REVIEW ARTICLE

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A Comprehensive Review and Update of the Use of Dexmedetomidine for Regional Blocks

By Ivan Urits, Celina Guadalupe Virgen, Hamed Alattar, Jai Won Jung, Amnon A. Berger, Hisham Kassem, Islam Mohammad Shehata, Amir Elhassan, Alan D. Kaye, Omar Viswanath

ABSTRACT ~ ***Purpose of Review****: This evidence-based systematic review will focus on the use of dexmedetomidine and its role as adjuvant anesthetics in regional blocks to help better guide physicians in their practice. This review will cover background and mechanism of dexmedetomidine as well as the use in various regional blocks.* ***Recent Findings:*** *Local anesthetics are preferred for nerve blocks over opioids; however, both due come with its own side effects. Local anesthetics may be toxic as they disrupt cell membrane and proteins, but by using adjuvants such as dexmedetomidine, that can prolong sensory and motor blocks can reduce total amount of local anesthetics needed. Dexmedetomidine is an alpha-2-adrenergic agonist used as additive for regional nerve block. It has a relatively low side effect profile and have been researched in various regional blocks (intrathecal, paravertebral, axillary, infraclavicular brachial plexus, interscalene). Dexmedetomidine shows promising results as adjuvant anesthetics in most regional blocks.* ***Summary:*** *Many studies have been done and many show promising results for the use of dexmedetomidine in regional blocks. It may significantly increase in duration of sensory and motor blocks that correlates with lower pain scores and less need of morphine in various regional blocks.* Psychopharmacology Bulletin. *2020;50(4, suppl. 1):121–141.*

Urits, MD, Department of Anesthesiology, Louisiana State University School of Medicine, Shreveport, LA; Beth Israel Deaconess Medical Center, Department of Anesthesiology, Critical Care and Pain Medicine, Harvard Medical School, Boston, MA. Berger, MD, PhD, Beth Israel Deaconess Medical Center, Department of Anesthesiology, Critical Care, and Pain Medicine, Harvard Medical School, Boston, MA. Kaye, MD, PhD, Departments of Anesthesiology and Pharmacology, Toxicology and Neurosciences, Louisiana State University School of Medicine, Shreveport, LA. Virgen, BS, Alattar, BS, University of Arizona College of Medicine-Phoenix, Department of Anesthesiology, Phoenix, AZ. Jung, BS, Georgetown University School of Medicine, MedStar Georgetown University Hospital, Washington, DC. Kassem, MD, Mount Sinai Medical Center, Department of Anesthesiology, Miami Beach, FL. Shehata, MD, Ain Shams University, Department of Anesthesiology, Cairo, Egypt. Elhassan, MD, Desert Regional Medical Center, Department of Anesthesiology, Palm Springs, CA. Viswanath, MD, Department of Anesthesiology, Louisiana State University School of Medicine, Shreveport, LA; Valley Pain Consultants – Envision Physician Services, Phoenix, AZ; University of Arizona College of Medicine-Phoenix, Department of Anesthesiology, Phoenix, AZ; Creighton University School of Medicine, Department of Anesthesiology, Omaha, NE Department of Anesthesiology, Louisiana State University School of Medicine, Shreveport, LA; Valley Pain Consultants – Envision Physician Services, Phoenix, AZ; University of Arizona College of Medicine-Phoenix, Department of Anesthesiology, Phoenix, AZ; Creighton University School of Medicine, Department of Anesthesiology, Omaha, NE.

To whom correspondence should be addressed: Ivan Urits, MD, Beth Israel Deaconess Medical Center Department of Anesthesia, Critical Care, and Pain Medicine, Boston, MA, 02215. Phone: (732)-501-7220; E-mail: ivanurits@gmail.com

Introduction

Local anesthetics are a preferred method for nerve blocks over opioids. There is less concern for adverse effects and dependence caused by opiates. Many of the commonly used local anesthetics such as ropivacaine have a greater safety profile than opiates that can minimize the pain experienced by patients.[1] However, the use of local anesthetics produces its own toxic effects on neurons as they disrupt cell membranes and proteins.[2] Several studies have shown neurotoxicity can be reduced with adjuvants as they cause a slowed absorption of anesthetics.[3] Additionally, adjuvants can assist in prolonging sensory and motor block duration with a rapid onset that can reduce the total amount of local anesthetic needed.[1] This can produce protective effects on the neurons while providing superior analgesia. Adjuvants such as dexmedetomidine and clonidine have demonstrated to have longer analgesic effects postoperatively for nerve blockade.[4] The administration of alpha-2-adrenergic agonist as adjuvants is useful in ambulatory procedures blocking the release of catecholamines. This reduction leads to a decrease pain signaling making it a less painful experience for the patient.[5] Dexmedetomidine is an alpha-2-adrenergic agonist used as an additive for regional nerve block. It has shown to significantly reduce onset time with longer duration of action compared to local anesthetics alone while having better postoperative analgesia.[6,7] When determining the type of adjuvant used in conjunction with local anesthetics, the route of administration and location is a decisive factor for the specific nerves being targeted. Dexmedetomidine is an effective additive for nerve blockade in multiple locations and it may inclusively decrease the risk of nerve injury elicited by administration of local anesthetics.

