Dexmedetomidine: the new all-in-one drug in paediatric anaesthesia?

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\textbf{Purpose of review}  
Dexmedetomidine is a drug with sedative, anxiolytic, sympatholytic and analgesic properties, which is finding widespread practice in paediatric anaesthesia and related practices. The present review summarizes its pharmacology and current experience with the drug.

\textbf{Recent findings}  
Dexmedetomidine is proving useful in many diverse areas in paediatric anaesthesia where its sedative properties are useful for premedication, fibreoptic intubation and radiologic procedures. Its use as an adjunct for balanced anaesthesia where it can decrease the use of other drugs, reduce emergence delirium, postoperative shivering and vomiting. Muted apoptotic neuroprotective effects may realize benefits in neonates. Cardiac conduction delay, an adverse effect, may prove beneficial for arrhythmias after congenital cardiac surgery.

\textbf{Summary}  
Most of the paediatric published studies concerning dexmedetomidine are observational in nature, with limited control groups or comparators. Adverse effects (e.g. bradycardia) still require greater scrutiny in the paediatric population and particularly with respect to different age groups. Dexmedetomidine currently has a firm position in the armamentarium of anaesthesia pharmacology. It is not the new all-in-one drug, but it is shaping up as a valuable adjunct for diverse indications within paediatric anaesthesia.

\textbf{Video abstract}  
http://links.lww.com/COAN/A44.

\textbf{Keywords}  
$\alpha_2$ adrenoceptor agonist, anaesthesia, children, pharmacology

\section*{INTRODUCTION}

Dexmedetomidine is a selective $\alpha_2$-agonist. It is in the same class as clonidine but differs from clonidine in that its affinity for $\alpha_2$-compared with $\alpha_1$-adrenoreceptors is eight-fold greater. An advantage is that it may be administered by intravenous, intramuscular, subcutaneous, nasal, buccal, rectal and oral routes.

The $\alpha_2$-adrenoreceptors are located ubiquitously throughout the body with effects that include sedation, anxiolysis and analgesia. Heart rate slows by blocking the cardio-accelerator nerves and by augmenting vagal activity. This $\alpha_2$-agonist action on the autonomic ganglia includes decreasing sympathetic outflow, which leads to hypotension. Actions on the peripheral vasculature depend on the concentration of dexmedetomidine: vasodilation is the result of sympatholysis at low concentrations and vasoconstriction is the result of direct action on smooth muscle vasculature at high concentrations.

Other manifestations of $\alpha_2$-adrenoreceptors include inhibition of shivering and promoting diuresis, although the mechanisms by which these are affected remain elusive \cite{1,2}. Consequently dexmedetomidine use in neonates and children has expanded to include prevention of emergence delirium, postoperative pain management, invasive and noninvasive procedural sedation and the management of opioid withdrawal \cite{3–11}. Is this drug the new all-in-one drug for paediatric anaesthesia?
Dexmedetomidine, a relatively recent drug in the field of paediatric anaesthesia, has raised great interest because of its sedative property without respiratory compromise.

It could be less damaging to the developing brain than other anaesthesia drugs currently used.

It seems particularly well suited for painless procedures that require a motionless patient (e.g., radiology procedures, fibreoptic intubation) or procedures that would benefit from nonsupressed cortical activity (e.g., electroencephalographic studies or epilepsy surgery).

The drug is often cited as one of choice for cardiac surgery, notably for its antiarythmogenic and postoperative sedation properties, although superiority over other drugs currently used has yet to be demonstrated.

Although effective to treat many common situations in paediatric anaesthesia such as postoperative delirium, shivering, nausea and vomiting, use of dexmedetomidine is more an adjunct to the current therapies than a new gold standard.

Dexmedetomidine has effects on cerebral, respiratory, analgesic and cardiovascular systems.

Sedation
Dexmedetomidine provides sedation that permits arousal with gentle stimulation [12]. A plasma concentration in excess of 0.6 μg/l is estimated to produce satisfactory sedation in adult ICU patients [13], and similar target concentrations are estimated in postoperative children after cardiac surgery who require sedation in the intensive care unit [14].

