Tabari Biomedical Student Research Journal

OPEN ACCESS

REVIEW: Dexmedetomidine as an Adjuvant to Local Anesthetics for Postoperative Pain Control: Applications in Neuraxial and Fascial Plane Blocks

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ARTICLE INFO

Submitted: 25 Apr 2026
Accepted: 18 May 2026
Published: 21 Jun 2026

Keywords:
Dexmedetomidine; Local Anesthetics; Postoperative Pain; Neuraxial Anesthesia; Fascial Plane Block; Regional Anesthesia

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Citation:
Hojjati M, Sobhani S. Dexmedetomidine as an Adjuvant to Local Anesthetics for Postoperative Pain Control: Applications in Neuraxial and Fascial Plane Blocks. Tabari Biomed Stu Res J. 2026;8(2): 52- 63.

ABSTRACT

Dexmedetomidine is a highly selective alpha-2 adrenergic agonist increasingly used off-label as an adjuvant to local anesthetics in neuraxial and peripheral regional anesthesia. Its appeal in postoperative pain management stems from the ability to prolong sensory blockade and analgesia while reducing systemic opioid requirements; however, these benefits are counterbalanced by dose-dependent bradycardia, hypotension, sedation, and, in neuraxial techniques, prolongation of motor block. This narrative review provides a route-specific synthesis of clinically relevant evidence for intrathecal, epidural, and pediatric caudal administration and for contemporary fascial plane and related truncal blocks, including transversus abdominis plane, erector spinae plane, quadratus lumborum, pectoral/interpectoral, pectoserratus, serratus anterior plane, and paravertebral blocks. Randomized trials and meta-analyses generally demonstrate longer time to first rescue analgesia and lower postoperative opioid consumption when dexmedetomidine is added to bupivacaine, ropivacaine, or levobupivacaine. The magnitude and consistency of pain-score improvement are more variable and are influenced by surgical population, local anesthetic regimen, dexmedetomidine dose, block approach, and background multimodal analgesia. Intrathecal doses around 3-5 micrograms and perifascial doses near 0.5-1 microgram/kg are frequently studied, but no universal dose can be recommended across techniques. Mechanistically, spinal alpha-2 receptor activation, inhibition of hyperpolarization-activated cation currents, local effects on neural conduction and vascular uptake, and systemic sympatholysis may all contribute. Current U.S. labeling is for intravenous administration; neuraxial and perineural/perifascial administration remains off-label, and long-term human neurotoxicity data are limited. Dexmedetomidine is therefore best viewed as a potentially useful, technique-specific opioid-sparing adjunct whose use requires deliberate dose selection, hemodynamic monitoring, an appropriate preservative-free formulation for regional use, and explicit institutional governance.

1. Introduction

Postoperative pain remains a major target of enhanced-recovery pathways because inadequately controlled pain delays mobilization, impairs respiratory function, increases opioid exposure, and may contribute to persistent postsurgical pain. Regional anesthesia can attenuate these problems, but the duration of a single-injection block is ultimately constrained by the pharmacology of the local anesthetic. Catheters can extend analgesia but require additional equipment, expertise, follow-up,

and management of catheter-related failure or infection. Consequently, adjuvants that prolong a single-shot block without materially increasing toxicity are attractive.

Dexmedetomidine is a potent and highly selective alpha-2 adrenoceptor agonist (alpha-2:alpha-1 selectivity approximately 1620:1) with sedative, sympatholytic, anxiolytic, and analgesic-sparing properties and relatively little direct respiratory depression (1). Experimental and human evidence indicates that dexmedetomidine can extend local-anesthetic action through mechanisms that are partly route dependent. Animal studies support a direct peripheral contribution, including dose-dependent prolongation of ropivacaine block and inhibition of the hyperpolarization-activated cation current (Ih), while volunteer and clinical studies demonstrate meaningful prolongation of peripheral nerve blockade (2-4). Meta-analyses subsequently confirmed prolonged sensory and motor block and longer analgesia, although bradycardia and hypotension become more relevant as dose increases (5-8). The clinical literature is now sufficiently broad to require a route-specific interpretation. Evidence for intrathecal and epidural administration is mechanistically and clinically distinct from evidence for high-volume interfascial injections. Fascial plane blocks also differ from classic perineural blocks because local anesthetic spreads within tissue planes, may reach multiple neural targets, and can produce clinically important systemic absorption. The purpose of this narrative review is therefore to synthesize current evidence on dexmedetomidine as a local-anesthetic adjuvant for postoperative analgesia with particular attention to neuraxial techniques and fascial plane blocks, to compare dose-response and safety signals, and to identify areas in which evidence is sufficiently consistent to inform clinical interpretation versus areas that remain investigational.