Dexmedetomidine Mechanism of Action as an Adjuvant to Local Anesthesia in Regional Blocks

The use of adjuvants combined with local anesthetics are meant to prolong analgesia while lessening the dose needed for anesthetic effect. Dexmedetomidine is commonly used as an adjuvant in various surgical procedures. Dexmedetomidine is an alpha-2 adrenergic agonist functioning similar to clonidine and has been studied for its anti-inflammatory effects. Expression of inflammatory cytokines can facilitate sensitivity to pain and injury to the nerves which is of concern for patients in recovery.[8] However, utilization of dexmedetomidine has shown to significantly weaken the transcription of NF-κB and iNOS leading to a decrease in response from TNF-α, IL-1β and IL-6 resulting in controlled neuropathic pain.[8] Its addition prolongs the effect

of decreased sensation to pain through motor and sensory blockade.[9] In a study examining the sciatic nerve in rats with administration of dexmedetomidine, it demonstrated to lower compound muscle action potential further adding to its effect on prolonging motor block. These injections did not produce toxic effects on the nerves tested.[10] The results of prolonged analgesia may even double in some cases with dexmedetomidine as an adjuvant as it targets hyperpolarized cation channels. Reversal of the blockade produces no response using an alpha-2 adrenergic antagonist, instead a hyperpolarized activated cation channel enhancer is used for its reversal.[11] When used in combination with local anesthetics such as ropivacaine and bupivacaine it has shown significant differences in its effects. One study specifically compared ropivacaine alone and in combination with dexmedetomidine and found a significant anti-inflammatory effect when combined.[12] A separate study examined its use with bupivacaine and mast cell degranulation. Mast cells are essential in creating an inflammatory immune response that damages the nerve.[13] Results showed that the group with dexmedetomidine with bupivacaine had no mast cells degranulation with less edema on the nerve. The group with bupivacaine alone developed nerve injury and higher mast cell expression. In this case the authors concluded a beneficial use of dexmedetomidine serving as a protective adjuvant to regional anesthesia.[13]

Preclinical Studies Assessing Neurotoxicity of Dexmedetomidine Used in Regional Anesthesia

Studies have examined the effect of dexmedetomidine as an adjuvant and its effectiveness, however patient safety is important for making treatment management decisions. It is essential to use a treatment option knowing the possible benefits and adverse effects it can produce. A study from Wang, H. et al. in which 30 rabbits that were injected for a femoral nerve block with dexmedetomidine and ropivacaine demonstrated no pathological changes in nerves with low doses of 1–2 μg/mL. When injected with higher doses, myelin sheath fibers became loose and presented as demyelination.[14] A separate study investigated injecting dexmedetomidine and ropivacaine compared to ropivacaine alone in the sciatic nerve of diabetic rats. Results showed that non-diabetic rats had no neurotoxic effects.[15] Those that were diabetic had damage to the nerves with ropivacaine alone. Addition of dexmedetomidine further exacerbated nerve damage by decreasing axon density and diameter including the demyelination and removal of axons. The authors concluded that ropivacaine caused the nerve damage and not dexmedetomidine, but its use as an adjuvant enhanced the injury in

diabetic rats.[15] Another study utilizing rats as well for sciatic nerve blockade with ropivacaine and dexmedetomidine found that the combination enhanced duration of blockage but did not produce nerve damage. Concluding that dexmedetomidine's anti-inflammatory effects was protective against the possible damage produced by local anesthetics.[16] Bupivacaine is another commonly used local anesthetic for sensory and motor nerve block. In a study by Elham, M. et al. the sciatic nerves of rats were administered bupivacaine as a control comparing it to bupivacaine with dexmedetomidine. The combination of bupivacaine and dexmedetomidine resulted in less inflammation but had nerve injury although less than that of bupivacaine alone. Nerves had less loss of myelination and degeneration reducing the neurotoxic effect of bupivacaine.[17] The experimental studies agree upon the reduction of nerve injury when local anesthetics are administered with dexmedetomidine as the adjuvant. Although, based on one of the studies, its use in diabetics may not produce the same protective outcome. The results support its use as a beneficial adjuvant for nerve blocks.

