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Mini-Review

Neuraxial Dexmedetomidine-Help or Hype?

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Abstract

Neuraxial dexmedetomidine, high selective alpha-2 adrenergic agonist has gained attention as adjuvant in neuraxial anesthesia. Dexmedetomidine enhances sensory and motor block quality, prolongs postoperative analgesia, and offers stable hemodynamic profiles with fewer side effects like respiratory depression or pruritus compared to opioids. It is associated with dose-dependent risks: bradycardia and hypotension. Although promising, dexmedetomidine's widespread adoption in neuraxial anesthesia is tempered by the need for robust data for long-term safety and optimal dosing.

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INTRODUCTION

Neuraxial anesthesia encompasses epidural and spinal techniques, is a critical modality for providing analgesia in surgical and obstetric settings [1]. Traditionally, local anesthetics and opioids have been utilized to achieve effective blocks [2]. Optimizing block duration and reducing side effects like hypotension, motor blockade, and respiratory depression remain clinical challenges [3]. Dexmedetomidine, a maximum selective alpha-2 adrenergic agonist, gained attention for its utility in neuraxial anesthesia. Unlike traditional agents, dexmedetomidine induces sedation, analgesia, and anxiolysis without significant respiratory depression, making it suitable for neuraxial administration [4] Dexmedetomidine enhances sensory and motor blockade quality and prolongs its duration when used in neuraxial blocks. This effect is mediated through its action on alpha-2 receptors in the spinal cord's dorsal horn inhibiting nociceptive transmission and reducing substance P release [5]. Research demonstrated if used as an adjuvant, neuraxial dexmedetomidine reduces required dose of local anesthetics while providing superior hemodynamic stability and extended postoperative analgesia [6,7]. Determining optimal dosing remains a debated subject but average recommended dose ranges from 3µg to 10µg, balancing efficacy against potential adverse effects such as bradycardia and hypotension [8,9]. Unlike opioids, dexmedetomidine has a lower incidence of pruritus and urinary retention. Despite this, widespread adoption of dexmedetomidine in neuraxial anesthesia still being explored. We need more data on long-term outcomes, neurotoxicity, and patient-specific responses. We aim to evaluate current evidence regarding the efficacy, safety, and mechanisms underlying neuraxial dexmedetomidine [10].

NEURAXIAL ANESTHESIA AND DEXMEDETOMIDINE

Neuraxial anesthesia is widely-known anesthetic practice and is being used through epidural, subarachnoid, and caudal blocks. Primary indications for these blocks are postoperative analgesia, intraoperative anesthesia, labor analgesia, and chronic pain management. Local Anesthetics (LAs) are the primary agents employed in these blocks, often enhanced with adjuvants to optimize their efficacy by reducing time of onset while enhancing block quality and prolonging analgesic duration. Among adjuvants, α2-adrenergic receptor DEX agonists have gained prominence due to their favorable pharmacological profile [11]. Dexmedetomidine bind with ratio of α1 to α2 receptors 1:1620, demonstrates superior selectivity compared to clonidine. FDA in 1999 initially approved it for short-term sedation in intensive care settings, DEX has since been extensively explored for off-label use in neuraxial blocks. Although not FDA-approved for this purpose, its use in subarachnoid and epidural spaces has shown promising results in animal and clinical studies [12].

DEX exerts analgesic effects through spinal α2 receptors, inhibiting C-fiber neurotransmission and induce postsynaptic dorsal horn neurons hyperpolarization. These mechanisms explain its ability to reduce motor and sensory block onset time, prolong sensory block duration, delay motor regression, and extend postoperative analgesia [11]. Additionally, DEX minimizes postoperative shivering and reduces the need for rescue analgesics. The effective dose range in spinal anesthesia is typically between 3 to 15 µg, with studies indicating a significant prolongation of postoperative analgesia then certain adjuvants like clonidine and fentanyl [11].

Clinical applications extend to epidural and caudal blocks. DEX has been shown to enhance intraoperative analgesia and postoperative recovery, often leading to reduced anesthetic requirements and improved maternal satisfaction during labor without adverse effects on fetal outcomes. However, as an adjuvant, DEX is associated with dose-dependent adverse effects, including hypotension or bradycardia, which are more prevalent with higher doses and in older or cardiovascular-compromised patients. Despite these risks, no long-term neurotoxic effects have been documented in human studies, and DEX has even demonstrated neuroprotective properties in experimental settings [13,14].