2. Material and Methods

This article was prepared as a focused narrative clinical review. PubMed/MEDLINE and publisher-indexed web sources were searched iteratively, with backward citation chaining from major reviews, meta-analyses, and clinically relevant trials. Search concepts combined “dexmedetomidine” with terms including “local anesthetic,” “intrathecal,” “spinal,” “epidural,” “caudal,” “transversus abdominis plane,” “erector spinae plane,” “quadratus lumborum,” “pectoral,” “interpectoral,” “pectoserratus,” “serratus anterior,” “paravertebral,” “perineural,” “postoperative pain,” and “analgesia.” Literature available through September 2026 was considered. The search was deliberately targeted and iterative rather than designed as an exhaustive systematic search, and no review protocol or PRISMA-style workflow was used.

3. Pharmacologic Rationale and Mechanisms

3.1. Central and Spinal Alpha-2 Adrenergic Effects

Dexmedetomidine activates presynaptic and postsynaptic alpha-2 receptors in the central nervous system. At the spinal dorsal horn, presynaptic receptor activation reduces calcium influx and release of excitatory neurotransmitters, whereas postsynaptic activation increases potassium conductance and neuronal hyperpolarization. These actions dampen nociceptive transmission and provide a biologically plausible explanation for the prolongation of neuraxial analgesia. Supraspinal activity in the locus coeruleus reduces central noradrenergic output, producing sympatholysis and a sleep-like, arousable sedation phenotype (1). These central actions also explain why a fraction of the apparent “local” benefit after perifascial injection may result from systemic absorption rather than exclusively from a peripheral neural mechanism.

3.2. Peripheral Neural and Vascular Effects

Peripheral actions appear to be more than a simple consequence of sedation. In rat sciatic nerve models, adding dexmedetomidine to ropivacaine prolonged thermal

antinociception in a dose-dependent fashion (2). Subsequent experiments implicated inhibition of the Ih current, which normally opposes membrane hyperpolarization; suppression of this current can stabilize a hyperpolarized state and delay recovery of nerve excitability (3). In human volunteers, dexmedetomidine added to ropivacaine prolonged peripheral nerve blockade (4). Local vasoconstriction and reduced vascular uptake of local anesthetic have also been proposed, although their quantitative contribution in modern ultrasound-guided fascial plane blocks is uncertain.

3.3. Local versus Systemic Contributions

The distinction between local and systemic dexmedetomidine effects is clinically important. A randomized interscalene trial found that both perineural and intravenous dexmedetomidine prolonged analgesia compared with control, with broadly similar clinical effects (33). A 2023 meta-analysis comparing perineural and intravenous administration found modest advantages for the perineural route in analgesic and sensory-block duration, but heterogeneity was substantial (8). Accordingly, enhanced block duration after a fascial plane injection should not automatically be interpreted as proof of a purely local neural effect. High-volume blocks may deliver enough dexmedetomidine into the systemic circulation to generate sympatholytic and analgesic-sparing effects.