Neuraxial

Intrathecal

Several studies have examined the efficacy of intrathecal administration of local anesthetics for spinal anesthesia or pain management. The anesthetic is typically administered into the subarachnoid space. Injecting medication into this location creates the possibly of neurological side effects. Two randomized control trials and a systematic review with meta-analysis all demonstrated that local anesthetics given with adjuvant of dexmedetomidine did not produce significant neurological effects.[18–20] Addition of dexmedetomidine allows for less need of postoperative opioid use while maintaining effective motor and sensory blockade. In a study by Safari et al. dexmedetomidine was used as an adjuvant for spinal blocks in comparison with fentanyl. The dexmedetomidine group had a more rapid onset of sensory and motor block as well as prolonged duration than fentanyl and a control group.[18] Participants reported lower pain scores and less need of postoperative morphine before 12 hours but reported no significant difference after 12 hour.[18] Xia et al. described similar findings with intrathecal administration of bupivacaine with dexmedetomidine for cesarean section. The study found an increase in duration of sensory and motor block in spinal anesthesia. The authors additionally used a lower dose of dexmedetomidine of 5 mcg and reported less incidents of hypotension that may be caused by the anesthetics.[19] Five other studies from a systematic review

with meta-analysis found a 72% increase in duration of sensory and motor block when compared to a local anesthetic alone.[20] These studies also indicated a longer time between its use and need for additional analgesia. However, the authors described no significant difference in onset of motor blockade.[20] While Xia et al. indicated less incidence of hypotension Abdallah et al. found no difference between the dexmedetomidine group compared to controls.[20] Overall, studies agree that dexmedetomidine provides a significant prolongation of sensory and motor block when given intrathecally. Based on the studies, further evaluation on onset of motor block is necessary for procedures benefiting from intrathecal administration of anesthetics (Table 1).

Paravertebral

Paravertebral blocks are a convenient form of regional anesthesia that targets the space between the spinal nerves and creates a unilateral blockade. It is a commonly used in thoracic surgery given its effectiveness in pain control using local anesthetics. In a study by Hong et al. examining the effectiveness of paravertebral blocks using dexmedetomidine combined with ropivacaine compared to a ropivacaine only found it to be significantly more effective in reducing postoperative pain.[21] Patients on dexmedetomidine required less fentanyl after 24 hours and recorded to have lower numerical rating scales (NRS) pain scores. However, the authors note there was no significant difference in length of stay or rescue analgesia.[21] The use of paravertebral blocks with dexmedetomidine as an adjuvant show promise in its effectiveness for pain control in regional anesthesia.

Brachial Plexus

Axillary

The axillary approach to brachial plexus blocks is commonly used in upper extremity orthopedic surgeries. Over the last ten years, numerous clinical trials have examined the efficacy of using dexmedetomidine as an adjuvant to perineural anesthetics in axillary brachial plexus blocks (ABPB). These trials provide a foundation for characterizing the change in onset and duration of sensory and motor block, duration of analgesia, and patient hemodynamics when using dexmedetomidine as an adjuvant in ABPBs.

Consistently, data show that dexmedetomidine increases the duration of motor and sensory block when used as an adjuvant in ABPBs. Recently, Koraki et al. observed an increase in duration of sensory block,

TABLE 1

Intrathecal

AUTHOR (YEAR)	GROUPS STUDIED AND INTERVENTION	RESULTS AND FINDINGS	CONCLUSIONS
Safari, 2016[18]	A triple blinded randomized clinical trial with three groups of 28 patients each age 18–60 undergoing abdominal or lower extremity. First group was given 5 μg of dexmedetomidine, 12.5 mg of 0.5% hyperbaric bupivacaine and 0.5 mL normal saline. Second group received 25 μg of fentanyl with 12.5 mg of 0.5% hyperbaric bupivacaine. The control group received only 12.5 mg of 0.5% hyperbaric bupivacaine along with 0.5 mL normal saline.	The dexmedetomidine group sensory block onset was lower compared with other two groups and produced longer block duration for both sensory (P = 0.043, P = 0.016) and motor (P = 0.014). Lower pain scores postoperatively were recorded.	Dexmedetomidine showed to be significantly more effective for sensory and motor blockade onset and duration compared to combined fentanyl and bupivacaine.
Xia, 2018[19]	A prospective double-blinded randomized control trial on 90 patients having elective cesarian section. The first group received 5 μg dexmedetomidine with 0.75% hyperbaric bupivacaine. The control group received 0.75% bupivacaine with normal saline.	Results showed there was no difference between both groups for the time of onset for motor block ($P > 0.05$). Significant difference was found for duration of sensory blockade ($P < 0.05$) in the dexmedetomidine group.	The use of dexmedetomidine prolonged sensory block requiring less postoperative analgesia with no significant side effects compared to bupivacaine alone.
Abdallah, 2013[20]	A systematic review and meta-analysis were conducted to examine randomized control trials comparing dexmedetomidine adjuvant compared to local anesthetics alone.	Most studies compared dexmedetomidine to ropivacaine, bupivacaine and levobupivacaine. Results indicated dexmedetomidine prolonged the duration of sensory and motor block ($P = 0.00001$, $P = 0.04$) with rapid onset. The time to request from next analgesic was delayed with its use.	Addition of dexmedetomidine significantly prolonged duration of sensory and motor block compared to local anesthetics alone.

