Targeting patients for use of dexmedetomidine

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Conflicts

• None

• Talking about off-label uses of dexmedetomidine
Dexmedetomidine

- Alpha-2 agonist
- 7 times more selective than clonidine for the receptor

- Infusion only
- 0.2 to 1.5 μg/kg/hr PER HOUR
- Loading dose of 1 mcg/kg over 10 min

- Distribution half-life of 6 minutes
- Terminal elimination half-life of 2 hours
- Hepatic clearance, renal excretion of metabolites
US FDA approval

1999/2000
• Mechanically ventilated patients in the intensive care setting up to 24 hrs
• 0.2 to 0.7 μg/kg/hr

2008
• Non-intubated patients requiring sedation prior to and/or during surgical and other procedures
Sedation of initially intubated and mechanically ventilated postsurgical patients during treatment in an intensive care setting by continuous intravenous infusion (must not exceed 24 hours).

Sedation of non-intubated patients prior to and/or during surgical and other procedures:
- Monitored Anesthesia Care (MAC)
- Awake Fiberoptic Intubation (AFI)
Clinical profile

- Anxiolysis
- Some analgesia
- No respiratory depression
  - *Can keep it going during extubation*
- No amnesia
- Bradycardia
- Hypotension
Does it help with delirium?
Delirium

- 4 large RCTs recently in *JAMA*
  - MENDS
    - (vs lorazepam)
  - SEDCOM
    - (vs midazolam)
  - MIDEX/PRODEX
    - (vs midazolam and vs propofol)
Effect of Sedation With Dexmedetomidine vs Lorazepam on Acute Brain Dysfunction in Mechanically Ventilated Patients: The MENDS Randomized Controlled Trial

Pratik P. Pandharipande; Brenda T. Pun; Daniel L. Herr; et al.


Figure 2. Delirium-Free and Coma-Free Days During Study

- Dexmedetomidine
- Lorazepam

Coma-Free Days

P = .01

P = .09

P < .001
Figure 2. Daily Prevalence of Delirium Among Intubated Intensive Care Unit Patients Treated With Dexmedetomidine vs Midazolam
Dexmedetomidine vs Midazolam or Propofol for Sedation During Prolonged Mechanical Ventilation
Two Randomized Controlled Trials

Figure 2. Duration of Mechanical Ventilation and Intensive Care Unit Stay
Table 3. Patients’ Arousalability, Ability to Communicate Pain, and Ability to Cooperate With Nursing Care

<table>
<thead>
<tr>
<th></th>
<th>Adjusted Mean Estimate (95% CI)</th>
<th>Estimate of Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 249)</td>
<td>(n = 251)</td>
</tr>
<tr>
<td><strong>Dexmedetomidine vs midazolam (MIDEX)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total VAS score^b</td>
<td>49.7 (45.5 to 53.8)</td>
<td>30.0 (25.9 to 34.1)</td>
</tr>
<tr>
<td>Can the patient communicate pain?</td>
<td>46.3 (41.7 to 50.9)</td>
<td>24.2 (19.7 to 28.8)</td>
</tr>
<tr>
<td>How arousable is the patient?</td>
<td>58.2 (53.7 to 62.6)</td>
<td>40.7 (36.3 to 45.1)</td>
</tr>
<tr>
<td>How cooperative is the patient?</td>
<td>44.8 (40.3 to 49.2)</td>
<td>25.1 (20.8 to 29.5)</td>
</tr>
<tr>
<td><strong>Dexmedetomidine vs propofol (PRODEX)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total VAS score^b</td>
<td>51.3 (46.9 to 55.7)</td>
<td>40.1 (35.7 to 44.6)</td>
</tr>
<tr>
<td>Can the patient communicate pain?</td>
<td>49.3 (44.5 to 54.2)</td>
<td>35.4 (30.5 to 40.4)</td>
</tr>
<tr>
<td>How arousable is the patient?</td>
<td>59.1 (54.7 to 63.4)</td>
<td>47.8 (43.4 to 52.3)</td>
</tr>
<tr>
<td>How cooperative is the patient?</td>
<td>47.2 (42.3 to 52.2)</td>
<td>38.0 (33.0 to 43.0)</td>
</tr>
</tbody>
</table>

^b VAS = Visual Analog Scale

a p < 0.001
Question of doses...

