Intraoperative Administration of Dexmedetomidine and Dexamethasone in Local Anesthetic Infiltration to Improve Postoperative Pain Control After Posterior Cervical Fusion

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Abstract
Dexmedetomidine, a selective and potent α2-adrenoceptor agonist, is used for its anxiolytic, sedative, and analgesic properties. Dexamethasone is a high-potency, long-acting glucocorticoid that has been shown to provide analgesic and anti-inflammatory effects. At present, little has been published with regard to the effectiveness of these drugs as dual agents with local anesthetics for analgesia. In this report, a case of a 50-year-old man who underwent a cervical spine orthopedic procedure is described, in which an intraoperative injection of ropivacaine was administered with the adjuvants dexmedetomidine and dexamethasone, providing extended postoperative pain relief. In summary, we present a patient who had an injection of ropivacaine with dexmedetomidine and dexamethasone into the erector spinae muscles in the cervical region, which provided improvement in postoperative pain and reduced opioid consumption for five days post-surgery, demonstrating additive and/or synergistic effects beyond the normal local anesthetic duration.

Introduction
Dexmedetomidine, a selective and potent α2-adrenoceptor agonist, is clinically used for its anxiolytic, sedative, and analgesic properties [1]. Compared to clonidine, another α2-agonist that has been in use for decades, it has greater selectivity for the α2-receptors and, as such, is a more potent sedative than clonidine. Dexmedetomidine has other features that make it an attractive alternative sedative choice as well, including minimal influence on respiration, and when administered, patients remain easily arousable. The main adverse effects of dexmedetomidine are alterations in hemodynamic status, which can include hypertension, bradycardia, and hypotension via pre- and postsynaptic α2-receptor activation. This can lead to vasoconstriction, vasodilatation, and reflex bradycardia [2]. Originally, it was approved for intravenous (IV) administration for sedation of patients who were mechanically ventilated in the intensive care unit. It could be administered for up to 24 hours. In 2008, indications of dexmedetomidine were expanded for the sedation of non-intubated patients periprocedurally [2]. In addition, dexmedetomidine has been used in regional anesthesia as an adjunct to local anesthetics to prolong the density and duration of peripheral nerve blocks [3,4].

Dexamethasone is a high-potency, long-acting glucocorticoid, which has been demonstrated to provide analgesic and anti-inflammatory effects [5]. Its analgesic mechanism of action is not completely understood, but it may arise from decreased nociceptive C-fiber activity from a direct effect on the glucocorticoid receptor [6]. Vasoconstrictive effects leading to reduced local anesthetic vascular uptake [7], and/or delivering systemic anti-inflammatory effects [8]. Dexamethasone has many clinical uses, including its use in interventional pain procedures to reduce swelling and/or inflammation of nerves as well as being an adjunct to local anesthetics for peripheral nerve blocks [3-5,9].

In this report, we present a case of a 50-year-old man who underwent a posterior cervical fusion with intraoperative wound infiltration using 20 mL of 0.2% ropivacaine plus 25 mcg dexmedetomidine and 5 mg preservative-free dexamethasone for improved postoperative analgesia.

Case Presentation
A 50-year-old Caucasian male with a history of hypertension, diabetes mellitus type II, previous hemorrhagic stroke, and cervical spondylitis with concomitant stenosis complicated by myelopathy was admitted for surgery. The patient presented for a laminectomy and fusion at cervical levels C5 through C7. Prior to the procedure, anesthesia and surgical informed consents were obtained from the patient by the...
their efficacy together has not been thoroughly researched. As shown in our case, the use of both agents Dex-Dex has been shown to be effective adjuncts to local anesthetics in peripheral nerve blocks. However, intraoperative infiltrate is warranted. Continued research into dexmedetomidine with dexamethasone as an adjunct as well. A study by Schnepper et al. showed that increased block duration was associated with receiving any dose of perineural dexamethasone (p < 0.01) [12]. Multiple studies have also shown that perineural dexamethasone is superior to systemic administration for prolonged analgesia [9,13]. Postoperative pain control is an issue with orthopedic surgery, including spine surgery [14,15]. Multimodal analgesia has been the preferred choice over opioids in recent years, including regional anesthesia with peripheral nerve blocks. This case shows how an intraoperative wound infiltration with Dex-Dex can help with postoperative pain.