motor block, and analgesia in the 1 μg/kg dexmedetomidine group as compared to the ropivacaine only control.[22] The study also noted a decrease in onset of sensory block but no significant decrease in onset motor block. These findings are comparable to two previous studies examining the use of dexmedetomidine as an adjuvant to ropivacaine in ABPBs.[23,24] Thakur et al. also described an increase in duration of sensory block, motor block, and analgesia with perineural administration of 1 μg/kg dexmedetomidine combined with 2% lignocaine with adrenaline.[25] The study reported a significant decrease in onset of motor block in the 1 μg/kg dexmedetomidine group as compared to normal saline.[25] Importantly, Thakur et al. noted improved effects on block quality in the 1 μg/kg dexmedetomidine group as compared to the 0.5 μg/kg group with no adverse effects, suggesting optimal adjuvant dose is near 1 μg/kg.[25] Both Koraki et al. and Thakur et al. add to the database established in previous meta-analyses reporting an overall shortening of both sensory and motor onset as well as an increased duration of sensory block, motor block, and analgesia.[26]

While the effects of dexmedetomidine on the characteristics of the blockade are important intraoperatively, the short-term analgesic effects are essential in determining clinical use. In two prior studies, dexmedetomidine extended duration of analgesia.[23,27] Several other trials examined total use of analgesics or use of rescue analgesics as primary outcomes and observed a decrease in each parameter when using dexmedetomidine as compared to the control.[28,29] Building off these trials, Koraki et al. and Thakur et al. reported an increase in duration of analgesia.[22,25] Thakur et al. also described a delay in first rescue analgesic use with 80% of patients in the 1μg/kg dexmedetomidine group requiring analgesic rescue after 6 hours, as compared to the control with 100% analgesic use within 6 hours post operation ($p < 0.005$).[25] In addition to analgesic consumption, the effects of dexmedetomidine on hemodynamic profile are necessary for patient safety. When examining the hemodynamic profiles of both magnesium sulfate and dexmedetomidine, Shahtaheri et al. reported lower heart rates and blood pressure in the dexmedetomidine group as compared to both the 100 mg magnesium sulfate and 1.5% lidocaine only groups.[30] Additional studies by Thakur et al. and Shahtaheri et al. also observed a decrease in heart rate and blood pressure.[25,31] Notably, none of these studies reported adverse effects such as bradycardia or hypotension requiring treatment in any group.[25,30,31]

Previous studies have evaluated efficacy of dexmedetomidine alongside other adjuvants such as clonidine and dexamethasone; however, none have compared the perineural adjuvant to magnesium sulfate.[24,29] In two recent publications, Shahtaheri et al. examined the hemodynamic

effects and block quality of dexmedetomidine in comparison with magnesium sulfate and 1.5% lidocaine control. Both studies reported a decrease in heart rate and blood pressure but with no associated adverse effects.[30,31] In the clinical comparison, Shahtaheri et al. noted a decrease in onset and stabilization of sensory and motor block in the magnesium sulfate group but dexmedetomidine increased duration of block and decreased opioid consumption postoperatively.[31]

Dexmedetomidine is an effective adjuvant that can be used in ABPBs and can provide better pain control and longer duration of sensorimotor block. The decision to use dexmedetomidine should always be weighed against the hemodynamic risks. Further studies are needed to compare the use of dexmedetomidine to other potential adjuvants in axillary brachial plexus blocks (Table 2).

Infraclavicular

The infraclavicular brachial plexus block is another technique where the effects of dexmedetomidine have been extensively studied during different procedures such as distal arm and forearm surgeries.[32] The effectiveness of dexmedetomidine in an infraclavicular block has been compared in many randomized control trials to other analgesics such as ketorolac, bupivacaine, buprenorphine, and dexamethasone. This section will outline the studies performed in regard to dexmedetomidine's utility in an infraclavicular brachial plexus block as well as compare its effectiveness to other anesthetic agents.

The effects of dexmedetomidine compared to ketorolac was examined in a clinical trial in three groups of 37 patients who were selected to undergo elective distal arm and forearm surgeries with an ultrasound guided brachial plexus block.[32] The patients were divided into three separate groups: a dexmedetomidine group with 30 mL of a solution with 25 mL lidocaine1.5% plus 4 mL saline and 100 μg dexmedetomidine, a ketorolac group with 30 mL of a solution made of 24 mL of lidocaine 1.5% plus 5 mL of ketorolac and a control group with 30 mL of a solution containing 25 mL of lidocaine 1.5% plus 5 mL of normal saline.[32] All three groups had 10 mL of their respective solution injected into every cord. The study found that the motor block onset was statistically less in the dexmedetomidine group when compared to the ketorolac and placebo groups ($P < 0.001$) and that the duration of the sensory block was also longer in the dexmedetomidine group as well ($P < 0.001$).[32] Overall, there were no significant differences in terms of the onset of the sensory block in the three groups ($P = 0.177$).[32] Furthermore, the time to request the first analgesic after the procedure was longer in the ketorolac group when compared to the dexmedetomidine ($P = 0.016$)

