Malaysian Society of Paediatric Anaesthesiologists (MSPA)

Asian Society of Paediatric Anaesthesiologists

Dexmedetomidine in Pediatric Anesthesia

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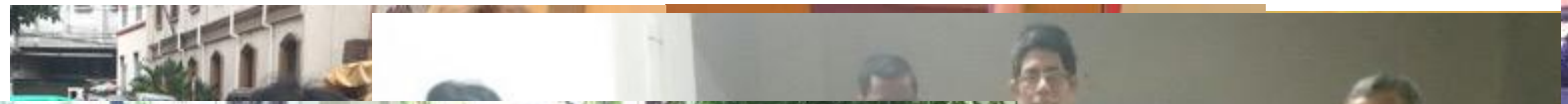
ACIBADEM ÜNİVERSİTESİ

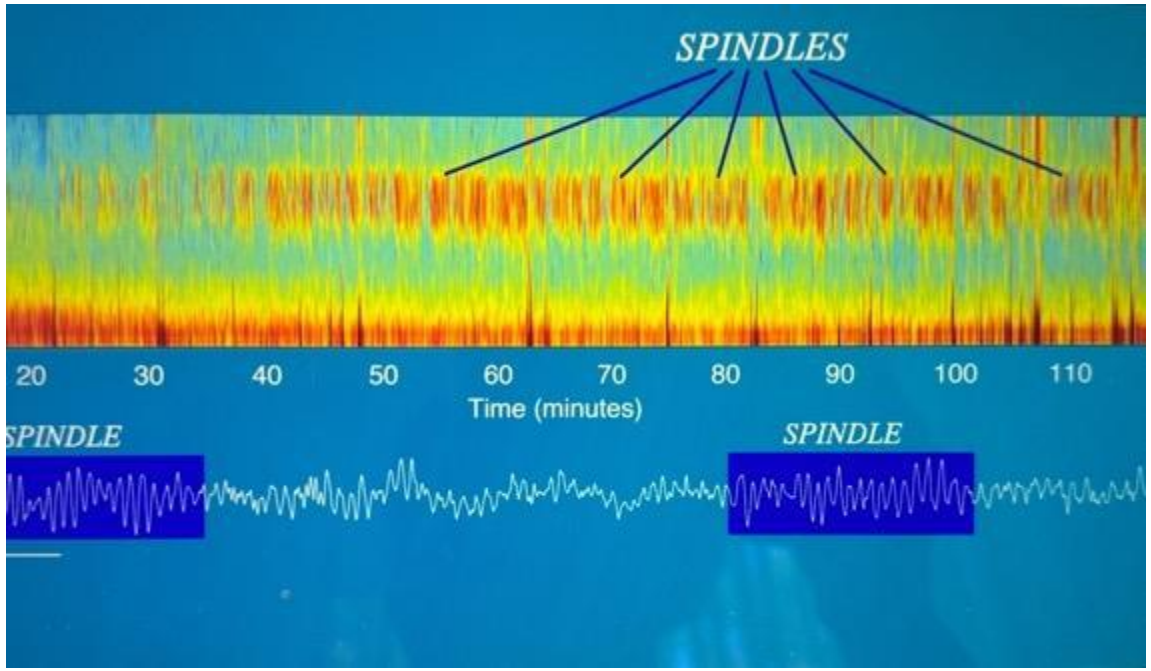
Disclosures ASPA Family





Outline

- Benefits of dex in ped anesthesia
- Potential adverse effects
- Indications for use
- Clinical applications
- Updates, Effective doses
- Safety considerations
- Future directions and research



What is dexmedetomidine?

