HOT TOPIC

SHOULD DEXMEDETOMIDINE BE USEDFOR PAEDIATRIC PROCEDURAL SEDATION?

SUMMARY OF KEY POINTS:

- Dexmedetomidine is a useful drug for pre-operative anxiolysis and procedural sedation owing to its various routes of administration and preservation of spontaneous ventilation
- The intranasal route has a particularly favourable efficacy and safety profile
- Appropriate dosing allows for safe use avoiding intubation and ventilation in several stimulating and non-stimulating procedures

REVIEW OF EVIDENCE

Dexmedetomidine is an alpha 2 adrenoreceptor agonist that acts in a similar manner to Clonidine albeit with a much higher selective potency for alpha 2 receptors. Its use in adult practice has increased in recent years, however despite its various routes of administration making it an attractive target for use in children, use is still not common in paediatric anaesthesia likely at least partially because its use remains off licence.

The aim of this review is to focus on Dexmedetomidine for the use of procedural sedation although it is important to note its scope extends much further. Owing to its properties of anxiolysis, suppression of sympathetic nervous response and mimicking of natural sleep with maintenance of spontaneous ventilation and airway reflexes it can be a useful tool in the paediatric anaesthetist's arsenal. It can be administered via the buccal, intranasal, IV, IM, SC, oral, nebulised, and rectal routes depending on the indication and desired effect. A single bolus used as an adjunct has been demonstrated to reduce postoperative analgesic requirements, facilitate smoother emergence from anaesthesia and prolong regional block time. Use in PICU has expanded and it is now used for procedural sedation, to ameliorate withdrawal and facilitate sedation weaning, and for reducing agitation in children and infants requiring NIV. In addition, there is amounting evidence that Dexmedetomidine is not only less neurotoxic to the developing brain than other drugs used for anaesthesia but that it may also confer a degree of neuroprotection which further adds to its appeal in paediatric anaesthesia.

Why not use it?

Dexmedetomidine is comparatively more expensive than other sedative agents and this, along with its use in children being off licence and its unfamiliarity to many anaesthetists, may account for some of the reluctance encountered to its routine use in clinical practice. The main adverse effects of Dexmedetomidine are its cardiovascular instability; administration causes bradycardia and hypotension in a dose dependent manner and can cause hypertension if large boluses are given too rapidly. Tolerance and tachyphylaxis can occur after 24 hours of infusion and rebound hypertension after cessation is possible.

Dexmedetomidine should not be used in patients with cardiac conduction abnormalities, chronic hypertension, or hepatic disease. Its use is also precluded in patients being treated with drugs that may cause hypotension and bradycardia such as digoxin, beta-adrenergic blockers, calcium channel blockers or monoamine oxidase inhibitors. It should be used with caution in patients with significant hypotension such as septic shock. Rapid boluses should be avoided, and boluses used with caution in patients with a concurrent high MAC of volatile anaesthetics.

Pre-operative anxiolysis

Intranasal (IN) Dexmedetomidine is less irritant to the nose and has a more pleasant taste than IN Midazolam and therefore may be preferable for preprocedural anxiolysis. Studies suggest that administration of 2-3mcg/kg IN Dexmedetomidine provides effective sedation within 45 minutes, with the child being rousable to voice[1]. The bioavailability of oral Dexmedetomidine is poor because of first pass metabolism, making it a less viable route. Further, although the buccal route has a superior bioavailability to the IN route, no benefit has been demonstrated clinically for buccal over IN administration. IN administration also confers more cardiovascular stability than the IV route and therefore demands a lower training requirement for administration; this, combined with its safety profile and less intense monitoring protocols make it an ideal pre-med for the anxious child.

Procedural Sedation

IN and IV Dexmedetomidine are now being used with increased frequency for procedural sedation. In non-stimulating procedures such as MRI scan and transthoracic echo IN Dexmedetomidine has been shown to be useful at a dose of 2-4mcg/kg as a sole agent, although a repeat dose of 1-1.5mcg/kg may be required at 30 minutes. This can be done with a relatively safe side effect profile and can be used as part of nurse led sedation protocols[2].