Respiration
The lack of respiratory depression distinguishes this sedative from opioids, benzodiazepines and other sedatives. Although dexmedetomidine blunts the CO₂ response curve [15], it does not lead to extreme hypoxia or hypercapnia. Indeed, respiratory rate, CO₂ tension, and oxygen saturation are generally maintained during dexmedetomidine sedation in children [11,12,16–18].

Anaesthesia
The MAC-sparing effect of isoflurane or sevoflurane in adults using dexmedetomidine is concentration dependent; estimated up to 50% at dexmedetomidine 0.7 μg/l [19–21]. Premedication with intranasal dexmedetomidine (1 and 2 μg/kg) in children 3–7 years decreased the MAC required for tracheal intubation using sevoflurane by 20 and 35%, respectively [22]. Similar results have been reported when infusion (0.5 and 1 μg/kg/h) were continued after an intravenous bolus (1 and 2 μg/kg) [23].

The propofol dose required for sedation and induction of anaesthesia is reduced in the presence of dexmedetomidine in adults [24,25]. The concomitant use of dexmedetomidine (0.5 μg/kg/h) in adolescents undergoing spinal fusion reduced propofol infusion requirements (71 SD 11 μg/kg/min) when compared with those (12–21 years) receiving only propofol and remifentanil (101 SD 33 μg/kg/min) [26].

Dexmedetomidine is often used as an adjunct to other drugs to improve sedation or anaesthesia, for example when added to midazolam it assists achievement of a motionless state for MRI [11,27,28]. Total intravenous anaesthesia with dexmedetomidine and ketamine in children is described [29]. This combination has also been administered as premedication for children 3–6 years using a nebulizer [30*]. Combined nebulized dexmedetomidine (1 μg/kg) and ketamine (1 mg/kg) proved more effective than either dexmedetomidine 2 μg/kg or ketamine 2 mg/kg.

Analgesia
Several adult [2,31,32] and paediatric [33*] studies have demonstrated that dexmedetomidine spares opioid requirements during surgery. Effect is short lived after surgery. A meta-analysis of perioperative analgesic effect in children, infants, and neonates showed intraoperative dexmedetomidine administration was associated with reduced postoperative opioid consumption in the postanaesthetic care unit (PACU) [risk ratio (RR) = 0.31; 95% confidence interval (CI), 0.17–0.59], decreased pain intensity (standardized mean difference = −1.18; 95% CI, −1.88 to −0.48) but had no effect upon postoperative nausea and vomiting (RR = 0.67; 95% CI, 0.41–1.08). The optimal bolus dose was 0.5 μg/kg or more [34**]. Although effective after short duration anaesthesia (e.g., myringotomy) [35], recovery may be delayed [36].

Cardiovascular
Dexmedetomidine decreases heart rate in a dose-dependent manner in children [12,19,37–40]. Decreasing the dose of dexmedetomidine restores the heart rate to normal values [41]. With very large doses of dexmedetomidine (2–3 μg/kg over 10 min followed by 1.5–2 μg/kg/h), 12 children under 6 years of age experienced heart rates less than 60.
50 beats/min, although their blood pressures were maintained [39]. Administration of anticholinergics or other medications to increase the heart rate have not been required, but it should be noted that severe and persistent hypertension has been reported when glycopyrrolate was used to treat high-dose dexmedetomidine-induced bradycardia [42].

There are conflicting data regarding its safety in children with congenital heart disease [43–46]. Sinus node and atrioventricular nodal function are both depressed. This adverse effect may be useful for control of supraventricular arrhythmias.

THE CLINICAL MULTIPURPOSE DRUG

The diverse effects that characterize dexmedetomidine pharmacodynamics have been harnessed for a number of purposes in paediatric anaesthesia and fields associated with our specialty.

Sedation

Early use for sedation was almost exclusively with the intravenous route. An initial bolus of 0.5 μg/kg over 10–15 min was followed by an infusion of 0.5–1 μg/kg/h. These regimens were associated with less delirium and tachycardia, lower blood pressure and fewer ventilator days when compared to midazolam in the adult intensive care environment [47*,48].

