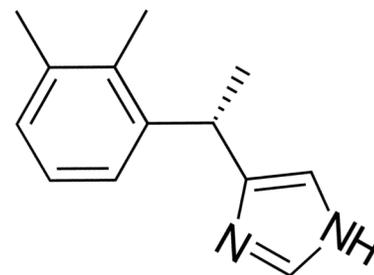


Dexmedetomidine

Mechanism of Action^{1,2}

- Highly selective α_2 receptor agonist (G-protein coupled receptor)
 - 8 times more specific for α_2 adrenoreceptors than clonidine (ratio of α_2 : α_1 activity 1620:1 for dexmedetomidine, 220:1 for clonidine)
- Presynaptic activation of α_2 receptor inhibits release of norepinephrine, terminating propagation of pain signals
- Postsynaptic activation of α_2 receptor inhibits sympathetic activity
- Sedative and analgesic effects via locus ceruleus and additional analgesic effects via spinal cord



Pharmacokinetics^{1,2,3}

- Plasma half-life = 2-2.5 hours
- 94% protein-bound (mostly albumin)
- Distribution half-life = 5-6min
- Elimination half-life = 2 hours
- Metabolized by liver via glucuronidation and cytochrome P450
- 95% renal excretion

Dosing^{3,4}

- Intravenous (analgesia, sedation, withdrawal):
 - Loading dose: 0.5-1.0mcg/kg over 10min
 - Infusion: 0.2-0.7mcg/kg/hr
- Intramuscular (premedication):
 - 2.5mcg/kg
- Neuraxial/Regional (analgesia):
 - Epidural – 1-2mcg/kg
 - Spinal – 0.1-0.2mcg/kg
 - Peripheral nerve block – 1mcg/kg

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Side Effects & Limitations⁴

- No absolute contraindications
- Mainly hemodynamic including hypertension, hypotension, and bradycardia as a result of vasoconstriction, sympatholysis, and baroreflex-mediated parasympathetic activation
- No reversal agent currently approved for use in humans

Opioid Reduction^{5,6}

- Multiple studies investigating a variety of surgical cases have demonstrated significant reduction in postoperative pain scores and opioid consumption with use of dexmedetomidine
- Several meta-analyses investigating dexmedetomidine's role in perioperative opioid reduction are shown below:

Author, year	Study	Comparison	Conclusions
Blaudszun, 2012	Meta-analysis of 30 RCTs in noncardiac surgery under GA	Systemic α_2 agonists compared with placebo or no treatment	Perioperative α_2 agonists DECREASED postoperative opioid consumption, pain intensity, and nausea
Liu, 2017	Meta-analysis of 11 RCTs in neurosurgery	Dex compared with placebo or opioids	Dex REDUCED pain intensity and perioperative opioid consumption
Bot, 2015	Meta-analysis of 18 RCTs in adults	Dex compared with placebo	Dex REDUCED postoperative opioid consumption and pain

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