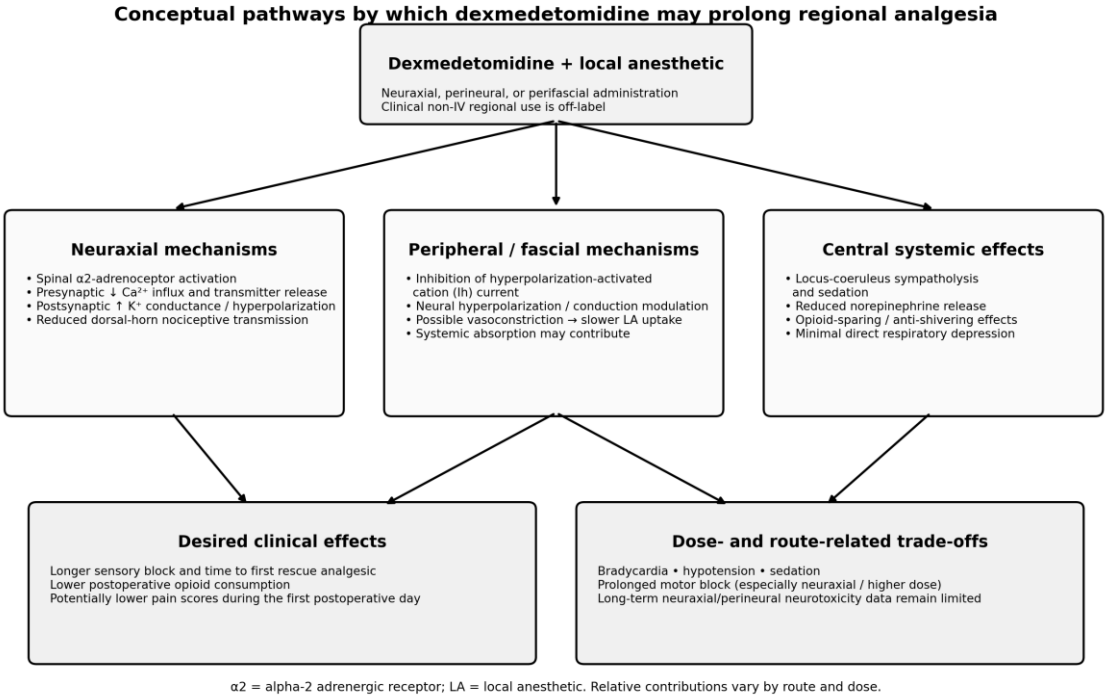

Figure 1. Conceptual mechanisms by which dexmedetomidine may prolong regional analgesia. The relative contributions of spinal, peripheral neural, vascular, and systemic effects differ according to route, dose, local-anesthetic regimen, and block technique. Non-intravenous regional administration is off-label.

4. Neuraxial Applications

4.1. Intrathecal Dexmedetomidine

Intrathecal dexmedetomidine is the most extensively studied neuraxial application. Early randomized trials showed that small doses added to bupivacaine or ropivacaine accelerate or preserve block onset while substantially prolonging sensory and motor regression. Kanazi et al. reported that 3 micrograms added to hyperbaric bupivacaine prolonged sensory regression to S1 and motor recovery compared with bupivacaine alone (10). Al-Mustafa et al. demonstrated a dose-response relationship with 5 and 10 micrograms in urologic surgery (11), while

Gupta et al. found that 5 micrograms added to intrathecal ropivacaine prolonged postoperative analgesia (12). A comparative trial by Mahendru et al. also supported dexmedetomidine as a potent spinal adjuvant relative to clonidine and fentanyl (13).

The aggregate evidence is more informative than any single trial. In a meta-analysis of 24 randomized trials involving 1,460 patients, Paramasivan et al. found that intrathecal dexmedetomidine prolonged the time to first analgesic request by approximately 191 minutes and reduced 24-hour pain intensity and shivering without a statistically detectable increase in most adverse events (14). A separate meta-analysis focused specifically on a fixed 5-microgram intrathecal dose included 25 studies and 1,478 patients; sensory block was prolonged by about 134 minutes, motor block by about 114 minutes, and time to first rescue analgesia by about 217 minutes (15). The same analysis showed increased point estimates for bradycardia and hypotension, highlighting that efficacy cannot be separated from autonomic effects.

For postoperative pain control, the practical advantage of intrathecal dexmedetomidine is the robust extension of analgesia from a very small mass of drug. The main clinical trade-off is prolonged motor block, which may be undesirable in ambulatory surgery or enhanced-recovery pathways in which early mobilization is prioritized. The literature commonly examines 3-5 micrograms and sometimes 10 micrograms; the higher end usually extends block further but also deepens concern for delayed motor recovery and hemodynamic effects. The available evidence supports a dose-response relationship rather than a universal “best” intrathecal dose.

4.2. Epidural Dexmedetomidine

Epidural dexmedetomidine has been studied as an adjuvant to local anesthetics for surgical anesthesia and postoperative epidural analgesia. In a systematic review and meta-analysis of randomized trials, Zhang et al. found that adding dexmedetomidine improved analgesic efficacy, prolonged analgesia, reduced rescue analgesic requirements, and increased sedation while tending to lower heart rate (16). Compared with the intrathecal route, epidural administration usually uses larger absolute or weight-based doses because of the larger epidural volume and different pharmacokinetics. Published regimens vary substantially, which limits a single pooled dose recommendation.