TABLE 2

Efficacy in Axillary Nerve Block

AUTHOR (YEAR)	GROUP STUDIED	INTERVENTION	RESULTS AND FINDINGS	CONCLUSION
Shahtaheri 2020	99 patients Double blind clinical trial	Placebo (33): lidocaine 1.5% in 35 mL NS Dexmedetomidine (33): Lidocaine 1.5% and dexmedetomidine 0.5 ug/kg in 35 mL NS Magnesium sulfate (33): lidocaine 1.5% with magnesium sulfate 100 mg in 35 mL NS	As compared to placebo and dexmedetomidine, magnesium sulfate lowered sensory block start time (Magnesium: 2.23 < 3.93 min, Dexmedetomidine: 1.07 < 4.90 min, Placebo: 1.16 < 6.12 min; P < 0.001) and motor block start time (Magnesium: 1.82 < 3.42 min, Dexmedetomidine: 1.39 < 4.00 min, Placebo: 1.80 < 6.06 min; P < 0.001). As compared to magnesium sulfate and placebo, the dexmedetomine group demonstrated prolonged motor block duration (Dexmedetomidine: 322.14 < 20.30 min, Magnesium: 207.00 < 19.64 min, placebo 148.22 < 22.52 min, p < 0.001), lower pain scores at 2,4,6,12, and 24 hours post op, and decreased pethidine use (Dexmedetomidine: 1.81 < 40.70 mg, Magnesium sulfate: 2.70 < 60.50 mg, and placebo 2.25 < 110.80 mg).	While magnesium sulfate improves onset properties of axillary brachial plexus block, dexmedetomidine increases motor block duration, demonstrates lower pain scores, and decrease analgesic consumption.

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TABLE 2 (*Continued*)

Efficacy in Axillary Nerve Block

AUTHOR (YEAR)	GROUP STUDIED	INTERVENTION	RESULTS AND FINDINGS	CONCLUSION
Shahtaheri 2019	99 patients Forearm ad hand surgery	Group 1 (33): Lidocaine 1.5% and dexmedetomidine 0.5 ug/kg in 35 mL NS Group 2 (33): lidocaine 1.5% with magnesium sulfate 100 mg in 35 mL NS Group 3 (33): lidocaine 1.5% in 35 mL NS	Blood pressure was lower in the dexmedetomidine group, as compared to magnesium and placebo, except in the 20–25 minute range ($p < 0.05$). At all times, patients in the dexmedetomidine group demonstrated a lower heart rate. There were no differences in oxygen saturation between groups.	Heart rate and blood pressure were lower in the dexmedetomidine group at varying times, as compared to magnesium sulfate and lidocaine only.
Koraki 2017	37 patients ASA I, II Elective forearm and hand surgery US-G A-BPB Randomly divided	Group R (18): 15 mL 0.5% ropivacaine with 1 mL NS Group RD (19): 15 mL 0.5% ropivacaine with 100 ug (1 mL) dexmedetomidine	The dexmedetomidine group demonstrated a shorter onset of sensory block (Group RD:39.63 < 46.77 seconds; Group R: 281.1 < 442.62 seconds; $p = 0.001$), no change in onset of motor block (Group RD: 147.11 < 85.1 seconds; Group R: 1130.56 < 1560.9 seconds; $p = 0.096$), increased duration of sensory block (Group RD: 723.684 < 266.94 minutes; Group R: 315.83 < 171.23 minutes; $p < 0.001$), increased duration of motor block (Group RD: 888.33 < 272.424 minutes; Group R: 581.39 < 237.275 minutes; 0.001), and increased duration of analgesia (Group	The addition of dexmedetomidine to 15 ml of 0.5% ropivacaine in an axillary brachial plexus block increases sensorimotor block duration, shortens sensory block onset, and prolongs analgesia.

			RD: 751.58 < 249.294 minutes; Group R: 349.64 < 122.983 minutes; $p < 0.001$). Adverse reactions were reported only in the dexmedetomidine group where two patients experienced bradycardia and three patients experienced hypotension.	
Thakur 2017	104 patients ASA I, II Forearm surgeries Randomized	Group L (30): 23 mL of 2% lignocaine with adrenaline + 7 mL saline Group $LD_{0.5}$ (30): 23 mL of 2% lignocaine with adrenaline + 0.5 ug/kg of dexmedetomidine diluted to 7 mL in saline Group LD1 (30): 23 mL of 2% lignocaine with adrenaline + 1 ug/kg of dexmedetomidine diluted to 7 mL in saline	Onset of sensory block was the most prompt in group L followed by group LD0.5 ($p > 0.05$) and LD1 ($p < 0.01$). Onset of motor block was earliest in group L (20.73 < 4.58 minutes) followed by group LD0.5 (22.27 < 7.04 minutes, $p > 0.05$) and group LD1 ($p < 0.01$). Duration of motor block (275.43 < 40.10 minutes, $p < 0.05$), sensory block (336.03 < 38.66 minutes, $p < 0.05$), and analgesia (395.90 < 52.89 minutes, $p < 0.05$) was longest in group LD1 as compared to group L. All patients in group L required analgesia prior to 6 hours, whereas 30% of patients in group LD0.5 and 80% of group LD1 patients required analgesia after 6 hours ($p < 0.05$).	When used as an adjuvant to 2% lignocaine in an axillary brachial plexus block, dexmedetomidine delays onset of sensory block, increases duration of sensory and motor block, and delays time until first rescue analgesia.

and the placebo groups ($P < 0.001$).[32] Overall, the study demonstrated that dexmedetomidine has better effects on the sensory and motor block duration when compared to ketorolac.