Dosing regimens are currently more liberal as practitioners either titrate drug to effect or add supplemental drugs to improve effect. Although undoubtedly effective, dose-finding studies and studies with sedation score-based outcomes in children are still needed for both clonidine and dexmedetomidine [49*]. Certainly experience in infants and neonates (age <36 months, n = 187) with congenital heart disease and pulmonary arterial hypertension is less convincing than adult reports showing advantages over midazolam. However, neonates and infants given dexmedetomidine required fewer sedative or analgesic drugs and had a lower incidence of delirium than those given midazolam [50]. Comparisons with clonidine are few, despite widespread use of that drug in intensive care [51,52,53**].

Dexmedetomidine sedation outside the operating room is increasing. A review of 13 072 children (ASA 1 or 2) sedated using dexmedetomidine reported an adverse event rate of 3.6% (95% CI, 3.3–3.9%). Airway obstruction was the most common adverse event (0.27%; 95% CI, 0.19–0.37%). Sedation was successful in 99.7% of children [54**]. Although concerns about the effect of bradycardia associated with dexmedetomidine exist, the use of a prophylactic anticholinergic (atropine or glycopyrrolate) showed no advantage in children other than a transient increase in heart rate and systolic blood pressure. Further, anticholinergics may precipitate transient exaggerated systolic blood pressure changes in children given dexmedetomidine [55**].

A meta-analysis comparing dexmedetomidine and propofol in children (n = 337) undergoing sedation for MRI demonstrated dexmedetomidine increased the recovery time by 10.7 min (95% CI, 4.3–17.1) [56*]. Discharge readiness may be slightly delayed but the importance of this in children who are obliged to be monitored for a requisite time after sedation, regardless of sedative agent, is debated [57]. The nasal route has gained popularity in the radiology suite because of ease of administration, reliable effectiveness and ability to administer further doses or supplement with other sedative drugs [58*]. Intranasal dexmedetomidine (2.5 μg/kg) was found to be superior to oral midazolam (0.5 mg/kg) for producing satisfactory sedation for computed tomography (CT) imaging [59**]. When used as rescue therapy after failure of chloral hydrate (50 mg/kg), the ED₅₀ of intranasal dexmedetomidine for rescue sedation was 0.4 μg/kg in children aged 1–6 months, 0.5 μg/kg in children aged 7–12 months, 0.9 μg/kg in children aged 13–24 months and 1.0 μg/kg in children aged 25–36 months [60*]. Higher doses in those children 1–6 months age caused increased sedation in a dose-dependent manner [61*].

Intranasal administration (2.5–3 μg/kg with a repeat dose of 1–1.5 μg/kg if needed 30 min later) is also finding use for electroencephalogram and auditory brain response testing. Onset time was 25 min [interquartile range (IQR), 20–32 min] and the median duration of sedation was 107 min (IQR, 90–131 min) [62*]. Others have reported similar results with a larger single dose (4 μg/kg) [63*,64*]. Aerosolized intranasal dexmedetomidine 2.5–3.0 μg/kg offered satisfactory conditions for thoracic echocardiography in children (3 months to 3 years) [65**] and was comparable to chloral hydrate 70 mg/kg [66]. The mean wake up time after dexmedetomidine 3 μg/kg was 44.3 min (range 12–123 min) [67*].

The indications for the use of dexmedetomidine sedation are increasing as familiarity with the drug increases, for example cardiac catheterization [68], craniectomy radiosurgery [69–71,72*] and even those children with preexisting respiratory problems [73,74]. Use in children suffering burns using doses of dexmedetomidine with a median infusion dose of 0.57 μg/kg/h (range 0.11–1.17 μg/kg/h) was well tolerated and effective [75], but higher doses have proved problematic because of hypotension.

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A bolus dose of dexmedetomidine (1.0 μg/kg for 10 min) and high infusion rates (0.7–2.5 μg/kg/h) may require fluid resuscitation or vasoressor support to maintain normotension in critically injured paediatric burn patients [76]. There remains a lack of information about relative recovery times after infusion with this drug compared to others using validated, objective measures that are reproducible form one institution to another.