Wu HH, et al. [10] in their meta-analysis evaluated the safety and efficacy of neuraxial DEX as an adjuvant in regional anesthesia. In inclusion, sixteen Randomized Controlled Trials (RCTs) with 1,092 participants, aiming to determine whether DEX improves analgesia and anesthesia outcomes and this analysis found that neuraxial DEX reduced postoperative pain intensity (SMD, -1.29; 95% CI, -1.70 to -0.89; P<0.00001) and extended analgesic duration (WMD, 6.93 hours; 95% CI, 5.23 to 8.62; P<0.00001). These results suggest that DEX provides effective and prolonged pain relief when used as an adjunct to local anesthetics, which is also confirmed by Choi S, et al. [15]. DEX improved postoperative sedation scores, reduced the need for additional analgesics, and positively influenced sensory and motor block characteristics. This study concern of DEX safety and risk of bradycardia was increased (OR, 2.68; 95% CI, 1.18 to 6.10; P = 0.02) although there was no significant increase in the risk of hypotension (OR, 1.54; 95% CI, 0.83 to 2.85; P = 0.17). Increased incidence remained concern that warrants careful monitoring and further investigation.

Research reported that DEX, when used as an adjuvant in neuraxial anesthesia, significantly reduces postoperative pain intensity within the first 24 hours and prolongs analgesia duration for 7 hours. It additionally results in a faster initiation of sensory blockade while prolonging the effects of both sensory and motor blocks. During surgery, DEX influences Heart Rate (HR) and Mean Arterial Pressure (MAP) without substantially raising the likelihood of other adverse reactions like hypotension, nausea, or vomiting, except for bradycardia, which remains a crucial concern [16]. Several reviews and studies support α2-Adrenergic Receptor (α2AR) agonists use like DEX for effective postoperative pain management. Compared to clonidine, another α2AR agonist, DEX is considered to have more favorable pharmacokinetic and pharmacodynamic properties. DEX's selective affinity for spinal α2ARs is approximately 8 to 10 times higher than that of clonidine potentially contributing to its enhanced analgesic effects. Although there is no direct comparison of dose equivalence and peri-operative costs between DEX and clonidine, existing data suggest that DEX is used in lower doses (1.5 to 4 times less) than clonidine when administered epidurally. The analgesic effects of DEX are primarily mediated through α2AR, which helps minimize cardio-respiratory adverse events often associated with α1AR activation. Studies have also shown that neuraxial DEX is associated with a reduced requirement for inhalation anesthetics and lower Bispectral Index (BIS) values, indicating a synergistic effect with Local Anesthetics (LAs) that enhances overall anesthesia and reduces anesthetic consumption [10,17,18].

Rivadeneira KV, et al. [4] suggested unlike opioids, dexmedetomidine has a rapid onset (approximately 5 minutes) and a relatively short duration of action (about 2 hours), which can be advantageous in tailoring analgesia and minimizing side effects. Its role in neuraxial anesthesia in spinal and epidural techniques is under evaluation for improving pain management while avoiding the adverse effects associated with opioids such as pruritus, respiratory depression, and nausea. Current papers demonstrate dexmedetomidine provides adequate analgesia and sedation without the common opioid-related side effects [19], as it works by activating alpha-2 adrenergic receptors, which modulate neurotransmitters release in pain perception while enhancing analgesia, reducing rescue medications necessity. This mechanism is beneficial in obstetric and orthopedic settings where traditional opioids cause pruritus in most of the cases, which compromises patient comfort his satisfaction. Dexmedetomidine's use in neuraxial anesthesia is not without challenges. The risk of bradycardia and hypotension are also discussed in this evidence which requires careful patient monitoring and limited duration of action compared to long-acting opioids necessitates more frequent dosing or adjunctive strategies for prolonged procedures [4].