Using dexmedetomidine as an adjuvant to established anesthetic treatments has been explored as well. A randomized control study explored the effectiveness of bupivacaine alone compared with dexmedetomidine and bupivacaine in an infraclavicular brachial plexus block.[33] The study divided 60 patients into 2 groups with one group receiving 30 mL of 0.33% bupivacaine and the second group receiving 30 mL of 0.33% bupivacaine along with 0.75 μg/kg of dexmedetomidine.[33] The group with combined dexmedetomidine and bupivacaine block had a statistically significant faster time to onset of the sensory block of 13.2 minutes when compared to the 19.4 minutes of the bupivacaine block alone ($P = 0.003$).[33] Furthermore, the dexmedetomidine group showed a longer duration of sensory block ($P = 0.002$) and a longer motor block duration ($P = 0.002$) as well as lower morphine requirements up to 48 hours after the surgery.[33] The study revealed the effectiveness of dexmedetomidine when mixed with local anesthetics for an infraclavicular brachial plexus block.

Lastly, when looking at other agents in comparison with dexmedetomidine for infraclavicular brachial plexus blocks, other randomized control trials have demonstrated that dexmedetomidine is more effective than buprenorphine in terms of the duration of the sensory and motor blocks.[34] Furthermore, some clinical trials have shown that dexmedetomidine added to lidocaine in an infraclavicular block in patients receiving forearm fracture surgery provided a longer sensory block duration than dexamethasone, yet there was no significant difference in postoperative pain when comparing the two groups.[35] Other studies comparing dexamethasone with dexmedetomidine have demonstrated that 5 mg of dexamethasone has a longer sensorimotor block and duration when compared to 100 μg dexmedetomidine (Table 3).[36]

Interscalene

The effect of dexmedetomidine in an interscalene brachial plexus block has been explored as well. One study has compared the effects of IV versus perineural dexmedetomidine in an interscalene brachial plexus block.[37] A randomized clinical trial compared 999 patients who were randomized to either a group receiving 15 mL ropivacaine, 0.5% with 0.5 μg/kg dexmedetomidine administered perineurally, a group receiving 15 mL ropivacaine, 0.5% with 0.5 μg/kg dexmedetomidine administered via an IV, or a control group receiving 15 mL ropivacaine, 0.5%.[37] The patients received a single injection of an interscalene

TABLE 3

Characteristics of Dexmedetomidine used in an Infraclavicular Brachial Plexus Block

DEXMEDETOMIDINE VS. INJECTATE TYPE	ARTICLE	GROUPS STUDIED AND INTERVENTION	RESULTS AND FINDINGS	CONCLUSIONS
Keterolac	Mirkhesti 2014	Clinical trial study of 3 groups of 37 patients undergoing an ultrasound guided brachial plexus block for an elective distal arm and forearm surgery divided into a dexmedetomidine group, a ketorolac group, and a control group	There were no significant differences in terms of the onset of the sensory block in the three groups ($P = 0.177$). The motor block onset was statistically less in the dexmedetomidine group when compared to the ketorolac and placebo groups ($P < 0.001$) and that the duration of the sensory block was also longer the dexmedetomidine group as well ($P < 0.001$)	When compared with ketorolac, dexmedetomidine is more effective at sensory and motor block duration in an infraclavicular brachial plexus block
Bupivacaine	Amany 2012	A randomized control study with 60 patients divided into 2 groups: one group received 30 mL of 0.33% bupivacaine and the second group received 30 mL of 0.33% bupivacaine along with 0.75 μg/kg of dexmedetomidine.	The combined dexmedetomidine and bupivacaine block had a statistically significant faster time to onset of the sensory block ($P = 0.003$), a longer duration of sensory block ($P = 0.002$) and a longer motor block duration ($P = 0.002$) as well as lower morphine requirements up to 48 hours after the surgery.	Combining dexmedetomidine with bupivacaine during an infraclavicular brachial plexus block enhances the onset and duration of the sensory and motor block.
Buprenorphine	Lomate 2020	Randomized control trial of 100 patients receiving an ultrasound guided infraclavicular brachial plexus block divided into two groups with one receiving	The duration of the sensory and motor block was prolonged in the dexmedetomidine group ($P < 0.05$). The onset of the sensory and motor block ($P < 0.05$) and the duration of the	When compared to buprenorphine, a dexmedetomidine block in an infraclavicular brachial plexus block showed an

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TABLE 3 (*Continued*)

Characteristics of Dexmedetomidine used in an Infraclavicular Brachial Plexus Block

