The Use of Dexmedetomidine for Sedation in the Pediatric Intensive Care Unit

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Introduction

Abstract

Dexmedetomidine is a centrally acting alpha2-adrenergic agonist that provides sedation with minimal respiratory depression. The medication's targeted activation of alpha2 receptors mediates its sedative, anxiolytic, and analgesic effects. Although dexmedetomidine is approved only for sedation in adults, it is currently being used off-label as an adjunctive agent in pediatric patients for sedation and analgesia in the critical care unit and for sedation during non-invasive procedures in radiology. Despite the lack of large randomized controlled trials, available literature and case studies suggest dexmedetomidine may be an effective alternative or adjunctive sedative in pediatric patients.

The purpose of this study is to evaluate the use of dexmedetomidine in the Pediatric Intensive Care Unit (PICU) at Blank Children’s Hospital (BCH) by assessing safety, efficacy, dosing, and duration of dexmedetomidine courses in mechanically ventilated infants and children. The study will also assess length of stay, time on the ventilator, extubation while receiving dexmedetomidine infusion, and necessity for use of other sedatives and analgesics.

These objectives will be assessed through retrospective chart review of all patients who received dexmedetomidine while in the PICU between March 2007 and January 2009. Analysis will include descriptive statistics on the data obtained. The results will add to the small volume of existing evidence regarding dexmedetomidine’s use in the pediatric population.

Dexmedetomidine (Precedex®)

- Approved for use by the FDA in 1999 for sedation of mechanically ventilated patients in the ICU.
- 2008 update includes non-inhaled patients.
- Dosing range: 0.2 to 0.7 µg/kg/hr.
- Mechanism of action:
  - Centrally-acting α2-adrenergic agonist
  - Sedative, anxiolytic, and analgesic
  - Mediates sedation with minimal respiratory depression
  - Analgesia related to effects on release of substance P

Dexmedetomidine & Pediatrics

- Off-label use in pediatrics as adjunctive agent for sedation and analgesia
- Available literature is small, case studies and reports
- Potential advantages over other sedatives
- Minimal respiratory depression
- Analgesia: decreased supplemental opioid needs

Objectives

To evaluate the use of dexmedetomidine in intensive care infants and children.

- Patients were grouped as <12 months and >12 months of age.
- Safety and efficacy of the drug were determined as follows:
  - Length of stay in the intensive care unit
  - Ability to extubate off of other sedatives and narcotics
  - Time on the ventilator and extubation while receiving dexmedetomidine

Methods

- Retrospective chart review
- March 2007 through January 2009
- Pediatric Intensive Care Unit (PICU) at Blank Children’s Hospital
- Iowa Methodist Medical Center – Des Moines, Iowa

Table 1: Patient Population

Baseline characteristics (n = 17)

<table>
<thead>
<tr>
<th>Age, median, yrs</th>
<th>3.5 (19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;12 months, n%</td>
<td>5 (29)</td>
</tr>
<tr>
<td>Male, n%</td>
<td>12 (70)</td>
</tr>
</tbody>
</table>

- Underlying medical conditions, n%:
  - Respiratory: 8 (47)
  - Neurological and/or Behavioral: 7 (41)
  - Other: 4 (24)

- Admission diagnosis, n%:
  - Respiratory: 14 (82)
  - Neurological: 5 (9)
  - Trauma: 4 (9)

- PRISM III score on admission:
  - Mean (range): 2 (0-8)

Figure 1: Dexmedetomidine’s Effect on the Alpha, Receptor

Figure 2: Alpha2 receptors in the locus ceruleus of the brain stem generate sedative and anxiolytic effects

Figure 3: Dexmedetomidine has an effect on opioid and locu ceruleus

Data

Table 2: Dexmedetomidine Dosing

<table>
<thead>
<tr>
<th>Dose, mg</th>
<th>Start/mg/kg/hr</th>
<th>Max, mean (mg/kg/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3</td>
<td>0.2-0.3</td>
<td>0.2-0.3</td>
</tr>
<tr>
<td>0.5</td>
<td>0.4-0.5</td>
<td>0.4-0.5</td>
</tr>
</tbody>
</table>

- Duration, hrs: 15-24
- Courses: 45 courses in 17 patients

Table 3: Opioid and Sedative

<table>
<thead>
<tr>
<th>Opioid and Sedative Dosing</th>
<th>Start/dose, hrs</th>
<th>Max, mean (mg/kg/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Off-label, 24 hrs, n%</td>
<td>94%</td>
<td>80%</td>
</tr>
<tr>
<td>Intravenous, n%</td>
<td>96%</td>
<td>96%</td>
</tr>
</tbody>
</table>

Table 4: Hospital Outcomes

<table>
<thead>
<tr>
<th>Hospital Course (n = 17)</th>
<th>Days: 0-1</th>
<th>2-3</th>
<th>&gt;3</th>
</tr>
</thead>
<tbody>
<tr>
<td>PICU</td>
<td>14</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Intubated</td>
<td>14</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

Conclusions

Dexmedetomidine overall was safe and effective in the 17 patients and 21 treatment courses analyzed for the study. The ability to titrate off of other sedatives and narcotics with the use of dexmedetomidine was difficult because of the drug's sedative effects. Mortal data was available concerning reason for use of dexmedetomidine. All patients died prior to the start of dexmedetomidine as well as their adjustments during dexmedetomidine infusions were not controlled.

No patients were noted to have severe adverse effects directly related to dexmedetomidine. The effects on blood pressure and heart rate were very difficult to attribute to dexmedetomidine. For the transitions back to other sedatives and opioid infusions, reasoning was because of inadequate sedation and not related to adverse effects of dexmedetomidine.

The use of dexmedetomidine was safe and effective in infants both greater than and less than 12 months of age as well as for durations of greater than 24 hours. Dexmedetomidine can be used to minimize the use of other sedatives and opioids and potentially decrease time of intubation. 59% of the patients were not extubated on dexmedetomidine. Several of the patients who were not extubated on dexmedetomidine, were extubated soon after it was discontinued.

References


Figure 2: Alpha2 receptors in the locus ceruleus of the brain stem generate sedative and anxiolytic effects

Figure 3: Dexmedetomidine has an effect on opioid and locus ceruleus

Figure 1: Dexmedetomidine’s Effect on the Alpha, Receptor