The use of both dexamethasone and dexmedetomidine together has been theorized to prolong the duration of local anesthetics and provide longer analgesia, as seen in our described patient [16]. The actual mechanism by which the drugs interact to produce this effect is not known but may arise from multiple factors. For example, vasoconstriction caused by both dexamethasone and dexmedetomidine maintains the concentration of local anesthetic around the targeted nerve and inhibits the nociceptive signal transmission by myelinated C fibers [16]. Dexmedetomidine may also inhibit hyperpolarization-activated cation current, stimulate the release of enkephalin-like substances at peripheral sites, and block the signals through C and Aδ fibers [16]. Due to the various and different ways the two agents can prolong the duration of action of local anesthetics and analgesia, a synergistic effect can arise from an additive effect from these actions.

The efficacy of either agent as adjuncts in peripheral nerve blocks has been compared [17]. Longer sensorimotor block and analgesia were demonstrated by dexamethasone.

As for their potential synergistic effect, Zhang et al. found that the addition of combined perineural dexmedetomidine and dexamethasone to ropivacaine for intercostal nerve blocks provided prolonged analgesia for patients undergoing thoracoscopic pneumonectomies [16]. Additionally, the study monitored for potential side effects from the two-drug combination, including hypotension, hypoxemia, respiratory depression, vomiting, nausea, pruritus, and dizziness [16]. No significant differences were observed in the incidences of side effects among the four study groups (intercostal nerve block with ropivacaine only, ropivacaine and dexamethasone, ropivacaine and dexmedetomidine, and ropivacaine/dexamethasone/dexmedetomidine) [16]. Recently, some authors demonstrated that the Dex-Dex combination could provide several days of postoperative pain relief from perineural administration [18-20]. Continued research into dexmedetomidine with dexamethasone as an intraoperative infiltrate is warranted.

**Conclusions**

Dex-Dex has been shown to be effective adjuncts to local anesthetics in peripheral nerve blocks. However, their efficacy together has not been thoroughly researched. As shown in our case, the use of both agents...
together as an intraoperative injection improved postoperative pain control and reduced opioid consumption in a patient undergoing cervical spine surgery. These findings point towards a possible additive and/or synergistic effect, which can potentially help improve postoperative pain control for spine surgery patients and potentially increase the efficacy of other peripheral nerve blocks. Further studies are needed to confirm the potential benefits of the combination of Dex-Dex extending the analgesic duration when combined with local anesthetics.

