PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #280
DEXMEDETOMIDINE

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Background Dexmedetomidine (Precedex) is a relatively new drug with sedative and analgesic properties. It is FDA approved for short-term sedation of non-intubated patients undergoing surgery or a medical procedure or in intubated patients in the intensive care unit (ICU) unit. There has been increasing interest in its use in end-of-life settings. This *Fast Fact* reviews dexmedetomidine's use relevant to palliative care.

Pharmacology Dexmedetomidine is an intravenous, relatively selective, alpha-2 adrenergic receptor agonist. In the ICU, its FDA approved use is only up to 24 hours, however, published reports indicate it is being used for longer periods (1-3). It can be given as a infusion (e.g., for ventilator sedation) or a bolus (e.g., for procedural sedation). Its onset of action is 5-10 min, peak affect 15-30 min, with duration of action of 60-120 min after a bolus. It is 94% protein bound and metabolized in the liver to renally excreted metabolites. Its elimination half-life in healthy adults is ~2 hours (4). Besides sedation and analgesia, its major clinical effects are related to the generally sympatholytic effects of alpha-2 agonism: bradycardia and hypotension. When administered at standard infusion rates, a transient increase in blood pressure often occurs followed by a sustained lower blood pressure of ~10-20% below baseline (5). Unlike most sedatives, it is not known to suppress respiratory drive at clinically relevant doses (6,7).

Clinical Findings – Mechanically Ventilated Patients There has been much interest in investigating dexmedetomidine's promise as a superior sedative for mechanically ventilated patients in the ICU. Results have been mixed as to whether it provides a meaningful improvement over other agents, notably benzodiazepines and propofol. Some studies have shown dexmedetomidine use is associated with less delirium, shorter ICU lengths of stay, and decreased time to extubation (8-13), but these finding have not been universal (10). Compared to propofol and midazolam, at any given level of sedation, dexmedetomidine does improve patients' ability to communicate pain (8,11). In all these studies, bradycardia was found to be significantly worse in dexmedetomidine patients compared to benzodiazepines or propofol.

Clinical Findings – Pain Sub-sedating doses of dexmedetomidine have been used as an analgesic, although there are no controlled clinical trials investigating this specific use. Two case reports in patients with severe, refractory cancer pain found the temporary use (~3-6 days) of dexmedetomidine at 0.2-0.6 mcg/kg/hour greatly reduced the patient's pain, while alternative analgesic modalities were explored (1,14). There has also been an intriguing case series published, describing the use of dexmedetomidine for suspected opioid-induced hyperalgesia (OIH; see *Fast Fact* #142) (3). In this case series, patients on high-dose opioids with suspected OIH were transferred to the ICU, if not already there, and given dexmedetomidine at rates of 0.2-0.7 mcg/kg/hour for 2-7 days. Coincident with initiating the infusion, opioid doses were decreased, and on average patients' opioid doses were decreased by ~70% with apparently equal or better analgesia. The authors note they suspect dexmedetomidine "'reboots' opioid sensitivity," although the true mechanism of action for this effect, if even real, has not been determined.

Clinical Findings – Symptoms at the End-of-Life Given the observation that patients sedated with dexmedetomidine appear to remain more arousable and interactive compared to patients sedated with benzodiazepines, there has been interest in using dexmedetomidine to manage delirium as well as provide sedation, anxiolysis, and analgesia for patients with severe symptoms near the end-of-life, while avoiding the need to deeply sedate patients to unconsciousness (see *Fast Facts* #106, 107) (14,15). One case series indicated some success with this practice (15). In this series, boluses of 1 mcg/kg were used, followed by infusions of 0.2-0.6 mcg/kg/h for 5-48 hours. A pilot-study is underway to further investigate this use of dexmedetomidine (16), but currently there are no more data to guide clinicians.

Cost: Dexmedetomidine is available in a 200 mcg vial for $55.00 (17). For comparison midazolam is available in a 5 mg vial for $5.00 and propofol in a 200mg vial for $10.00 (17,18). Thus, dexmedetomidine is ~3-4 times more expensive than midazolam and propofol.

Summary Dexmedetomidine is a unique sedative, and there is interest in its use as an analgesic and for end-of-life symptom control. Its expense, need for close monitoring during its use (including, for most institutions, ICU monitoring), and lack of controlled clinical trials, currently prohibit any recommendation for its use outside of the ICU setting.

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