From a postoperative perspective, epidural dexmedetomidine may be most relevant when clinicians seek to reduce epidural opioid exposure while maintaining dense analgesia. However, the same sympatholytic pharmacology that makes dexmedetomidine attractive can be additive with neuraxial sympathectomy and local anesthetic, particularly in hypovolemic, elderly, or conduction-system-vulnerable patients. Continuous epidural regimens also create cumulative exposure that is not directly comparable with single-dose spinal or perifascial injection.

4.3. Pediatric Caudal Block

Caudal analgesia is the best-developed pediatric neuraxial application. A review by Trifa et al. identified 21 publications involving 1,590 children and concluded that caudal dexmedetomidine added to a local anesthetic generally prolongs postoperative analgesia compared with local anesthetic alone (17). Sedation was more frequent, while clinically important hemodynamic effects were uncommon in most studies and appeared more likely at higher doses. Many trials use approximately 0.5-1 microgram/kg, with some evaluating 2 micrograms/kg. The pediatric setting deserves separate consideration because developmental pharmacology, weight-based dosing, postoperative monitoring, and the ethical threshold for off-label neuraxial exposure differ from adult practice.

5. Fascial Plane and Related Truncal Blocks

Fascial plane blocks have expanded rapidly because they can provide somatic and,

depending on the approach, partial visceral analgesia without deliberate needle-to-nerve contact. Dexmedetomidine has been tested in most major truncal plane blocks. Across techniques, the most reproducible outcomes are longer time to first rescue analgesia and lower opioid use; effects on numerical pain scores are less consistent and are often small relative to baseline multimodal analgesia. Because fascial planes differ in vascularity, neural targets, and injectate spread, evidence from one block should not be uncritically extrapolated to another.

5.1. Transversus Abdominis Plane Block

The transversus abdominis plane (TAP) block has the largest fascial-plane evidence base. Sun et al. analyzed 20 trials involving 1,212 patients and found that adding dexmedetomidine to local anesthetic reduced early postoperative pain, decreased opioid consumption, and prolonged TAP-block duration by approximately 3.3 hours (18). A second meta-analysis of nine randomized trials (598 patients) likewise found lower 24-hour opioid use and a mean prolongation of time to rescue analgesia of about 172 minutes, although pain-score estimates were heterogeneous and sensitive to analysis assumptions (19). Doses in the underlying studies varied, commonly including 0.5, 0.75, or 1 microgram/kg and occasional fixed doses.

These findings make TAP block a useful example of the distinction between statistically significant and clinically meaningful outcomes. Opioid-sparing and delayed rescue analgesia are relatively consistent, whereas absolute reductions in pain scores are often modest. The benefit also depends on whether the TAP block is a primary analgesic technique or one component of a regimen that already includes acetaminophen, nonsteroidal anti-inflammatory drugs, intrathecal morphine, or systemic dexamethasone.

5.2. Erector Spinae Plane Block

Evidence for erector spinae plane block (ESPB) has matured rapidly. A 2024 meta-analysis of 13 randomized trials involving 823 patients evaluated dexmedetomidine concentrations corresponding predominantly to 0.5 or 1 microgram/kg. Both dose ranges improved resting and dynamic pain scores at several postoperative time points, prolonged sensory block and time to first analgesic request, reduced morphine consumption, and reduced the need for rescue analgesia (21). The analysis suggests that efficacy is present at both commonly studied doses, but the certainty of a direct dose-response relationship is constrained by differences in surgery, local-anesthetic concentration, and injection level.

Individual trials reinforce the signal across diverse operations. Abu El Hassan et al. reported improved analgesic outcomes when dexmedetomidine was added to bupivacaine for bilateral ESPB in posterior lumbosacral spine fixation (27). More recently, Abraham et al. studied 0.5 microgram/kg dexmedetomidine added to bupivacaine for ESPB after cesarean delivery and found reduced analgesic requirements and prolonged block duration (29). These newer studies broaden external validity but remain relatively small and single-center; they do not resolve the optimal dose or the fraction of benefit attributable to systemic absorption.

5.3. Quadratus Lumborum Block

Quadratus lumborum block (QLB) is particularly relevant to abdominal, pelvic, renal, and obstetric surgery because injectate may spread toward thoracolumbar fascia and paravertebral spaces. In an open renal surgery trial, Alansary et al. added 1 microgram/kg dexmedetomidine to bupivacaine in a transincisional QLB and observed a marked prolongation of time to first analgesic request (18.6 versus 7.3 hours), lower morphine consumption, and lower pain scores, but also more bradycardia and higher sedation scores (25). Singh et al. similarly found a longer time to rescue analgesia and lower tramadol use with dexmedetomidine-enhanced QLB after cesarean delivery (26).