**Awake fibreoptic intubation**

Drugs or combinations of drugs with anxiolytic and analgesic properties are popular to facilitate awake fiberoptic intubation; benzodiazepines, propofol, opioids, \(\alpha_2\)-adrenoceptor agonists and ketamine are commonly used. Dexmedetomidine 1.5 μg/kg has proven effective for awake fiberoptic intubation in adults [77]. Augmentation with ketamine, a drug known for its airway protection properties, also offers advantages in adults [78]. Paediatric practitioners are no strangers to this approach [79].

**Premedication**

Sedative premedication has long been used in paediatric practice. The cynical older generation of practitioners might suggest that a third of premedicants administered work well, a third have some variable success and that a third fail. Midazolam retains popularity despite criticisms concerning amnesia, confusion and long-term behavioural disturbances [80]. The \(\alpha_2\)-adrenoceptor agonist, clonidine, has long been advocated as an alternative premedicant [81]. Dexmedetomidine is now competing for that role [82]. Onset time after oral administration (4 μg/kg) is slower than midazolam 0.75 mg/kg (18.9 SD 3.7 vs. 30.5 SD 4.4 min) [83]. Modest dose comparisons (midazolam 0.5 mg/kg, dexmedetomidine 2 μg/kg) in children (3.96 SD 2.04 years) presenting for cardiac surgery were equally effective [84]. However, a meta-analysis (n = 1033 children) comparing dexmedetomidine to midazolam reported a higher incidence of satisfactory sedation at separation from parents (74 vs. 50%, RR = 1.30), a reduced incidence of postoperative agitation (10 vs. 40%, RR = 0.31), and a reduction in the rescue doses of analgesic drugs (20 vs. 39%, RR = 0.52) [85]. Dexmedetomidine was also superior for providing satisfactory intravenous cannulation compared to placebo [86]. Part of dexmedetomidine’s appeal as a premedicant is the ability to administer the drug intranasally [87–89].

**Balanced anaesthesia**

The traditional trilogy of sedation, analgesia and neuromuscular blockade can be refined with the introduction of dexmedetomidine to the mix, allowing reduction of analgesia or sedative requirements. This can be advantageous in spinal instrumentation surgery where inhaled anaesthetic vapours or propofol can lessen the value of neurophysiological evoked potential monitoring. Dexmedetomidine added to a propofol infusion in adolescents (14–18 years) reduced propofol requirements by more than 50%, provided moderate hypotension, decreased blood loss, and allowed monitoring of motor and somatosensory evoked potentials [90]. Similarly, the addition of a dexmedetomidine 1–2 μg/kg before propofol administered for MRI sedation resulted in fewer sedation-related adverse events, particularly upper airway obstruction [91].

Dexmedetomidine (0.5 μg/kg over 10 min, followed by an infusion 0.5 μg/kg/h) in children 1–6 years undergoing cardiac surgery reduced sevoflurane requirements and decreased the incidence of emergence delirium [92]. A meta-analysis confirmed a shorter length of postoperative mechanical ventilation, lower postoperative and morphine requirements, reduced stress responses, and lower risk of delirium. Dexmedetomidine increased the bradycardia and hypotension risk [odds ratio (OR) = 3.14; 95% CI, 1.47–6.69] [93].

The addition of ketamine to either propofol [94,95] or dexmedetomidine offers analgesia, better airway protection and greater cardiovascular stability than either drug alone. Fewer oxygen desaturations and a higher rate of successful completion of drug-induced sleep endoscopy were reported in children suffering obstructive sleep apnoea when a combination of dexmedetomidine and ketamine was used compared to propofol alone [96]. Although both combinations ketamine–dexmedetomidine and ketamine–midazolam offered effective sedation–analgesia without causing noteworthy adverse effects in children undergoing burns dressing changes, the former resulted in higher sedation and less hemodynamic discrepancy [97]. Low-dose intravenous ketamine 0.15 mg/kg followed by dexmedetomidine 0.3 μg/kg reduced the incidence and severity of emergence agitation in children (3–7 years) undergoing adenotonsillectomy following sevoflurane-based anaesthesia and provided smooth extubation [98].