The study by Alselaiti AA, et al. [20] investigated efficacy of combining caudal morphine with dexmedetomidine for postoperative pain management in children undergoing scoliosis correction. Alselaiti et al included seven pediatric patients who received a caudal epidural injection of morphine (50mcg/kg) and dexmedetomidine (4mcg) along with normal saline (0.5ml/kg). Pain-free durations ranged was 2 to 48 hours with one patient experiencing a delay of only 2 hours before needing rescue analgesia. Reported adverse events were minimal with only one case of postoperative nausea and vomiting reported and there was respiratory distress, pruritus, or shivering among patients. Its primary outcome was duration of effective analgesia which was notably prolonged compared to historical controls. The use of dexmedetomidine, an α2-adrenergic agonist known for its sedative and analgesic properties helped extend the period before additional pain relief was required. Enalgesia duration extension is consistent with findings from Wang, et al. who reported that dexmedetomidine prolonged postoperative analgesia and reduced intraoperative sevoflurane levels. It was confirmed that dexmedetomidine's administered dose did not interfere with neurophysiological monitoring during surgery and combination of caudal morphine and dexmedetomidine showed high efficacy in managing postoperative pain for scoliosis surgery. It resulted prolonged analgesia with minimal adverse effects which concluded combination can be a valuable component of multimodal analgesia strategies in similar surgical settings.

A previous case of 73-year-old male with severe bradycardia and asystole during Transurethral Lithotomy (TUL) under spinal

anesthesia with dexmedetomidine was added for sedation and the procedure began with spinal anesthesia using 3.4mL of 0.5% hyperbaric bupivacaine. Dexmedetomidine was administered at a loading dose of 3μg/kg over 10 minutes followed by a continuous infusion at 0.4μg/kg/h. Patient's vital signs initially remained stable a drop in SpO2 to 93% led to a reduction in dexmedetomidine dosage and the initiation of oxygen supplementation. Shortly after that, patient's heart rate decreased to 30bpm during ureteral stent placement and eventually leading to a 32-second period of asystole. Dexmedetomidine infusion immediately stopped and 0.5mg of atropine was given which restored his heart rhythm and consciousness and he experienced no further complications and was discharged the next day. The authors attributed the asystole to dexmedetomidine's effects spinal anesthesia, and a possible vagal reflex, stressing need of vigilant ECG and hemodynamic monitoring during similar procedures.

Smith J, et al. [21] evaluated impact of two different doses of intrathecal dexmedetomidine and fentanyl as adjuvants to hyperbaric bupivacaine in spinal anesthesia. In inclusion, about 100 patients scheduled for elective surgeries of the lower abdomen or lower limbs were randomly assigned to four groups; Group I received hyperbaric bupivacaine alone, Group II received bupivacaine with 3μg dexmedetomidine, Group III bupivacaine with 5μg dexmedetomidine, and Group IV was given with bupivacaine with 25μg fentanyl. Results showed adding dexmedetomidine or fentanyl notably extended the duration of both sensory and motor block compared to bupivacaine alone which is also confirmed by Sun Y, et al. [22]. Group I exhibited a shorter interval before the first request for postoperative analgesia and reported higher postoperative pain scores. Interestingly, only Group II exhibited a rise in blood glucose levels. Intraoperative hemodynamic parameters, heart rate and mean arterial pressure were consistent across all groups. Both dexmedetomidine and fentanyl enhanced block duration, maintained stable hemodynamics, minimized blood glucose effects, and improved postoperative analgesia compared to bupivacaine alone, with dexmedetomidine offering superior analgesic effects and a longer duration of sensory and motor block relative to fentanyl [23,24]. It reduces opioid-related side effects and enhances hemodynamic stability while fentanyl, an opioid, provides rapid analgesic onset but may lead to increased side effects like nausea and respiratory depression. Dexmedetomidine is more preferred for its prolonged analgesic effect and minimal opioid-related complications and is more advantageous in longer procedures or for patients at risk of opioid adverse effects. Fentanyl is effective but is chosen for shorter procedures due to its quicker onset but requires careful monitoring for opioid-related side effects.

CONCLUSION

Neuraxial dexmedetomidine valuable in enhancing anesthetic quality and duration while maintaining hemodynamic stability. Its unique pharmacological profile makes it a strong candidate for neuraxial anesthesia, predominantly in patients where minimizing respiratory depression and motor blockade is crucial. Its benefits must be weighed against the potential for dose-dependent adverse effects such as bradycardia and hypotension. The evidence supports its efficacy. We conclude neuraxial dexmedetomidine, when used as an adjuvant in spinal anesthesia, prolongs both sensory and motor block durations while enhancing postoperative analgesia with a lower incidence of respiratory depression compared to other adjuvants like opioids. We recommend further trials that confirm long-term safety, optimize dosing, and better understand patient-specific responses. Therefore, while dexmedetomidine is promising, cautious application is recommended.

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