A 2026 randomized trial by Qi et al. in gynecologic laparoscopic surgery found that dexmedetomidine added to ropivacaine for posterior QLB reduced postoperative morphine consumption and pain scores without a statistically significant increase in adverse events (30). These data support the analgesic signal but also illustrate why safety cannot be inferred from one trial: baseline autonomic tone, dose, block volume, timing, and hemodynamic definitions differ substantially across studies.

5.4. Pectoral, Interpectoral, and Pectoserratus Plane Blocks

For breast surgery, dexmedetomidine has been evaluated in pectoral nerve (PECS) and related interfascial blocks. In a randomized double-blind study, Manzoor et al. used a total dexmedetomidine dose of 1 microgram/kg with bupivacaine for PECS I and II blocks and reported approximately 40% longer complete analgesia, lower rescue diclofenac consumption, and higher patient satisfaction without serious adverse effects (3ᵛ). Hefni et al. later compared ketamine and dexmedetomidine as adjuvants to bupivacaine in PECS II block and found favorable postoperative analgesia with dexmedetomidine (23). Arun et al. reported that adding dexmedetomidine to levobupivacaine in a thoracic interfascial plane block improved analgesia after modified radical mastectomy (24).

The terminology of anterior chest-wall fascial blocks has evolved, and older “PECS II” protocols overlap with what is now described as interpectoral and pectoserratus plane injections. For interpretation of the dexmedetomidine literature, the exact needle plane, injectate volume, and targeted dermatomes matter more than the label alone. Trials should therefore be compared on anatomical technique rather than nomenclature only.

5.5. Serratus Anterior Plane Block

Serratus anterior plane block (SAPB) is used for thoracic surgery, rib fractures, breast surgery, and lateral chest-wall analgesia. Rashidi et al. randomized thoracotomy patients to ropivacaine alone or ropivacaine plus 0.5 microgram/kg dexmedetomidine and found lower pain scores at several postoperative time points and lower narcotic consumption in the dexmedetomidine group. Two transient episodes of bradycardia occurred in the dexmedetomidine group, and heart rate and mean arterial pressure were lower at intermediate time points (28). The study illustrates a recurring pattern: improved analgesia and opioid sparing accompanied by a detectable sympatholytic signal even at moderate doses.

5.6. Paravertebral Block as a Related Deep Regional Comparator

Thoracic paravertebral block is not, strictly speaking, a classic fascial plane block; it is included here because it is anatomically and clinically relevant to truncal analgesia and provides a useful comparator for deep regional injection. Tang et al. analyzed 12 randomized trials with 701 patients and found that dexmedetomidine added to local anesthetic reduced pain at 12 and 24 hours, prolonged analgesia by roughly 173 minutes, and reduced morphine consumption by approximately 18 mg, without a statistically significant increase in hemodynamic complications (20). The evidence was rated moderate for major pain outcomes. The PVB data therefore strengthen the broader conclusion that dexmedetomidine can enhance truncal regional analgesia, while not proving equivalence across anatomical planes.

6. Dose, Route, and Local Anesthetic Interactions

6.1. No Single Dose Applies to All Regional Techniques

The literature does not support a universal dexmedetomidine dose across intrathecal, epidural, caudal, perineural, and fascial-plane techniques. Intrathecal studies use microgram quantities because the drug is delivered directly into cerebrospinal fluid, whereas perifascial studies often use a weight-based

dose diluted into 20-40 mL of local anesthetic. Importantly, "dose" in a fascial plane block is inseparable from injection volume, bilateral versus unilateral administration, local-anesthetic concentration, vascularity of the plane, and patient size. A regimen that is well tolerated in a unilateral upper-extremity block cannot be assumed to have the same pharmacokinetic profile in a bilateral truncal block.

Table 1. Summary of clinical evidence for dexmedetomidine as a regional anesthesia adjuvant.

