Dexmedetomidine in Regional Anesthesia: The Current Perspective

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Abstract
Dexmedetomidine is a highly selective alpha-2 agonist and is increasingly being used in anaesthesia for its sedative, analgesic and cardiovascular stabilizing effects. Recently a lot of research is being conducted to study the effect of dexmedetomidine as an adjuvant to local anaesthetics in regional anaesthesia. This review examines the currently available literature on the use of dexmedetomidine as an anaesthetic adjunct for regional anaesthesia.

Keywords: Alpha-2 agonists, dexmedetomidine, regional anaesthesia

INTRODUCTION
Alpha-2 receptor agonists are increasingly being used in anaesthesia for their sedative, analgesic and cardiovascular stabilizing effects. Dexmedetomidine is a highly selective newer prototype of alpha-2 agonists with $\alpha_2:\alpha_1$ selectivity of approximately eight times more in comparison to clonidine.1 It is a short acting drug and has an antidote for its sedative effects, antipamezole.2,3 Dexmedetomidine was approved by the Food and Drug Association in 1999 for its use in the intensive care units as a sedative. Since then dexmedetomidine has been used extensively in the intensive care. Plethora of studies have been conducted on animals to study the effect of dexmedetomidine in regional anaesthesia.4,5 Recently the use of dexmedetomidine as an adjuvant in regional anaesthesia in humans is gaining popularity.

MECHANISM OF ACTION
Alpha-2 adrenoceptors are distributed at numerous sites in the central nervous system, peripheral nervous system and variety of other organs including liver, pancreas, kidney and eye.6,7

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Dexmedetomidine is a pharmacological active isomer of medomitidine with selective agonism for alpha-2 adrenoceptors.\(^8\)

Presynaptic activation of alpha-2 adrenoceptor causes inhibition of the release of norepinephrine, terminating the propagation of pain.\(^9\) Post synapatic activation of alpha-2 adrenoceptors causes decrease in the sympathetic outflow which manifests as hypotension and bradycardia.\(^10\)

The mechanisms of the analgesic actions of alpha-2 agonists are not yet completely understood. It has been postulated that the anti-nociceptive effects of dexmedetomidine may be due to its action at supraspinal and spinal sites.\(^11\) Even the peripheral alpha-2 adrenoceptors may mediate anti-nociception. The alpha-2 adrenoceptors located at the nerve endings have the analgesic mechanisms of alpha-2 adrenoceptor agonists by preventing release of norepinephrine.\(^12,13\) At the spinal cord, stimulation of alpha-2 receptors at the substantia gelatinosa of the dorsal horn leads to the firing of nociceptive neurons and inhibition of the release of substance P.\(^14\)

The hypnotic and sedative effects of alpha-2 adrenoceptor agonists are due to its action at locus ceruleus.\(^15\) Locus ceruleus is also the site of origin of medullospinal noradrenergic pathway which forms an important modulator of nociceptive pathway.\(^16\)

**Role in Epidural Anaesthesia**

Asano et al in 2000 observed that spinal antinociception caused by the epidural administration of alpha-2 agonists correlated with their binding affinity to spinal alpha-2 adrenoceptors in spinal cord and brain of rats.\(^17\) Jellish et al in 2003, studied the effect of epidural clonidine for potentiating spinal anaesthesia in patients undergoing lumber laminectomy.\(^18\)

Dexmedetomidine, a newer prototype of alpha-2 agonists has similar effects as clonidine. The use of dexmedetomidine in regional anaesthesia has been extensively studied in animals by various workers, however its role in humans is deficient in literature.\(^19,20\) Fukushima et al were one of the first to conduct a human trial on the use of epidural dexmedetomidine in patients undergoing surgery under general anaesthesia. They concluded that following epidural injection of dexmedetomidine at the culmination of surgery, there was a significant depression in the electroencephalography (EEG). Dexmedetomidine decreased the requirement of analgesic drugs by 70% for 24 hours and duration of analgesia lasted for 4-6 hours post-operatively.\(^21\) Fukushima et al in 1997 also conducted a placebo controlled double blinded study to clarify the mechanisms of anaesthetic activity of dexmedetomidine. They postulated that the analgesic properties of dexmedetomidine might be due to its direct action on the dorsal root neuron where dexmedetomidine might inhibit P-substance in the nociceptive pathway. They found that the decrease in the blood pressure and heart rate could be caused by inhibition of norepinephrine and epinephrine release centrally and peripherally.\(^22\)

Antonio Mario Veira showed that epidural dexmedetomidine and clonidine with 0.75% ropivacaine prolonged analgesia and sedation for 2-4 hours postoperatively in patients undergoing cholecystectomy.\(^23\)
Maroof et al explored the effect of epidural dexmedetomidine on the incidence of postoperative shivering in 60 patients undergoing orthopaedic surgery. They found that patients who received dexmedetomidine at a dose of 100mcg added to 20ml 0.5% bupivacaine showed lower incidence in postoperative shivering when compared to patients receiving epidural bupivacaine alone (10% vs 36%).

Oriol Lopez SA et al in 2008 used epidural dexmedetomidine at a dose of 1mcg/kg with lidocaine and epinephrine at 3-4mg/kg. They concluded that dexmedetomidine was a good alternative to achieve anaesthetic quality that keeps the patient in active sedation. Fialho et al studied the synergistic effect of dexmedetomidine with 0.75% ropivacaine and found that epidural dexmedetomidine 1mcg/kg enhanced the motor and sensory blockade and prolonged the duration of analgesia.