Sedative

Despite a strong evidence base for the use of DEX in paediatric anaesthesia, its use is currently '**off-label**'

α_2 receptor activation

ELSEVIER

Revalidation FOR ANAESTHETISTS
RCA Revalidation matrix
Matrix codes: 1A01, 2D02, 2D05, 2D06, 2E01, 2G01, 3A01, 3A02, 3D00

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Dexmedetomidine in paediatric anaesthesia

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Highly selective α_2 agonist

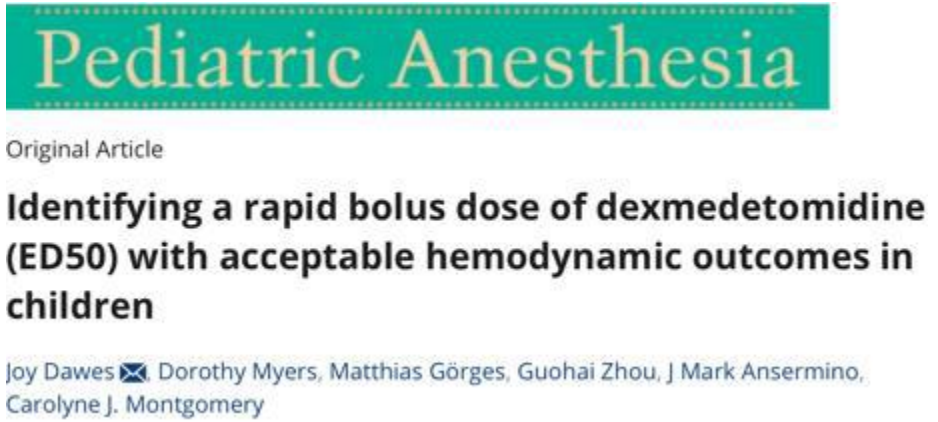
- Parallels natural sleep
- Anxiolysis
- Sympatholysis
- ***Without clinically significant respiratory depression***

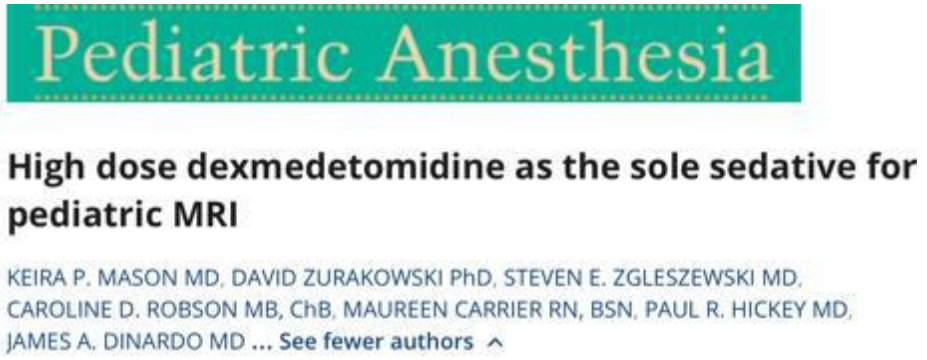
Pharmacokinetics vs Pharmacodynamics

Highly lipofilic
Vd high both in adults and children
Bound to plasma proteins; albumin and α_1 glycoprotein
Crosses BBB
Broken down by hepatic enxymes UDPGT and cytochrome P450 to inactive metabolites
Half-life 2 h (contex sensitive; 4 min after 10 min infusion, 250 min after 8 h infusion)
Clearance changes with age; Neonates and <1 y reduced

Updates on Pharmacology

- ***DEX clearance***; significantly decreased at birth and increases over the first month in full-term neonates following cardiac surgery
- Scaled pharmacokinetic models in term neonates showed higher clearance of intravenous DEX compared to previous reports
- Age, weight, duration of cardiac bypass, and presence of an intracardiac shunt contribute
- DEX clearance in children with compromised hepatic function is inversely proportional to the international normalized ratio (INR)



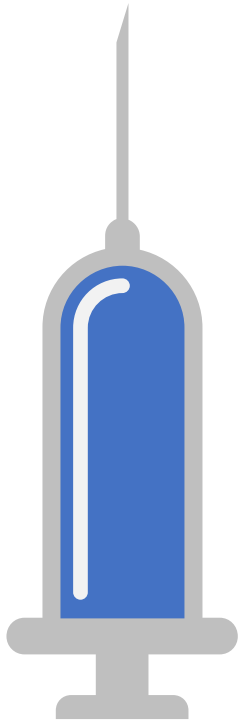


PK and PD

- Dose dependent effect on MAP and BP
- Mean ED50 i.v. given over 5 s without significant hemodynamic changes is 0.49 mic/kg TIVA
- Transient Dex-induced hypertension; after repeated boluses of 2-3 mic/kg
- Bradycardia %30 baseline