Technique / population	Common study regimen	Key evidence	Clinical signal	Main limitations / safety
Intrathecal (adults)	Often 3-5 micrograms; some trials 10 micrograms with bupivacaine/ropivacaine	24-RCT meta-analysis: time to rescue +191 min (14); fixed 5-microgram meta-analysis: sensory +134 min, motor +114 min (15)	Strong prolongation of spinal block and postoperative analgesia	Bradycardia/hypotension signal; prolonged motor block; off-label neuraxial use
Epidural (adults)	Variable; often weight-based bolus/infusion with local anesthetic	Meta-analysis of RCTs supports longer analgesia and fewer rescue analgesics (16)	Improved epidural analgesic quality and opioid sparing	Sedation and lower heart rate; heterogeneous dosing; cumulative exposure
Caudal (children)	Commonly 0.5-1 microgram/kg; higher doses studied	21 publications/1,590 children: longer analgesia versus local anesthetic alone (17)	Consistent prolongation of caudal analgesia	Sedation; limited long-term neuraxial safety data; pediatric off-label use
TAP block	Typically 0.5-1 microgram/kg or fixed dose with bupivacaine/ropivacaine	20-trial meta-analysis: lower opioid use, block +3.33 h (18); 9-RCT meta-analysis: rescue +172 min (19)	Opioid sparing and delayed rescue analgesia	Pain-score effect less robust; high heterogeneity
ESPB	Most often 0.5 or 1 microgram/kg	13 RCTs/823 patients: improved pain, sensory duration, rescue timing, morphine use (21)	Growing evidence across thoracic, spine, abdominal, and obstetric surgery	Optimal dose uncertain; many small single-center trials
QLB	Frequently 1 microgram/kg; 0.5-1 microgram/kg range emerging	RCTs show longer rescue time and lower opioids (25,26); 2026 RCT confirms opioid-sparing (30)	Potentially substantial extension of truncal analgesia	Bradycardia/sedation in some trials; technique-dependent spread
PECS / anterior chest wall	Commonly about 1 microgram/kg divided with block solution	PECS I/II RCT prolonged complete analgesia about 40% (36); additional RCTs favorable (23,24)	Longer analgesia after breast surgery	Nomenclature and plane definitions vary; modest sample sizes
SAPB	0.5 microgram/kg studied with ropivacaine	Thoracotomy RCT: lower pain and narcotic use (28)	Promising opioid-sparing effect	Transient bradycardia and lower heart rate/mean arterial pressure reported
Thoracic PVB (related comparator)	Variable, often 0.5-1 microgram/kg or fixed dose	12 RCTs/701: analgesia +173 min, morphine about 18 mg lower (20)	Moderate-certainty improvement in truncal analgesia	Not a classic fascial-plane block; between-study heterogeneity

Peripheral nerve-block meta-analyses offer a useful but imperfect reference. Vorobeichik et al. found that approximately 50-60 micrograms maximized sensory-block prolongation while minimizing hemodynamic adverse effects in brachial plexus block (6). Other analyses confirm efficacy but also show that larger doses increase bradycardia, hypotension, and somnolence (31). These findings should not be mechanically converted into a fascial-plane "ceiling dose," because interfascial absorption and target anatomy differ. They do, however, reinforce the principle of using the lowest dose that achieves a clinically meaningful prolongation.

6.2. Interaction with Local Anesthetic Choice and Background Analgesia

Most clinical studies combine dexmedetomidine with bupivacaine, ropivacaine, or levobupivacaine. The apparent effect size depends on the baseline duration of the local anesthetic: prolongation may look larger when control analgesia is relatively short. The interaction with other adjuncts is also clinically relevant. Intravenous dexamethasone, intrathecal morphine, nonsteroidal anti-inflammatory drugs, acetaminophen, and scheduled opioids can reduce the incremental benefit attributable to dexmedetomidine. Future trials

should therefore report standardized multimodal co-analgesia and should distinguish "block duration" from "time to first rescue analgesic," which is affected by many factors beyond sensory block.

Table 2. Dose ranges and safety signals by route and technique. Values are study ranges, not prescribing recommendations.

Setting / route	Frequently studied range	Expected effect	Key cautions	Evidence interpretation
Intrathecal	3-5 micrograms commonly; 10 micrograms in some trials	Longer sensory/motor block and time to rescue	Motor delay; bradycardia/hypotension; neuraxial off-label exposure	Best-established neuraxial evidence, but dose-response and safety must be balanced
Epidural	Variable; commonly weight-based bolus or infusion	Longer epidural analgesia; opioid sparing	Additive sympathectomy, sedation, cumulative exposure	Promising but heterogeneous regimens
Pediatric caudal	About 0.5-1 microgram/kg common; up to 2 micrograms/kg studied	Longer analgesia	Sedation and hemodynamic effects at higher dose; developmental safety	Evidence supports efficacy; long-term safety remains limited
TAP / ESPB / QLB / chest-wall planes	About 0.5-1 microgram/kg common in trials	Delayed rescue analgesia and lower opioids	Systemic absorption; bradycardia/hypotension; bilateral total dose	Technique-specific evidence; do not extrapolate one plane to another
Classic peripheral nerve blocks	About 30-60 micrograms often favorable in meta-analysis	Longer sensory block and analgesia	Higher doses increase hemodynamic adverse effects	Useful contextual evidence, not a direct fascial-plane dosing rule