DEXMEDETOMIDINE VS. INJECTATE TYPE	ARTICLE	GROUPS STUDIED AND INTERVENTION	RESULTS AND FINDINGS	CONCLUSIONS
		150 μg buprenorphine and the other receiving 50 μg dexmedetomidine both added to 30 ml of 0.375% bupivacaine	analgesia postoperatively was longer in the dexmedetomidine group.	improved duration and improved duration of postoperative analgesia
Dexamethasone	Aliste 2019	A randomized clinical trial of 120 patients receiving an ultrasound-guided infraclavicular block for upper limb surgery. Patients were randomly assigned to receive perineural dexamethasone (5 mg) or dexmedetomidine (100 μg).	Dexamethasone showed a longer duration of motor block ($p < 0.001$) and sensory block ($P < 0.001$) while dexmedetomidine showed a decrease in heart rate and blood pressure.	Dexamethasone was more effective in terms of sensory and motor block duration when compared to dexmedetomidine
	Yaghoobi 2019	A double-blinded randomized clinical trial of 75 patients undergoing forearm fracture surgery receiving an infraclavicular brachial plexus block. Patients were divided into three groups: a lidocaine group that received 28 mL lidocaine and 2 mL distilled water, a dexamethasone group that received 28 mL lidocaine and 2 mL dexamethasone and a dexmedetomidine group that received 28 mL lidocaine plus 2 mL dexmedetomidine	The duration of the sensory block and the motor block was longer in the dexmedetomidine group when compared to the lidocaine group. There was no overall difference in postoperative pain rating in the dexmedetomidine group when compared to the dexamethasone group	When comparing dexamethasone with dexmedetomidine, there was no difference in postoperative pain. Dexmedetomidine showed a longer sensory block duration.

brachial plexus block for a shoulder surgery. The study found that both dexmedetomidine received via IV and perineurally were effective in reducing pain and post-operative analgesics needed.[37] Furthermore, both routes were superior in terms of the duration of the analgesia with the perineural group having a duration of 10.9 hours and the IV group having a duration of 9.8 hours when compared to the control group of 6.7 hours ($P < 0.001$).[37]

Other studies have compared the effects of dexmedetomidine when compared to ropivacaine in an interscalene brachial plexus block. Patients receiving surgery on their upper limb receiving an interscalene block were randomly divided into two groups: a group receiving 30 ml of 0.75% ropivacaine with 0.5 ml normal saline and a group receiving 30 ml of 0.75% ropivacaine with 50 μg of dexmedetomidine.[38] The addition of dexmedetomidine produced a statistically significant longer duration of both the sensory and motor block ($P < 0.0001$) as well as a faster onset of the block as well ($P < 0.05$).[38] Further studies on the addition of dexmedetomidine to ropivacaine in an interscalene brachial plexus block have confirmed these results. In a prospective, randomized control trial of 62 patients receiving shoulder surgery, patients were divided into two groups: an interscalene block with 12 mL of 0.5% ropivacaine or an interscalene block with 12 mL of 0.5% ropivacaine and 150 μg dexmedetomidine.[39] The group receiving dexmedetomidine had lower pain scores ($P = 0.04$), faster onset of the block ($P = 0.002$), and a longer duration ($P = 0.0001$).[39] This study further supports the conclusion that dexmedetomidine added to ropivacaine in an interscalene brachial plexus block is superior in terms of its analgesic properties than ropivacaine alone (Table 4).[39]

Metanalysis and Systemic Review

Previous metanalyses and systemic reviews have explored the effectiveness of dexmedetomidine as an anesthetic by itself as well as an adjuvant to other local anesthetics. A metanalysis of 12 randomized clinical trials by Dai *et al*. looked at the effectiveness of dexmedetomidine added to ropivacaine in different types of blocks.[40] Their analyses found that there was no optimal dose of dexmedetomidine, however they did point out that Jung et al.'s research found that 2 μg/kg was the most optimal dose in comparison to the 1 and 1.5. μg/kg.[40,41] Their metanalysis also concluded that the addition of dexmedetomidine to ropivacaine prolonged the duration of the sensory and motor blocks and the axillary brachial plexus block produced the earliest onset and longest duration when compared to the supraclavicular and interscalene brachial plexus blocks.[40] Lastly, the most common adverse events associated with the