**Intrathecal Dexmedetomidine**

Alpha-2 agonists have been used to potentiate the quality and duration of the subarachnoid block. Intrathecal clonidine in a dose of 30-100mcg is being used safely as an adjuvant to local anaesthetics. Tuijl et al, in their study, showed that addition of 75mcg of clonidine to hyperbaric bupivacaine prolonged spinal anaesthesia after caesarean section without causing any maternal and neonatal side effects.

Li and Eisench et al examined the pharmacology of adrenergic agents in rats. They showed that intrathecal and epidural injections of alpha-2 agonists produced potent antinociception by altering spinal neurotransmitter release and effectively reduced pain.

Bouaziz, Hewitt and Eisenach administered clonidine and dexmedetomidine in subarachnoid spaces in eyes and found that both clonidine and dexmedetomidine produced dose dependent analgesia with similar potency.

Recently, there have been a few human trials to study the effect of intrathecal dexmedetomidine. Kanazi et al investigated the effect of adding a small dose of 3mcg dexmedetomidine intrathecally to 12 mg bupivacaine. They found a significant prolongation of sensory and motor block as compared to bupivacaine alone. They found the effect of 3mcg intrathecal dexmedetomidine comparable to 30mcg intrathecal clonidine. Al-Mustafa et al reported that intrathecal dexmedetomidine as an adjuvant to 12.5mg bupivacaine in spinal anesthesia had a dose dependent effect on the onset and regression of sensory and motor block. Al-Ghanem et al in their study found that 5mcg of dexmedetomidine added to 10mg bupivacaine prolonged motor and sensory block as compared with 25mcg of fentanyl.

**Role in Intravenous Regional Anaesthesia (IVRA)**

Intravenous regional anaesthesia is a simple technique meant for short surgical procedures of the upper limb. Its major disadvantage is inability to provide postoperative pain relief and tourniquet pain. Recently various studies have been conducted to evaluate the role of alpha-2 agonists in IVRA. It has been hypothesized that enhancement of the action of local anaesthetics is mediated via alpha-2 adrenoceptors. Dexmedetomidine causes vasoconstriction at the site of action, which
delays the absorption of lidocaine resulting in the prolongation of action in addition to with the direct action.

Memi et al found that addition of 0.5mcg/kg dexmedetomidine to 40 ml of 0.5% lidocaine enhanced the sensory and motor blockade, quality of anaesthesia, postoperative pain free period and sedation in IVRA. Esmaoglu A et al in their study demonstrated that the addition of 1μg/kg dexmedetomidine to lidocaine for IVRA improved quality of anaesthesia and postoperative analgesia, without causing side-effects. Kol I clalo et al in 2009 found out that addition of dexmedetomidine or lornoxicam to prilocaine in IVRA decreased the pain scores, improved anaesthesia quality and decreased analgesic requirement.

**Caudal Dexmedetomidine**

Caudal anaesthesia is one of the most commonly performed anaesthetic block in the paediatric population. Dexmedetomidine has been used increasingly in children without any untoward effects. Hennawy et al had compared the analgesic effects and side effects of caudal dexmedetomidine and clonidine when added to bupivacaine in patients undergoing lower abdominal surgeries and found that both the drugs promoted analgesia without any significant side effects. Saadawyl et al found that addition of 1mcg/kg of dexmedetomidine to bupivacaine in caudal space provided excellent analgesia and sedation in children undergoing inguinal hernia repair or orchidopexy without causing significant difference in the haemodynamics.

**ROLE IN PERIPHERAL NERVE BOCKS**

Clonidine has been extensively used in peripheral nerve block techniques to potentiate the action of local anaesthetics. Dexmedetomidine is known to enhance central neuraxial blockade, however, its role in the peripheral nerve block has not been fully elucidated. Yoshitomi et al had conducted a study to evaluate the peripheral action of dexmedetomidine. In their study they found that dexmedetomidine enhanced the local anaesthetic action of lidocaine via peripheral alpha-2 adrenoreceptor.

Brummet et al showed that peripheral administration of DEX in combination with bupivacaine enhanced sensory and motor blockade in sciatic nerve block without inducing any neurotoxicity in rats. Esmaoglu found out that dexmedetomidine added to levobupivacaine for axillary brachial plexus block shortened the onset time and prolonged the duration of the block and the duration of postoperative analgesia. Obayah et al demonstrated that addition of dexmedetomidine to bupivacaine for greater palatine nerve block prolonged postoperative analgesia after cleft palate repair.

**Intra-articular Dexmedetomidine**

Dexmedetomidine has been safely given intraarticularly at 0.1mcg/kg at the end of arthroscopic knee surgery in humans resulting in significant reduction in the degree of pain for six hours postoperatively. Dexmedetomidine, added as an adjunct to ropivacaine in patients undergoing arthroscopic knee surgery, improved the quality and duration of postoperative analgesia.

This review of the currently available literature on the use of dexmedetomidine in regional anaesthesia suggests that the drug has been a promising adjuvant to
local anaesthetics for various techniques of regional anaesthesia. Dexmedetomidine, administered intrathecally or epidurally, causes dose dependant antinociception and helps in the potentiation of the local anaesthetic block. Thus, it can be inferred that dexmedetomidine can be safely administered in regional anaesthesia techniques without causing serious side effects.

CONCLUSION

Dexmedetomidine is a newer and more selective prototype of alpha 2 agonists. Its role in anaesthesia as an anaesthetic adjunct is well established. This review article explored the currently available literature on the use of dexmedetomidine as an adjunct to local anaesthetics in regional anaesthesia and the possible mode of action. Various studies have now documented that dexmedetomidine potentiates the action of local anaesthetics and can be safely administered in regional anaesthesia techniques without causing any harmful side effects.

REFERENCES


42. Esmaoglu A, Yegenoglu F, Akin A, Yildirim C, Duxmedetomidine added to levobupivacaine

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