7. Safety, Tolerability, and Regulatory Considerations

7.1. Hemodynamic Effects: Bradycardia and Hypotension

Bradycardia and hypotension are the most consistent clinically relevant adverse effects of dexmedetomidine and are pharmacologically expected consequences of sympatholysis. The risk may be amplified by neuraxial sympathectomy, hypovolemia, beta-blockade or other negative chronotropic therapy, advanced age, conduction-system disease, and concomitant anesthetic agents. In the 2014 neuraxial meta-analysis by Wu et al., dexmedetomidine increased the odds of bradycardia while improving analgesia (9). Brachial plexus and femoral-block meta-analyses also identify bradycardia or hypotension as dose-sensitive trade-offs (6,31,35). Individual fascial-plane trials occasionally report transient bradycardia even when serious events are absent (25,28). These findings support close perioperative hemodynamic monitoring during the period of expected systemic absorption, particularly after larger or bilateral truncal injections.

7.2. Sedation and Motor Block

Dexmedetomidine produces a characteristic arousable sedation and relatively little direct respiratory depression at typical clinical concentrations (1). This profile can be useful when opioid sparing is desired, but sedation remains clinically relevant because it can delay readiness for discharge, complicate neurologic assessment, or interact with opioids and other sedatives. Sedation is more consistently observed in epidural and pediatric caudal studies and with larger peripheral doses (16,17,31). Motor-block prolongation is a separate functional trade-off, particularly after neuraxial administration. The fixed 5-microgram intrathecal meta-analysis documented substantial prolongation of motor blockade (15). This may be acceptable when dense surgical anesthesia is desired but undesirable in ambulatory or enhanced-recovery pathways that prioritize early mobilization and fall-risk reduction. Fascial plane blocks are less likely to produce direct limb motor block, although spread to motor nerves or excessive systemic sedation can still impede mobilization.

7.3. Neurotoxicity and Formulation Considerations

Long-term human neurotoxicity data for intrathecal, epidural, caudal, and perineural dexmedetomidine remain limited relative to the volume of clinical use. Preclinical work provides some reassurance and has not produced a simple signal of direct neural toxicity at commonly investigated exposures, but animal safety data cannot substitute for adequately powered, long-term human follow-up. Because regional administration is off-label, formulation matters: when dexmedetomidine is deliberately administered near neural structures, clinicians should use a formulation suitable for the intended institutional protocol and avoid unnecessary exposure to preservatives or excipients not intended for neuraxial or perineural use. Institutional procedures should address preparation, labeling, asepsis, consent, and adverse-event surveillance.

7.4. Regulatory Status and Off-Label Use

The current U.S. PRECEDEX prescribing information identifies dexmedetomidine injection for intravenous use and does not list intrathecal, epidural, caudal, perineural, or perifascial administration (37). The regional routes reviewed here are therefore off-label in the United States. Off-label use is not synonymous with inappropriate use, but it places greater responsibility on clinicians and institutions to justify the indication, use an appropriate formulation, discuss uncertainty when relevant, and avoid presenting study dose ranges as regulatory dosing recommendations. Local regulations and institutional policies may differ across jurisdictions.

8. Interpreting the Evidence for Postoperative Pain Control

Across neuraxial and fascial-plane studies, three efficacy outcomes recur: duration of sensory block, time to first rescue analgesic, and total postoperative opioid consumption. Dexmedetomidine performs most consistently on the first two outcomes. Pain intensity at fixed time points is less consistent because it is affected by rescue medication, background multimodal analgesia, surgical trajectory, and the timing of block resolution. A patient who receives earlier rescue opioid can have a low pain score despite a shorter block; conversely, a patient with a long block may still report visceral or non-covered pain. Consequently, time-to-event and opioid-sparing outcomes often provide a more coherent measure of the adjuvant effect than a single numerical rating scale value.