TABLE 4

Characteristics of Dexmedetomidine used in an Interscalene Plexus Block

TYPE OF INJECTATE	ARTICLE	GROUPS STUDIED AND INTERVENTION	RESULTS AND FINDINGS	CONCLUSIONS
IV vs. Perineural Dexmedetomidine	Abdallah 2016	A randomized, triple-masked, placebo-controlled clinical trial with 99 patients receiving an interscalene brachial plexus block for shoulder surgery. Patients were randomly divided into either the control group receiving 15 ml ropivacaine, 0.5%, the dexmedetomidine administered perineurally group with the above and 0.5 μg/kg dexmedetomidine, and the dexmedetomidine administered via IV group with the above and 0.5 μg/kg dexmedetomidine.	The duration of analgesia in both dexmedetomidine groups was longer than the control groups ($P < 0.001$). The 24 hours cumulative morphine consumption was reduced in the dexmedetomidine groups when compared to the control ($P < 0.001$). Both IV and perineural dexmedetomidine groups had similar outcomes in terms of pain reduction and amount of opioids consumed post-procedure.	In an interscalene brachial plexus block, the route of dexmedetomidine administration via IV or perineurally showed similar results in terms of the duration of analgesia and reduction of opioid consumption
Dexmedetomidine compared to Ropivacaine	Rashmi 2017	A prospective, randomized double-blind study in patients receiving an interscalene brachial plexus block for a surgery of the upper limb. Patients were randomly divided into two groups a.	The group with the combined dexmedetomidine and ropivacaine had a longer sensory and motor block duration ($P < 0.0001$) as well as a quicker onset of the sensory and motor block ($P < 0.05$)	Combining dexmedetomidine with 0.75% ropivacaine during an interscalene brachial plexus block reduces the onset of the sensory

	group receiving 30 ml of 0.75% ropivacaine with 0.5 ml normal saline and a group receiving 30 ml of 0.75% ropivacaine with 50 µg of dexmedetomidine		and motor block and prolongs the duration when compared to 0.75% ropivacaine alone
Fritsch 2014	A prospective, randomized, triple-blind control trial with 62 patients receiving shoulder survey with an interscalene block. Patients were divided into two groups: an interscalene block with 12 mL of 0.5% ropivacaine or an interscalene block with 12 mL of 0.5% ropivacaine and 150 µg dexmedetomidine.	The group receiving dexmedetomidine had lower pain scores (P = 0.04), faster onset of the block (P = 0.002), and a longer duration (P = 0.0001).	Dexmedetomidine used as an adjuvant to ropivacaine for an interscalene block increases the duration of the block, lowers pain scores and is more effective than ropivacaine by itself

dexmedetomidine block were bradycardia and hypotension and that the dosage of dexmedetomidine did not make a different in terms of the bradycardia and hypotension adverse events.[40] The authors concluded in their meta-analysis that the combination of dexmedetomidine with ropivacaine increases the sensory and motor block more than ropivacaine alone.[40]

Another meta-analysis explored perineural dexmedetomidine's effectiveness as a local anesthetic when compared to clonidine, an alpha-2 agonist in a supraclavicular brachial plexus block.[42] The meta-analysis focused on 14 trials and concluded that dexmedetomidine not only increased the duration of the sensory block, but also the motor block as well when compared to clonidine ($P < 0.00001$).[42] The authors discussed that this may be due to dexmedetomidine's greater affinity for the a-2 adrenoreceptors when compared to clonidine. The side effects associated with dexmedetomidine were bradycardia as well as sedation after the operation.[42]

Further meta-analyses have confirmed the efficacy of dexmedetomidine when used as an adjuvant in brachial plexus blocks.[43] A meta-analysis of 18 randomized clinical trials revealed that the addition of dexmedetomidine to brachial plexus blocks prolongs the duration of the motor and sensory blocks.[43] Furthermore, the review paper also discussed how the addition of dexmedetomidine can reduce the time of onset of the sensory and motor blocks. Ping *et al.*'s study also found similar adverse effects of dexmedetomidine such as bradycardia and hypotension which they hypothesized was due to its mechanism of action on the alpha-2 receptors.[43]

Conclusion

Dexmedetomidine is an effective additive for nerve blockade in multiple locations and it may inclusively decrease the risk of nerve injury elicited by administration of local anesthetics. Dexmedetomidine is an alpha-2-adrenergic agonist used as an additive for regional nerve block. The use of adjuvants combined with local anesthetics are meant to prolong analgesia while lessening the dose needed for anesthetic effect. When Dexmedetomidine combined with ropivacaine, it was found to have a significant anti-inflammatory effect as well. For neuraxial intrathecal blocks, addition of dexmedetomidine allows for less need of postoperative opioid use while maintaining effective motor and sensory blockade. Dexmedetomidine also resulted in lower pain scores and less need of morphine. Dexmedetomidine provided a significant prolongation of sensory and motor block when given intrathecally. For paravertebral blocks, using dexmedetomidine combined with ropivacaine

significantly reduced post-operative pain. For axillary brachial plexus blocks (ABPB), many studies showed dexmedetomidine as an effective adjuvant that can better control pain and also a longer duration of sensorimotor block. Similar results were seen for infraclavicular brachial plexus blocks and interscalene. In conclusion, dexmedetomidine as an adjuvant anesthetic showed very promising results in controlling pain and the duration of the sensorimotor blocks in various regions. Hypotension and bradycardia some of the side effects that can occur with dexmedetomidine, but it was not severe is most of the studies. More studies must be done to find the appropriate dosage and the optimal combination with other drugs. The many studies support its use as a beneficial adjuvant for nerve blocks. ✤

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