

**WHEN AND FOR HOW LONG SHOULD DEXMEDETOMIDINE BE USED IN THE INTENSIVE CARE UNIT**

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ABSTRACT

Dexmedetomidine is a novel sedative that was approved for use in the US at the end of the last century. Currently, the FDA labeling for its use are: sedation in non-intubated patients prior to and during surgical and other procedures, and in intubated and mechanically ventilated patients during treatment in an intensive care setting and to be administered by continuous infusion not to exceed 24 hours. Multiple investigations for other indications and prolonged durations have caused controversies for its use. Given the risks of this medication, strict adherence to guidelines for its use is recommended. The aim of this review is to discuss the approved and the not yet approved indications to use this medication.

Keywords: Sedation, analgesia, ICU

Dexmedetomidine is a potent α_2 -adrenoceptor agonist that has eight times greater specificity for α_2 receptors than does clonidine.^[1] It is a novel medication which was approved in the US in 1999. It has potent sedative, opioid sparing analgesic, and sympatholytic effects which has the additive benefit of sparing the respiratory drive, but with no anticonvulsant properties.^[2] The onset of sedation occurs within 15 minutes after a loading bolus and peak sedation occurs within 1 hour of starting continuous intra-venous infusion. It is rapidly redistributed into peripheral tissues and is metabolized by the liver with a half life of approximately 3 hours.^[3]

Side effects include: hypotension, bradycardia, sinus arrest usually occur during the loading dose but can occur during the continuous infusion. Withdrawal can occur in about 5% of patients who had prolonged infusion for more than 7 days, usually in the form of nausea, vomiting, agitation, tachycardia and hypotension.

Project IMPACT published in 2007^[4], showed that its use has significantly increased by 4% since 2001. As more studies appear in the literature, this review aims to clarify the current approved indications and duration of infusion from the non-approved ones.

Approved indications:

Sedation for mechanically ventilated patients post operatively (approved indication in 1999). Though there have been no differences in days of mechanical ventilation, ICU length of stay or mortality, the latest guidelines for pain, agitation and sedation published 2013, granted level 2B evidence for dexmedetomidine use in ICU, "We suggest that sedation strategies using non-benzodiazepine sedatives (either propofol or dexmedetomidine) may be preferred over sedation with (either midazolam or lorazepam) to improve clinical outcomes in mechanically ventilated adult ICU patients".^[5] Compared to conventional post operative management, the use of dexmedetomidine has shown better sedation and analgesia with less rescue therapy

with sedatives and analgesics in post operative patients that are undergoing mechanical ventilation for less than 24 hours.^[2,6] Sedation in non intubated patients undergoing surgical and other procedures (approved indication in 2008)

Dexmedetomidine safety and efficacy in non-intubated patients requiring sedation for surgical and diagnostic procedures has been evaluated prospectively.^[6] The MAC DEX study involving 326 patients, demonstrated that the use of dexmedetomidine for procedures requiring monitored anesthesia care is safe and superior to the combination of midazolam and fentanyl.^[7]

Non-approved indications:

Adjunctive therapy for alcohol withdrawal
Given its characteristic pharmacologic action as a potent alpha-2 receptor antagonist, case reports have examined the adjunctive role of dexmedetomidine to benzodiazepines in the treatment of alcohol withdrawal syndrome. Those reports found that “dexmedetomidine successfully controlled psychomimetic and sympathetic symptoms of withdrawal, an effect that was seen almost immediately following initiation of this medication”^[8]

ICU delirium

Compared to lorazepam, dexmedetomidine have shown reduction in the incidence of delirium and coma post mechanical ventilation.^[9] Similar results

were found in post operative cardiac surgical patients compared to propofol and midazolam.^[10] Another study demonstrated that dexmedetomidine was superior to haloperidol in treatment of ICU delirium.^[11]

Duration of more than 24 hours

The MENDS trial^[12] compared dexmedetomidine versus lorazepam for 5 days in medical patients with sepsis. The trial results showed less incidence of delirium, more ventilator free days, however, no mortality difference. Similar results were found in the SEDCOM trial when dexmedetomidine was compared to midazolam for more than 24 hours (3.5 days).^[13]

Treatment for acute and chronic pain:

Dexmedetomidine has been studied in the treatment of acute and chronic pain syndromes e.g. spasticity, myofascial pain, neuropathic pain, complex regional pain, chronic headaches, cancer pain, and palliative care.^[14]

Conclusion:

Despite the recent data and the promising results in the literature. More data are needed for its use outside the current FDA approved indications. Knowledge of its safety profile and adverse effects are crucial. We suggest restricting its use in specific inpatient areas (operating room, recovery room, ICU).

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