Routes of Administration

Dex other than vascular

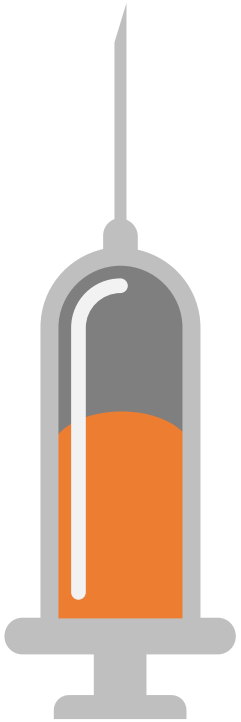


Intranasal

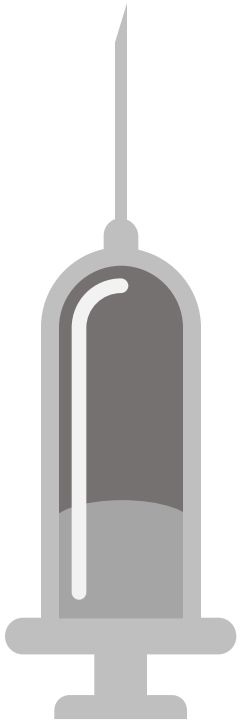
2-4 mic/kg, 1-3 mic/kg procedural sedation

Intranasal DEX achieved sedation within 20-45 minutes with 84% bioavai

Atomized

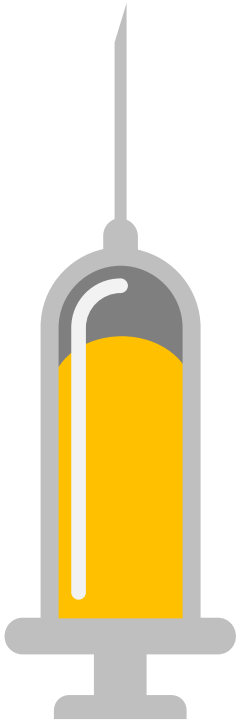


Intramuscular



Buccal

20% failure, may go oral



Subcutaneous

recently

Benefits of dexmedetomidine in pediatric anesthesia

- Sedative properties /preserving respiratory function
- Analgesic effects
- Anxiolytic properties
- Hemodynamic stability /ability to attenuate sympathetic responses to surgical stimuli

Indications for use

- Primary sedative agent
- Adjunct to general anesthesia
- Procedural sedation outside the OR
- Tailoring dosage based on weight and age; individualized dosing regimens to achieve optimal sedation and analgesia while minimizing adverse effects

Uses for Surgical and Nonsurgical Procedures

- ENT
- Cardiac
- Neonatal
- Neurosurgery
- ED
- Procedures in Radiology
- Use as an analgesic adjunct
- ‘Postmedication’

A Comparison of the Sedative, Hemodynamic, and Respiratory Effects of Dexmedetomidine and Propofol in Children Undergoing Magnetic Resonance Imaging

Ahmet Koroglu, MD*
Huseyin Teksan, MD†
Ozlem Sagır, MD*
Aytaç Yucel, MD*

We compared the sedative, hemodynamic, and respiratory effects of dexmedetomidine and propofol in children undergoing magnetic resonance imaging procedures. Sixty children were randomly distributed into two groups: The dexmedetomidine (D) group received 1 $\mu g/kg$ initial dose followed by continuous infusion of 0.5 $\mu g \cdot kg^{-1} \cdot h^{-1}$ and a propofol group (P) received 3 mg/kg initial dose followed by a continuous infusion of 100 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Inadequate sedation was defined as difficulty in completing the procedure because of the child's movement during magnetic resonance imaging. Mean arterial pressure (MAP), heart rate, peripheral oxygen saturation, and respiratory rate (RR) were recorded [illegible] of sedation, recovery, and discharge.

