the Popliteal Artery and Capsule of the Knee and Adductor Canal Block With Bupivacaine, Dexmedetomidine, and Dexamethasone for Total Knee Arthroplasty: A Propensity-Matched Analysis. Arthroplast Today. 2024 Feb;25:101292. doi:10.1016/j.artd.2023.101292

[28] Swain BP, Sharma P, Kant R. A randomized controlled trial evaluating the efficacy of combined dexamethasone and dexmedetomidine as adjuvants to ropivacaine in adductor canal block for postoperative analgesia in total knee arthroplasty. J Anaesthesiol Clin Pharmacol. 2026 Jan;42(1):112–9. doi:10.4103/joacp.joacp_118_25
[29] Zhao C, Liao Q, Yang D, Yang M, Xu P. Advances in perioperative pain management for total knee arthroplasty: a review of multimodal analgesic approaches. J Orthop Surg Res. 2024 Dec 19;19(1):843. doi:10.1186/s13018-024-05324-4
[30] Soffin EM, Wu CL. Regional and Multimodal Analgesia to Reduce Opioid Use after Total Joint Arthroplasty: A Narrative Review. HSS J. 2019 Feb 1;15(1):57–65. doi:10.1007/s11420-018-9652-2
[31] Pehora C, Pearson AM, Kaushal A, Crawford MW, Johnston B. Dexamethasone as an adjuvant to peripheral nerve block. Cochrane Database of Systematic Reviews. 2017 Nov 9;2017(11). doi:10.1002/14651858.CD011770.pub2
[32] Song ZG, Pang SY, Wang GY, Zhang Z. Comparison of postoperative analgesic effects in response to either dexamethasone or dexmedetomidine as local anesthetic adjuvants: a systematic review and meta-analysis of randomized controlled trials. J Anesth. 2021 Apr 30;35(2):270–87. doi:10.1007/s00540-021-02895-y
[33] Zufferey PJ, Chaux R, Lachaud PA, Capdevila X, Lanoiselée J, Ollier E. Dose–response relationships of intravenous and perineural dexamethasone as adjuvants to peripheral nerve blocks: a systematic review and model-based network meta-analysis. Br J Anaesth. 2024 May;132(5):1122–32. doi:10.1016/j.bja.2023.12.021
[34] Brummett CM, Hong EK, Janda AM, Amodeo FS, Lydic R. Perineural Dexmedetomidine Added to Ropivacaine for Sciatic Nerve Block in Rats Prolongs the Duration of Analgesia by Blocking the Hyperpolarization-activated Cation Current. Anesthesiology. 2011 Oct 1;115(4):836–43. doi:10.1097/ALN.0b013e318221fcc9
[35] Guo J, Hou M, Shi G, Bai N, Huo M. iPACK block (local anesthetic infiltration of the interspace between the popliteal artery and the posterior knee capsule) added to the adductor canal blocks versus the adductor canal blocks in the pain management after total knee arthroplasty: a systematic review and meta-analysis. J Orthop Surg Res. 2022 Aug 12;17(1):387. doi:10.1186/s13018-022-03272-5
[36] Jabur A, Nam HJ, Dixon A, Cox T, Randall H, Sun J. The effects of continuous catheter adductor canal block for pain management in knee replacement therapy: a meta-analysis. Knee Surg Relat Res. 2023 Jun 1;35(1):16. doi:10.1186/s43019-023-00188-0
[37] Lv J, Huang C, Wang Z, Ou S. Adductor canal block combined with local infiltration analgesia versus isolated adductor canal block in reducing pain and opioid consumption after total knee arthroplasty: a systematic review and meta-analysis. Journal of International Medical Research. 2020 Aug 10;48(8). doi:10.1177/0300060520926075
[38] Laigaard J, Pedersen C, Rønsbo TN, Mathiesen O, Karlsen APH. Minimal clinically important differences in randomised clinical trials on pain management after total hip and knee arthroplasty: a systematic review. Br J Anaesth. 2021 May;126(5):1029–37. doi:10.1016/j.bja.2021.01.021
[39] Kim DH, Lin Y, Goytizolo EA, Kahn RL, Maalouf DB, Manohar A, et al. Adductor Canal Block versus Femoral Nerve Block for Total Knee Arthroplasty. Anesthesiology. 2014 Mar;120(3):540–50. doi:10.1097/ALN.0000000000000119
[40] Wang D, Yang Y, Li Q, Tang SL, Zeng WN, Xu J, et al. Adductor canal block versus femoral nerve block for total knee arthroplasty: a meta-analysis of randomized controlled trials. Sci Rep. 2017 Jan 12;7(1):40721. doi:10.1038/srep40721
[41] Hussain N, Brull R, Vannabouathong C, Robinson C, Zhou S, D'Souza RS, et al. Analgesic Effectiveness of Motor-sparing Nerve Blocks for Total Knee Arthroplasty: A Network Meta-analysis. Anesthesiology. 2023 Oct 26;139(4):444–61. doi:10.1097/ALN.0000000000004667
[42] Turner JD, Henshaw DS, Weller RS, Jaffe JD, Edwards CJ, Reynolds JW, et al. Perineural dexamethasone successfully prolongs adductor canal block when assessed by objective pinprick sensory testing: A prospective, randomized, dose-dependent, placebo-controlled equivalency trial. J Clin Anesth. 2018 Aug;48:51–7. doi:10.1016/j.jclinane.2018.05.009