Current evidence does not substantiate any clinically significant interaction between dexmedetomidine and neuromuscular blockade [99].

**Apoptotic neuroprotection**

Dexmedetomidine was not associated with neuroapoptosis or other neurodegenerative effects in animal studies involving infant rodents and foetal
Emergence delirium occurs commonly after most postoperative shivering, pruritus and pain scores. Superior to placebo in attenuating the incidence of meta-analysis from adults who underwent gynaecological surgery. A num-
deral antiemetic therapy in paediatric anaesthesia. A current infant study investi-
gating sevoflurane neurotoxicity is using dexmedetomidine as the comparator (ClinicalTrials.gov Identifier: NCT02353182).

PONV

Ondansetron and dexamethasone remain the pillars of antiemetic therapy in paediatric anaesthesia. A meta-analysis from adults who underwent gynaecological surgery showed that dexmedetomidine was superior to placebo in attenuating the incidence of postoperative shivering, pruritus and pain scores. There was a reduction in the need for an antiemetic (RR = 0.62; 95% CI, 0.39–0.99) [108**]. However, this effect may be related to a lower consumption of intraoperative opioids, rather than specific antiemetic activity [109]. Paediatric studies are lacking.

Emergence delirium

Emergence delirium occurs commonly after most inhalational anaesthetics in children [110*]. A number of medications have been shown to attenuate the incidence of delirium after anaesthesia, including both clonidine and dexmedetomidine [8,111,112*]; odds ratio for dexmedetomidine are estimated at 0.18 (95% CI, 0.12–0.25), for clonidine 0.25 (95% CI, 0.14–0.46) and for propofol 0.32 (95% CI, 0.18–0.56) [113]. Dexmedetomidine decreased the incidence of agitation after sevoflurane anaesthesia: after an infusion of dexmedetomidine (0.2 μg/kg/h), recovery was not prolonged [114], whereas a single intravenous dose of 0.5 μg/kg, 5 min before the end of surgery, may prolong recovery [115*,116]. Unfortunately results are inconsistent [117–119] and depend on factors such as anaesthetic agents, analgesic delivery, age, delirium scoring system, time of assessment, underlying disorder and type of surgery. Clonidine, for example, may have minimal impact in children with good analgesia after adenotonsillectomy [120]. A higher dose of intravenous dexmedetomidine (1 μg/kg) is more effective than lower doses after strabismus surgery [121*], whereas nasal dexmedetomidine 1–2 μg/kg is effective after cataract surgery [122*] and ambulatory surgery in children 3–7 years [123].

Shivering after anaesthesia

No drug is effective enough to be considered the gold standard for the management of postoperative shivering. Dexmedetomidine 1 μg/kg has some action compared to placebo on cold-induced shivering in adults,[124] but so does relaxation, breath holding and mental arithmetic [125*]. An adult meta-analysis showed a decrease in postanaesthetic shivering for those given dexmedetomidine (RR = 0.27; 95% CI, 0.19–0.36). Similar results are reported in children [126]. Although onset of effect is relatively fast (3.5 SD 0.9 min) after dexmedetomidine 0.5 μg/kg infused over 5 min [127], dexmedetomidine is no better than other drugs that have been used (e.g., tramadol) [128].

Opioid withdrawal

Clonidine remains popular for the management of opioid and benzodiazepine withdrawal symptoms in paediatric intensive care. There is a growing body of literature describing the use of dexmedetomidine in adults for this purpose. Evidence supporting such use in children is mostly anecdotal [7,129]. Regimens such as loading dose of 0.5–1.0 μg/kg administered over 5–10 min, followed by a continuous infusion at 0.1–1.4 μg/kg/h for a period of 1–16 days have been proposed [130].

One reservation is the fear of a withdrawal from dexmedetomidine itself after prolonged use (>24 h). Up to 80% of children (0–17 years) in an intensive care experienced withdrawal symptoms after infusion (0.42 SD 0.17 μg/kg/h) [131**,132*]. Prospective, controlled studies are needed to characterize the safety of long-term dexmedetomidine therapy in critically ill children [131**].