Anesth Analg. 2006 Jul;103(1):63-7

Dex/propofol 60 pt.s

***Propofol*; onset of sedation, recovery, discharge times significantly shorter, significantly lower MAP and RR**

***Dex*; less hypotension and desaturation**

Less respiratory depression

Original Article

SAGE Open Medicine

SAGE Open Medicine
Volume 5: 1–7

DOI: 10.1177/2050312117729920
journals.sagepub.com/home/smo
SAGE

Dexmedetomidine provides less body motion and respiratory depression during sedation in double-balloon enteroscopy than midazolam

Hiroshi Oshima[1], Masanao Nakamura[1], Osamu Watanabe[1], Takeshi Yamamura[2], Kohei Funasaka[1], Eizaburo Ohno[1], Hiroki Kawashima[1], Ryoji Miyahara[1], Hidemi Goto[1] and Yoshiki Hirooka[2]

Updates

Postprocedural applications

Postanesthesia recovery	Neonatal ICU	Pediatric ICU	Palliative Care
Improves	**Sedation**	**Sedation**	**Sedation/Analgesia/ Anxiolysis**
Critically ill; bronchoscopy, first attempt extubation Decrease cough; intratracheal 1 mic/kg Decrease ED Nausea & vomiting? Ketamine delirium?	0.2 mic/kg bolus, 0.2 mic/kg inf ? <2 y decrease doses 0.2-0.3 mic/kg 0.5 mic/kg withdrawal symptoms	hasten weaning off ventilator facilitates NIV,ventilator synch, improves lung recruitment avoids invasive ventilatory support Prophy Tx (JET) post-cardiac surgery	Arousable, interactive Intractable sleep disorders

Dex 3 mic/kg
IN
Atomiser/drops

279 pt.s <3 years
undergoing Transthoracic ECHO
Success rate 84%/82%
Less successful in older children

Anaesthesia 2016, 71, 522–528

Original Article

A comparison of intranasal dexmedetomidine for sedation in children administered either by atomiser or by drops

B. L. Li,[1] N. Zhang,[2] J. X. Huang,[1] Q. Q. Qiu,[2] H. Tian,[3] J. Ni,[4] X. R. Song,[4] V. M. Yuen[5] and M. G. Irwin[6]

Updates
Airway collapsibility and Respiration

Mimicks natural sleep	Safe in OSA and Down Syndrome	Maintain spontaneous ventilation
Upper airway tone	DISA, Dynamic airway imaging	Pulmonary function testing IN 2.64 mic/kg

Airway collapsibility and Respiration

Improve intubating conditions

tracheal intubation without NMB

Increase tolerance to ETT

Decrease MAC Sevo smooth extubation

Diminish laryngeal responses

Obtunding airway reflexes

Broncoscopy

Updates
Inflammation and Immune System

Antiniflammatory properties

Supress surgical stress and inflammation, preserve immunity

Alleviates perioperative stress

Stabilize the integrity of blood-spinal cord barrier

Improve neuronal viability, protect the spinal cord from ischemia-reperfusion injury

Reduce inflammatory cytokine levels

Updates
Cardiovascular

- Caution: Bradycardia
- Depressed left ventricular function
- Recent high degree AV block
- Volume depletion
- Drugs; digoxin, beta blockers, Ca-canal blockers, Amiodarone

Relative Contraindications or precautions to the use of Dex in children

- Rapid bolus of dexmedetomidine with high blood concentrations of volatile anaesthetics
- Cardiac conduction abnormalities
- Septic shock
- Concurrent treatment with digoxin, β-adrenergic blockers, calcium channel blockers, monoamine oxidase inhibitors or other agents that predispose to bradycardia or hypotension[13]
- Chronic hypertension
- Hepatic disease

Synergistic Effects

Adjunct to LA;

increases duration, motor and esp sensory blockade

prolongs analgesia increases patient satisfaction

decreases postop opioid consumption

Propofol and remifentanil infusion

15-20 % decreases

0.5-2 mic/kg preop

Updates
Thermal Regulation

- Decreases vasoconstriction; role in thermoregulatory shivering
- Adult studies ; superiority over placebo
- Febrile episodes – case reports
- Temperature monitoring!