Use of IV Dexmedetomidine in children to facilitate awake craniotomy has been described. This allows for gold standard monitoring during resection close to eloquent areas of the brain, however patient selection and appropriate pre-operative preparation are crucial in order for this method to be successful[3].

Dexmedetomidine has been used successfully in burns care although higher doses may be required. This may necessitate concomitant vasopressor use or treatment of bradycardia. It should be noted that prophylactic anticholinergics confer no benefit and treating bradycardia with Atropine or Glycopyrrolate should be undertaken with caution as it can result in rebound hypertension [2].

Additional uses

Dexmedetomidine has been used in combination with TIVA for ENT procedures such as foreign body removal from the airway allowing for reduced doses of opiates and maintained spontaneous ventilation with less risk of apnoea. It has also been used in children with Obstructive sleep apnoea to reduce the amount of post-operative opiate requirements therefore reducing the number of post-operative complications associated with airway obstruction[4].

Use in neonates

The pharmacokinetics of Dexmedetomidine differ in the neonate compared to the infant, probably due to immature hepatic function and impaired metabolism via the p450 system. The resultant significantly prolonged half-life in this population necessitates dose alteration.

In experimental animal models Dexmedetomidine has been shown to attenuate the neurocognitive dysfunction associated with isoflurane. IV infusion of Dexmedetomidine has also been used in combination with caudal anaesthesia to perform inguinal hernia repair without the need for general anaesthesia, therefore avoiding the need to instrument the airway[5].

A summary table detailing suggested regimes for the use Dexmedetomidine in appropriate clinical situations is included below.

The full potential for the use of Dexmedetomidine in paediatric anaesthesia has not yet been reached. It can be considered a useful tool in the perioperative period for the paediatric anaesthetist and its use is likely to grow as clinician familiarity is increased.

REFERENCES:

1. Poonai N, Spohn J, Vandermeer B, et al. Intranasal Dexmedetomidine for Procedural Distress in Children: A Systematic Review. *Pediatrics* 2020; **145**: e20191623
2. Sottas CE, Anderson BJ. Dexmedetomidine: the new all-in-one drug in paediatric anaesthesia? *Curr Opin Anaesthesiol* 2017; **30**: 441–51
3. Lohkamp L-N, Mottolese C, Szathmari A, et al. Awake brain surgery in children—review of the literature and state-of-the-art. *Childs Nerv Syst* 2019; **35**: 2071–7
4. Mahmoud M, Barbi E, Mason KP. Dexmedetomidine: What's New for Pediatrics? A Narrative Review. *J Clin Med* Multidisciplinary Digital Publishing Institute; 2020; **9**: 2724
5. Lin R, Ansermino JM. Dexmedetomidine in paediatric anaesthesia. *BJA Educ* Elsevier; 2020; **20**: 348–53

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Indication	Route	Dosing	Onset	Considerations
Pre-med	IN	2-3mcg/kg	30-45 minutes	
Procedural sedation non-stimulating Eg. MR scan, TTE	IN	2-4mcg/kg	30-45 minutes	Many require a second dose at 1.5mcg/kg
	IV	0.5 - 2 mcg/kg followed by 0.5-1 microgram/kg/h	Load over 10 mins, can be repeated if inadequate sedation	
Procedural sedation stimulating Eg. Awake craniotomy	IV	0.5-1mcg/kg bolus over 10 minutes followed by 0.1-2mcg/kg/h		Higher rates more likely to cause cardiovascular instability necessitating vasopressors
Intraoperative				
ENT airway examination	IV	4mcg/kg over 10 mins followed by infusion		In combination with TIVA technique eg. Propofol/Remifentanil. Likely prolonged wake up time
In OSA	IV	1mcg/kg		
Post-op benefits eg. Emergence delirium, prolonging regional block, opioid sparing	IV	0.5 – 1mcg/kg		
PICU	IV	0.1- 1.4 mcg/kg/hr titrate to effect depending on indication		Avoid bolus doses. Rebound tachycardia associated with prolonged use.
Neonates In NICU	IV	0.05 to 0.2 mcg/kg/h		Consider differing pharmacokinetics
Neonates Peri-operative to avoid GA	IV	3µg/kg/h over 20 minutes followed by 0.2–1mcg/kg/h		Consider differing pharmacokinetics – prolonged duration of action