Epilepsy studies

Sedation for electroencephalography in uncooperative children is contentious because many
Regional blockade

The use of adjunct drugs in combination with local anaesthetics for neuraxial blockade both prolong block duration and improve block quality. Clonidine has direct central effects and has been long used as the preferred adjunct [144]. Dexmedetomidine has higher lipid solubility and is finding increasing use as an alternative to clonidine [145].

There is widespread use of dexmedetomidine to supplement local anaesthetics for paediatric caudal blockade. Although these studies demonstrate better pain scores compared to fentanyl [146], fewer adverse effects [147,148], prolongation of block duration [148,149*], dose optimization at 1 μg/kg [150*] and superiority of the single shot caudal route over the intravenous route [151], comparative data with clonidine are rare. A meta-analysis (n = 328) concluded longer duration of caudal analgesia compared to local anaesthesia alone (mean difference 8.21 h; 95% CI, 5.02–11.40) [152].

α2 adrenoceptor agonists together with local anaesthetics prolong the duration of peripheral nerve blockade. Whether this is a systemic effect or a local effect remains debated. Early exploratory data suggests that the use of dexmedetomidine as an adjunct to an ilioinguinal nerve block results in lower pain scores and less emergence agitation after paediatric inguinal hernia repair [153*]. A meta-analysis in children (n = 283, age: 0.8–13 years, weight 8–47 kg) determined block duration was prolonged with the use of α2-adrenoceptor agonists (9.75 vs. 3.75 h) compared to the use of plain local anaesthetics, that supplemental analgesics were reduced and that no serious adverse effects were evident. That meta-analysis did not provide specific support for dexmedetomidine over clonidine [154**].

CONCLUSION

Dexmedetomidine is proving useful in many diverse areas in paediatric anaesthesia. α2 receptors are certainly important in this field of medicine but have previously not been seen as the answer to so many vexing anaesthesia issues. Clonidine may be equally effective for some indications and monetary costs are far less. The shorter elimination half-life of dexmedetomidine may be beneficial in some
situations, and less useful in others. Unfortunately most of the published studies concerning dexmedetomidine are observational in nature, with limited control groups or comparators. Additional research in children is required before recommendations can be made regarding appropriate dosing, drug interactions and adverse effects (Table 1) [43,155,156,157*]. Dexmedetomidine currently has a firm position in the armamentarium of anaesthesia pharmacology. It is not the new all-in-one drug, but it is shaping up as a valuable adjunct for diverse indications within paediatric anaesthesia.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

• of special interest
•• of outstanding interest

34. Cardiac anesthesia using a lower dose of fentanyl 15 μg/kg when augmented with dexmedetomidine was as effective as fentanyl 30 μg/kg. Unfortunately, a dose-response relationship for fentanyl alone was not explored. The use of lower doses (10 μg/kg) without dexmedetomidine is now commonly used in recipes designed for early extubation.
36. A review of 14 randomized trials demonstrating dexmedetomidine (~0.5 μg/kg) administration in children reduces postoperative opioids consumption and post-operative pain in postanesthetic care unit (PACU). Impact on analgesia beyond PACU or effect of subsequent dexmedetomidine dosing requires further investigation.

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regardless of provider. Airway obstruction was the most common serious adverse event at 7 days. The trial used standard care rather than comparators such as midazolam, clonidine or propofol. Extrapolation of these results to children remains uncertain. An adult study pointing to benefits from sedation using dexmedetomidine in infants less than 36 months given fentanyl/dexmedetomidine rather than midazolam does not negate the usefulness of dexmedetomidine, a major benefit for many children.

Intranasal dexmedetomidine is easy to administer and a useful adjunct when chloride hydrate (50 mg/kg) fails to adequately sedate for MRI. The authors noted that rescue sedation 2 μg/kg increased time to arousal after the scan when compared to 1 μg/kg.

A retrospective review showing intranasal dexmedetomidine, like chloral hydrate, provides effective sedation for ABR examinations, with the benefits of an ability to begin the test sooner and complete the examination with a single dose, in addition to a decreased incidence of hypoxemia. The question of superiority of one drug over the other remains hanging.