Updates
Organ protective effects
Neuroprotective

- Alleviate brain damage caused by anesthetics, reducing apopitosis in cortical and subcortical regions (animal)
- Reversed the damage in cognitive decline and inflammation via vagomimetic and humoral pathways
- Protects spinal cord against lidocaine-induced spinal neurotoxicity
- TBI; prevented tissue loss and cell death, also reduced axonal injury and synaptic degeneration, resulting in improvement of motor function

Pan, W.; Lin, L.; Zhang, N.; Yuan, F.; Hua, X.; Wang, Y.; Mo, L. Neuroprotective Effects of Dexmedetomidine Against Hypoxia-Induced Nervous System Injury are Related to Inhibition of NF-kappaB/COX-2 Pathways. Cell. Mol. Neurobiol. 2016, 36, 1179–1188.

Perez-Zoghbi, J.F.; Zhu, W.; Grafe, M.R.; Brambrink, A.M. Dexmedetomidine-mediated neuroprotection against sevoflurane-induced neurotoxicity extends to several brain regions in neonatal rats. Br. J. Anaesth. 2017, 119, 506–516.

Shan, Y.; Yang, F.; Tang, Z.; Bi, C.; Sun, S.; Zhang, Y.; Liu, H. Dexmedetomidine Ameliorates the Neurotoxicity of Sevoflurane on the Immature Brain Through the BMP/SMAD Signaling Pathway. Front. Neurosci. 2018, 12, 964

Updates *Organ protective effects*

Renoprotective

- Possible protective effect on cardiac surgery-associated acute kidney injury
- Promotes renal blood flow via inhibiting vasoconstriction
- Promotes diuresis effect via decreasing renin and arginine vasopressin
- Increases glomerular filtration
- Reduces reactive oxygen species
- Decreases systemic inflammatory response
- Reduces renal cell death

Bayram, A.; Ulgey, A.; Baykan, A.; Narin, N.; Narin, F.; Esmaoglu, A.; Boyaci, A. The effects of dexmedetomidine on early stage renal functions in pediatric patients undergoing cardiac angiography using non-ionic contrast media: A double-blind, randomized clinical trial. Paediatr. Anaesth. 2014, 24, 426–432.

- (6 months–6 years) received intravenous iodine contrast for cardiac angiography
- The use of DEX as an adjuvant to sedative agents decreased elevation in plasma endothelin, renin, and markers of acute renal injury in these children- RCT

Updates
Organ protective effects
Cardioprotective

- Mediated via the cholinergic anti-inflammatory pathway
- Blocks the sympathetic nervous system
- Blunts hemodynamic responses to perioperative stress
- Controls heart rate
- Optimizes blood flow in the coronary arteries

- DEX-ketamine combination can attenuate myocardial ischemia-reperfusion injury during cardiac surgery

Ríha, H.; Kotulák, T.; Bˇrezina, A.; Hess, L.; Kramáˇr, P.; Szárszoi, O.; Netuka, I.; Pirk, J. Comparison of the effects of ketamine-dexmedetomidine and sevoflurane-sufentanil anesthesia on cardiac biomarkers after cardiac surgery: An observational study. Physiol. Res. 2012, 61, 63–72.

ketamine-DEX-based anesthesia on the release of cardiac biomarkers was compared with that of sevoflurane/sufentanil-based anesthesia

Safety considerations /Adverse effects and how to manage

Bradycardia, hypotension, prolonged sedation

Drug interactions and precautions

Dex induced bradycardia

- Anticholinergics should be avoided in the absence of hemodynamic instability
- Small doses of glycopyrolate – severe hypertension in pt.s receiving Dex
- Have not been reported of clinical relevance, like in natural sleep
- Positive effect on SVT – IN 4mic/kg –case report
- Not associated with a reduction in PSVT inducibility