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Review Article

Dexmedetomidine: A Review of Its Pharmacology and Use in Pediatric Dentistry

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ABSTRACT

Dexmedetomidine is an alpha 2 adrenergic receptor agonist having an analgesic, anaesthetic sparing effect and sympatholytic property, making it useful in dentistry especially in management of pediatric patients. The aim of this review is to make awareness of its role in present dentistry specially in behavior management of pediatric patients and discuss its effects along with other sedative agents used in moderate sedation.

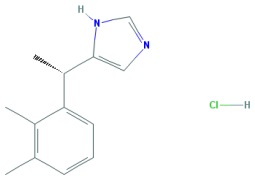
Keywords: dexmedetomidine, analgesic, pediatric dentistry, behavior management.

INTRODUCTION

One major aspect of child management in the dental chair is managing dental anxiety and this highlights the need for various behavior management techniques. These are mainly classified into non-pharmacological and pharmacological. In pharmacological management, use of dexmedetomidine alone and with other agents has produced successful results.

Dexmedetomidine (DEX) is a potent, highly selective alpha-2 adrenoceptor agonist with high selectivity for the alpha-2 compared with the alpha-1 receptor. Activation of these receptors in the central nervous system leads to inhibition of sympathetic activity, which causes reduction in blood pressure and heart rate, decreased arousal, sedation, and anxiolysis. [1] It is being regarded as a potentially successful sedative for pediatric dental procedure because of its additional stable respiratory profile, analgesia and antisalivatory properties. [2]

It was approved by the Food and Drug Administration in 1999 for use in humans. It is a selective a2 adrenergic receptor agonist [3] with a dose-dependent a2 selectivity that is approximately 7- to 8-fold greater than that of clonidine. [4]



The interactions with central nervous system and spinal cord a2 adrenergic receptors mediate dexmedetomidine's primary physiologic effects by stimulation of parasympathetic outflow and inhibition of sympathetic outflow. Main site of inhibition of noradrenergic outflow is locus coeruleus where it induces electroencephalographic activity similar to natural sleep. [5] Primary analgesic effects and potentiation of opioid-induced analgesia

result from the activation of a2-adrenergic receptors in the dorsal horn of the spinal cord and the inhibition of substance P release. [6] When delivered by non-IV routes, the bioavailability of dexmedetomidine follows the order of orogastric 16%, intranasal (IN) 65%, buccal 82%, and IM 104%. [7] In children, large doses of dexmedetomidine cause peripheral vasoconstriction, which may lead to transient systemic hypertension, whereas low doses cause central sympatholysis, which can lead to systemic hypotension. [8] Its induced sedation is characterized by an easy and quick arousal from sedation resembling natural sleep. One of dexmedetomidine's key advantages over other sedation medications is that it maintains ventilation and airway patency in the presence of increasing sedation. Respiratory rate and hemoglobin oxygen saturation are unchanged after 1 µg/kg dexmedetomidine infused over 10 minutes. [9] Dexmedetomidine has dose dependent sedative response. [10]

Effects on the central and peripheral nervous system includes decrease in cerebral perfusion pressure with no effect on intracranial pressure, [11] dose related opioid sparing and analgesic effect, [12] prevention of opioid-induced muscle rigidity and attenuation of shivering. [13]

Pharmacodynamics:

Dexmedetomidine is 8 to 10 times more selective towards α2-AR than clonidine. [14] Sedative actions are believed to be mediated primarily by post-synaptic α2-adrenoceptors. Dexmedetomidine has a low affinity for beta adrenergic, muscurinic, dopaminergic and serotonin receptors. It binds the α2 receptors of locus ceruleus and spinal cord and causes sedation and analgesia respectively. Higher affinity to α2 receptor selectively leads to vagomimetic action on heart (bradycardia) and vasodilatation. The role as an antishivering agent and diuretic is yet to be established. [15]

Pharmacokinetics:

In the manufacturer recommended dosing range of dexmedetomidine i.e. 0.2-0.7 µg/kg/h, the pharmacokinetics are linear. It exhibits 94% binding to serum albumin and a1-glycoprotein. Primary site of metabolism is liver with a small amount of unchanged drug being exchanged in urine and stool. [16] The pharmacokinetics of dexmedetomidine in pediatric patients are similar to those of adults [17] but, infants appear to clear dexmedetomidine more quickly than adults or older children.

Oral bioavailability is poor because of extensive first pass metabolism. However, after sublingual & intranasal administration bioavailability is high (84%), giving it a potential role in paediatric sedation and premedication. [18]

It undergoes almost complete biotransformation with very little unchanged dexmedetomidine excreted in urine (95%) and faeces (4%).Biotransformation involves both direct glucuronidisation (the major pathway) as well as cytochrome P450 mediated metabolism. [19]

Application In Pediatric dentistry:

Dexmedetomidine is being thought of as a potentially successful sedative for dental procedure because of its stable respiratory profile, analgesia and antisalivatory properties. [2]
Limited data on adult population undergoing dental procedural sedation with dexmedetomidine has shown it to be efficacious and safe with sufficient analgesia but limited amnesia. It shows prolonged recovery time of 82.2 - 24.3 min when compared with the total procedure time of 44.6 -27.9 min. [20] The most distinctive characteristic of dexmedetomidine is the high quality of its hypnotic action. Specifically, unlike existing sedatives, it has been described as inducing a state that is close to physiologic sleep, but allowing full awakening with stimulation. [20] However, sudden arousal in response to stimulation, especially sound, may be a disadvantage of the drug for dentistry.

Dexmedetomidine In Combinations With Other Agents:-

The rationale to combine any two drugs is either to achieve a synergy of desired beneficial drug actions or to achieve antagonism of potential adverse effects of the two.

DEXMEDETOMIDINE - KETAMINE COMBINATION:

Pharmacological profile of dexmedetomidine and ketamine suggest that combining these two may develop a nearly ideal sedative agent. This can simply be understood by considering the followings points:

The opposing hemodynamic profiles of two i.e. negative hemodynamic effects of dexmedetomidine and positive cardiostimulatory effects of ketamine may provide balanced hemodynamic parameters in sedated patients. Ketamine has an adverse effect of increased salivation which is undesirable especially during dental procedures owing to implications of increased salivary secretions in adverse airway events, while dexmedetomidine has antisialagogue properties on account of its sympatholytic potential. Dexmedetomidine has limited analgesia while ketamine has an effective analgesic action. [21]

Both of the agents act on different parts of central nervous system to produce sedation. Hence a combination of two may provide synergistic sedation with decreased dose. Also, faster onset of action on induction as well as faster recovery can be expected with combination when compared to dexmedetomidine alone.

DEXMEDETOMIDINE FENTANYL COMBINATION:

Recent systematic reviews found that dexmedetomidine could reduce opioid requirements and potentiate analgesia.

Dexmedetomidine has an analgesic-sparing effect, significantly reducing opioid requirements both during and after surgery. [22] Reduction in dose requirement of opioid could further reduce the postoperative complications of nausea, vomiting and physical dependence which are specifically associated with opioids. [23]

CONCLUSION

Dexmedetomidine is a very useful addition to the family of drugs used in dentistry. It can successfully be used as an alternative for sedation in pediatric patients.

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