A prospective study using intranasal dexmedetomidine, like chloral hydrate, for sedation of infants undergoing cranial ultrasound and the proportion of children whose parents reported a return to baseline activity on the day of testing was also greater. Better understanding of the usefulness of these two drugs could be made if the response or concentration-response curves for each drug were characterized.

A prospective study found that intranasal dexmedetomidine is well tolerated and safe for sedation in children of all ages during MRI. In this respect, the study showed that intranasal dexmedetomidine is an effective and safe sedative agent for EEG or auditory brain response testing. Pediatric Anesthesia 2016; 26:273–279.

A follow-up study to the one above where completion rates for ABR with a single dose of sedation (3 μg/kg) were higher than those given chloral hydrate (50 mg/kg). The time to successful testing start was shorter for dexmedetomidine and the proportion of children whose parents reported a return to baseline activity on the day of testing was also greater. Better understanding of the usefulness of these two drugs could be made if the response or concentration-response curves for each drug were characterized.

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73. Children with respiratory morbidities are at increased risk of developing adverse respiratory events, even with dexmedetomidine. Data from this retrospective review demonstrate that dexmedetomidine deep sedation was well tolerated in children with significant respiratory morbidities. Moreover, children younger than 1 year of age did not receive lower dexmedetomidine dose than children older than 1 year of age for the same sedation level, consistent with reduced clearance in that age group.
This prospective, randomized, controlled study in 60 children, aged 1-7 years old, showed premedication with oral dexmedetomidine 4 μg/kg produced equally effective preoperative sedation and a better recovery from anaesthesia in comparison to oral midazolam 0.75 mg/kg. The dose of both drugs differ from other similar studies, highlighting our lack of dose equivalence understanding.
Another study comparing midazolam (0.5 mg/kg) and dexmedetomidine (2 μg/kg) PO; similar results were reported in each group, although acceptance of a mask at induction was better in those given dexmedetomidine.
This meta-analysis showed dexmedetomidine was associated with shorter length of mechanical ventilation, lower postoperative fentanyl and morphine requirements, reduced stress response and lower risk of delirium. Dexmedetomidine caused an increase the bradycardia and hypotension risk. Unfortunately results rely on data from observational studies and randomized controlled trials are few.
101. It appears increasingly that all available drugs have some effect on cells involved in neurodevelopment. The meaning and the clinical significance of these findings in humans remains to be established. Dexmedetomidine produced significant cellular degeneration and apoptosis in primary sensory brain regions, but nonsignificant changes in limbic regions (as was observed with ketamine). Uncertainty remains about whether this makes dexmedetomidine a better drug than ketamine in human infants.
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Drugs in anesthesia


115. This paper is concerning because dexmedetomidine is increasingly used for sedation after cardiac surgery in children. Physicians should be aware of the potential for withdrawal seizures in infants after surgery for congenital heart disease.


117. The differences of dexmedetomidine and chloral hydrate in EEG power did not change the EEG qualitative interpretation, which was similar with the two drugs.

118. Other studies comparing natural sleep and sleep induced by these drugs are needed to clarify the clinical relevance of the observed EEG quantitative differences.


121. The authors also suggest an alternative management to amiodarone. It would be useful to know if these results can be reproduced in younger children.

122. The use of isoproterenol can interfere with the conduct of electrophysiological studies for SVT and the successful ablation of such arrhythmias. It did however result in a greater need for isoproterenol.

123. Perioperative use of dexmedetomidine or amiodarone infusion was associated with a lower incidence of JET as compared to placebo in children 2–18 years. These data suggest an alternative management to amiodarone. It would be useful to know if these results can be reproduced in younger children (<2 years), a higher risk group for undergoing tetrology of Fallot repair.

124. The authors argue that incorporating a drug that reduces emergence delirium into the technique used to prevent emergence delirium. Medications used for treatment of pediatric emergence delirium (TIVA) was considered by 38% of respondents as a good auxiliary drug.


126. This survey of Canadian Pediatric Anesthesiologists revealed that total intravenous anesthesia (TIVA) was considered by 38% of respondents as a good technique used to prevent emergence delirium. Medications used for treatment included propofol, midazolam, fentanyl, and lornoxicam (4%). 87% of respondents rated effectiveness of treatment as ‘usually works quickly with one dose’. The survey highlights the need for further investigation.