The overall evidence also shows substantial statistical and clinical heterogeneity. Meta-analyses mix surgeries, anesthetic concentrations, block approaches, unilateral and bilateral injections, dexmedetomidine doses, and definitions of “duration.” Some trials are small and single-center, and publication bias is plausible in a field where positive block-adjuvant studies may be easier to publish than negative studies. The most defensible narrative interpretation is therefore not that dexmedetomidine universally improves every regional block, but that it prolongs regional analgesia in many studied settings while introducing predictable dose- and route-related autonomic, sedative, and motor effects.

A 2024 meta-analysis focused on cancer surgery also found lower postoperative opioid consumption and prolonged rescue timing across several nerve-block strategies, with high heterogeneity but no signal of serious adverse events in the included studies (22). This supports generalizability to major oncologic surgery, including breast and abdominal procedures, while also emphasizing that the evidence base remains a mixture of block techniques rather than a single standardized intervention.

9. Clinical Application Framework

For clinicians considering dexmedetomidine as an adjunct, a route-specific framework is preferable to a universal protocol. The first question is the clinical objective: prolonging surgical neuraxial anesthesia, extending postoperative analgesia, reducing opioids, or avoiding a catheter. The next consideration is

whether prolonged motor block or sedation would conflict with early mobilization or ambulatory discharge. Patient-specific susceptibility to bradycardia and hypotension should then be considered, and dose evidence should be drawn from the same block type whenever possible rather than imported from a different anatomical compartment. Finally, non-intravenous regional administration should be handled within explicit institutional procedures, with careful preparation, labeling, monitoring, and documentation.

This framework also clarifies when dexmedetomidine may add little. If a long-acting block is already combined with intrathecal morphine or an effective continuous catheter, the incremental benefit of another adjuvant may be small. Conversely, when prolonged opioid-sparing analgesia is a high priority and hemodynamic reserve is adequate, a carefully selected low-to-moderate dose may be considered within the limits of the available technique-specific evidence. The literature supports individualized risk-benefit assessment rather than routine automatic addition to every local-anesthetic block.

10. Knowledge Gaps and Future Research

Future research should move beyond proof-of-concept comparisons of "local anesthetic plus dexmedetomidine" versus "local anesthetic alone." Dose-finding trials are needed within specific fascial planes, with pharmacokinetic sampling to separate local from systemic effects. Trials should standardize local-anesthetic dose, block volume, ultrasound endpoint, background multimodal analgesia, and definitions of block duration and rescue analgesia. Head-to-head comparisons with intravenous dexmedetomidine and intravenous dexamethasone would help determine whether the additional complexity of off-label regional mixing is justified.

Safety research should include prospective capture of clinically important bradycardia, hypotension requiring treatment, delayed discharge, falls, neurologic symptoms, and longer-term sensory or motor deficits. Pediatric and obstetric studies require particularly careful follow-up. Registry data could complement randomized trials for uncommon neurologic outcomes that are impossible to study adequately in small single-center samples.

Finally, modern regional anesthesia trials should incorporate patient-centered outcomes such as quality of recovery, functional mobilization, sleep, opioid-related adverse events, and persistent postsurgical pain. An adjuvant that prolongs a sensory block by several hours is clinically valuable only if that extension translates into better recovery without an offsetting burden of motor impairment, sedation, or hemodynamic intervention.

11. Conclusion

Dexmedetomidine is among the most extensively studied non-opioid adjuvants for prolonging local-anesthetic regional anesthesia. Evidence is strongest for intrathecal use and classic peripheral nerve blocks, with increasingly supportive data for TAP, ESPB, QLB, pectoral/interfascial, pectoserratus, and serratus anterior plane blocks. Across these settings, the most consistent benefits are longer analgesic duration, delayed first rescue analgesia, and reduced postoperative opioid consumption. Pain-score reductions are more variable, and clinically relevant bradycardia, hypotension, sedation, and motor-block prolongation remain dose- and route-dependent trade-offs. Because neuraxial and perineural/perifascial administration is off-label and long-term neural safety data remain incomplete, dexmedetomidine should be used selectively within route-specific evidence and institutional governance. Future work should define the lowest effective dose for individual fascial planes and determine whether local administration provides clinically important advantages over systemic administration within contemporary multimodal analgesia pathways.

Acknowledgments
Not declare.

Authorship
Mehdi Hojjati and Samira Sobhani both contributed substantially to the conception and scope of the review, interpretation of the literature, drafting or critical revision of the manuscript, and approval of the final version. Both authors agree to be accountable for the work. Samira Sobhani is the corresponding author.

Conflicts of interest
The authors declared no conflict of interest.

Funding
No financial support was received.

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