**Additional Information**

**Disclosures**

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**References**

1. Belleville JP, Ward DS, Bloor RC, Maze M: Effects of intravenous dexmedetomidine in humans. I. Sedation, ventilation, and metabolic rate. Anesthesiology. 1992, 77:1125-33. 10.1097/00000542-199212000-00015
2. Weerink MAS, Struys MMFM, Hannivoort LN, Barends CRM, Absalom AR, Colin P: Clinical pharmacokinetics and pharmacodynamics of dexmedetomidine. Clin Pharmacokinet. 2017, 56:895-91. 10.1007/s40262-017-0507-7
3. Brummell CM, Williams BA: Additives to local anesthetics for peripheral nerve blockade. Int Anesthesiol Clin. 2011, 49:104-16. 10.1097/IAN.0b013e328358aa49
4. Emeline PJ, Eng NR, Menard BL, Myers AS, Cornett EM, Urman RD, Kaye AD: Adjunct medications for peripheral and neuraxial anesthesia. Best Pract Res Clin Anaesthesiol. 2018, 32:83-99. 10.1016/j.bpa.2018.06.011
5. Albrecht E, Kern C, Kirkham KR: A systematic review and meta-analysis of perineural dexamethasone for peripheral nerve blocks. Anesthesia. 2015, 70:71-83. 10.1111/ane.12823
6. Johansson A, Hao J, Sjöland B: Local corticosteroid application blocks transmission in normal nociceptive C-fibres. Acta Anaesthesiol Scand. 1990, 34:535-8. 10.1111/j.1399-6566.1990.tb03097.x
7. Marks R, Barlow JW, Funder JW: Anti-inflammatory actions of glucocorticoids: molecular mechanisms. Clin Sci (Lond). 1998, 94:557-72. 10.1042/cs980557
8. Chong MA, Berbenets NM, Lin C, Singh S: Perineural versus intravenous dexamethasone as an adjuvant for peripheral nerve blocks: a systematic review and meta-analysis. Reg Anesth Pain Med. 2017, 42:519-26. 10.1097/AAP.0000000000000571
9. Obayah GM, Refaie A, Aboushanab O, Ibraheem N, Abdelazeem M: Addition of dexmedetomidine to bupivacaine for greater palatine nerve block prolongs postoperative analgesia after cleft palate repair. Eur J Anaesthesiol. 2010, 27:280-4. 10.1016/j.eja.2009.05.003
10. Abdallah FW, Abirshami A, Brull R: The facilitatory effects of intravenous dexmedetomidine on the duration of spinal anesthesia: a systematic review and meta-analysis. Anesth Analg. 2011, 113:271-8. 10.1213/ANE.0b013e318209b1c5
11. Schnepper GD, Kightlinger BI, Jiang Y, Wolf BJ, Bolin ED, Wilson SH: A retrospective study evaluating the effect of low doses of perineural dexamethasone on ropivacaine brachial plexus peripheral nerve block analgesic duration. Pain Med. 2018, 19:1485-95. 10.1093/pm/pxy205
12. Adhikary LN, Kundu AK, Mitra K, Mitra P, Das SK: A retrospective study to evaluate the efficacy of dexamethasone as a nerve block adjuvant in patients undergoing lumbar laminectomy. J Clin Anesth. 2017, 119:183-91. 10.1016/j.jclinane.2017.07.003
13. Jones J Jr, Sahtoryah F, Catalani B: The importance of optimizing acute pain in the orthopedic trauma patients. Orthop Clin North Am. 2017, 48:445-6. 10.1016/j.ocl.2017.06.003
14. Young JS, Ahn J, Buvanendran A, Singh K: Multimodal analgesia in pain management after spine surgery. J Spine Surg. 2019, 5:5154-9. 10.21037/jss.2019.05.04
15. Zhang P, Liu S, Zhu J, Yao Z, Liu C: Dexamethasone and dexmedetomidine as adjuvants to local anesthetic mixture in intercostal nerve block for thoracoscopic pneumonectomy: a prospective randomized study [Online ahead of print]. Reg Anesth Pain Med. 2019, 10.1136/rapm-2018-100221
16. Albrecht E, Vorobievich L, Jacot-Guillarmod A, Fournier N, Abdallah FW: Dexamethasone is superior to dexmedetomidine as a perineural adjunct for supraclavicular brachial plexus block: systematic review and indirect meta-analysis. Anesth Analg. 2019, 128:545-54. 10.1213/ANE.0000000000004386
17. Herman J, Urits I, Urman RD, Kaye AD, Viswanath O, Eskander JP: Synergistic effect of perineural dexamethasone and dexmedetomidine (Dex-Dex) extending the analgesic duration of a supraclavicular block. J Clin Anesth. 2020, 65:109750. 10.1016/j.jclinane.2020.109750
18. Schwartz BH, Urits I, Viswanath O, Urman RD, Kaye AD, Eskander JP: Successful combination of thoracodorsal interfascial plane block and erector spinae plane block for peri-operative pain control after lumbar laminectomy. J Clin Anesth. 2020, 62:109705. 10.1016/j.jclinane.2020.109705
19. Herman J, Urits I, Urman RD, Kaye AD, Viswanath O, Eskander JP: Combination of perineural dexamethasone and dexmedetomidine prolong analgesic duration of a supraclavicular block in a patient with complex regional pain syndrome. J Clin Anesth. 2020, 65:109873. 10.1016/j.jclinane.2020.109873

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