128. The authors argue that incorporating a drug that reduces emergence delirium into an anesthetic that uses sevoflurane is better than treating emergence agitation when it occurs postoperatively. Dexmedetomidine ranked highly compared to other drugs such as fentanyl, sufentanil, ketamine, clonidine, remifentanil, propofol, and midazolam.


132. Dexmedetomidine 0.3 µg/kg reduced the incidence of emergence delirium after intra-umbilical surgery but this was at the expense of greater incidence of sedation in the recovery period. These results are a little surprising given the low dose of dexmedetomidine used; they point to the need for a dose response relationship to be characterized.


139. Strabismus surgery is associated with a high incidence of emergence delirium. The use of nasal dexmedetomidine as a premedicant was associated with reduced emergence delirium in PACU. Comparative data with other drugs are lacking.


141. Intra nasal dexmedetomidine 1 µg/kg was more effective than clonidine 4 µg/kg in decreasing the incidence and severity of EA, when administered 45 min before the induction of anesthesia with sevoflurane for paediatric day care surgery. Interpretation of these data is difficult; an understanding of dose-response relationships for each drug would help.


145. While dexmedetomidine was effective to reduce shivering after anesthesia, its effect was similar to other widely used antishivering agents, such as fentanyl, meperidine, tramadol or clonidine.
This meta-analysis compared dexmedetomidine to clonidine as an intrathecal adjunct in adults. There was a slight difference in onset of sensory block (40 s). The duration of stable sensory block, duration of overall sensory block, and the time before the need for analgesic requirements were extended, 10.8, 22.3 and 38.6 min, respectively, when dexmedetomidine was used as an adjuvant to local anesthetics. Compared to clonidine, the addition of dexmedetomidine as an adjuvant to local anesthetics was associated with earlier, prolonged sensory block characteristics and later need for analgesic requirements. A similar study is required for children.


The mean duration of effective analgesia in those children undergoing infraumbilical surgery given dexmedetomidine as an adjunct (9.9 SD 0.9 h) was twice that of those without (4.3 SD 1.0 h). Although postoperative pain scores are reported less in those given dexmedetomidine, the clinical difference is minor. Similar results were posted by Kamal et al. (146).


Al-Zaben KR, Qudaisat IY, Alja’bari AN, et al. The effects of caudal or intravenous dexmedetomidine on postoperative analgesia produced by caudal bupivacaine in children: a randomized controlled double-blinded study. J Clin Anesth 2016; 33:386–394. Debate exists about whether effects of caudal dexmedetomidine are systemic or local. These authors noted that compared to IV administration, caudal administration of dexmedetomidine during caudal bupivacaine anaesthesia provided prolonged postoperative analgesia and a greater analgesic sparing effect without significant adverse effects. This suggests a greater role of neuraxial compared to that of peripheral α₂-adrenoceptors in pain processing.


This single centre study noted that the use of dexmedetomidine as an adjunct to iliopulvar or iliopulvagastic block resulted in less pain during early recovery following paediatric inguinal hernia repair. In addition, the use of adjunct dexmedetomidine was associated with a prolongation of the period to first supplemental analgesia demand.

Lundblad M, Trifa M, Kaabachi O, et al. α₂ adrenoceptor agonists as adjucents to peripheral nerve blocks in children: a meta-analysis. Pediatr Anesth 2016; 26:232–238. This is a follow-up study to the one above. Although raw data from only five studies were gathered and aggregated, this meta-analysis provides evidence-based support for the use of adjunct α₂ adrenoceptor agonists when performing peripheral nerve blocks in children. Block duration was significantly prolonged (9.75 vs. 3.75 h) compared to the use of plain local anaesthetic.

The authors report 1 μg/kg caudal dexmedetomidine achieved comparable prolongation of postoperative analgesia to 2 μg/kg dose, with shorter duration of postoperative sedation and lower incidence of other side effects.

The authors list suggestions for future studies that may improve our knowledge of this drug and how best to use it clinically.