MIDEX

- \(0.2 \ \mu g/kg/hr \text{ dex} = 2.1 \ \text{mg/hr midaz} \ (0.03 \ \text{mg/kg})

My version

- \(0.2 \ \mu g/kg/hr \text{ dex} = 0.5 \ \text{mg/hr midazolam}\)
### Goal RASS -3 to 0

<table>
<thead>
<tr>
<th></th>
<th>Dexmed</th>
<th>Midazolam</th>
<th>Dexmed</th>
<th>Propofol</th>
</tr>
</thead>
<tbody>
<tr>
<td>RASS Score during study period</td>
<td>-0.9 (-1.9 to -0.1)</td>
<td>-1.5 (-2.5 to -0.5)</td>
<td>-1.0 (-1.9 to -0.2)</td>
<td>-1.7 (-2.5 to -0.7)</td>
</tr>
<tr>
<td>Sedation stop performed</td>
<td>89.7%</td>
<td>93.3%</td>
<td>89.0%</td>
<td>90.1%</td>
</tr>
</tbody>
</table>

Jakob et al. *JAMA* 2012
Which patients get dexmedetomidine?
Cardiac surgery patients – use over time

Wunsch et al. Anesthesiology 2010
Why cardiac surgery patients?

- Prelim studies in cardiac surgery patients
- Generally <24 hrs on ventilator
- Low analgesia requirements (for surgical patients)
- More likely to be cared for by anesthesiologists
Our own experience
Patients who have received dexmedetomidine

- Post cardiac surgery
- Post general surgery
- Transplants (heart, lung, liver, kidney)
- ARDS
- Septic shock
- Etoh withdrawal
- Pancreatitis
- Etc...

We do not have IV clonidine
Potential problems

Barriers
- Dosing error (mcg/kg/HR)
- Staff anxiety regarding its sedative effects

‘Wrong’ patients
- Bradycardia
- Need for deeper sedation
- Need for long period of sedation
  - Rebound (a la clonidine) after many days
- Planning to transfer a patient out of the ICU
Deep sedation

> 200 μg/hr fentanyl

Pandharipande JAMA 2007
Economics

A cost-minimization analysis of dexmedetomidine compared with midazolam for long-term sedation in the intensive care unit*

Joseph F. Dasta, MSc, FCCM, FCCP; Sandra L. Kane-Gill, PharmD, MSc, FCCM, FCCP; Michael Pencina, PhD; Yahya Shehabi, MD, FJFICM, EMBA; Paula M. Bokesch, MD; Wayne Wiseman, MA; Richard R. Riker, MD

Table 1. Median (1st–3rd quartile) costsa between study arms

<table>
<thead>
<tr>
<th>Cost Driver</th>
<th>Dexmedetomidine (n = 244), $</th>
<th>Midazolam (n = 122), $</th>
<th>p \text{**}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonparametric censoring</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>method</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total ICU cost</td>
<td>40,365 (27,557–60,971)</td>
<td>50,149 (32,730–71,861)</td>
<td>.010</td>
</tr>
<tr>
<td>ICU component</td>
<td>36,571 (21,017–45,010)</td>
<td>40,501 (25,063–51,206)</td>
<td>.028</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>7022 (3,293–12,762)</td>
<td>10,885 (5257–16,790)</td>
<td>.010</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>1541 (542–3143)</td>
<td>1293 (533–11,274)</td>
<td>.040</td>
</tr>
<tr>
<td>Adverse drug reaction</td>
<td>507 (175–1167)</td>
<td>810 (265–1694)</td>
<td>.013</td>
</tr>
</tbody>
</table>

SEDCOM data

Midazolam patients were generally more sedated
Costs of drugs

- $58.31 per 200-microgm vial, and the midazolam cost was $1.56 per 5-mg vial
- 0.7 mcg/kg/hr = 49 mcg/hr = 1,176 mcg/day
- 6 vials (at 200 mcgs) = $350.00
- Dosing of 1.5 mcg/kg/hr = $700.00
Areas for potential use

- That patient who is agitated and/or delirious every time you try to wake them up
- Anxious patient not receiving mechanical ventilation
- Neurological ICU: shivering
- ?Alcohol withdrawal
- ?Sleep deprived
So who are those ‘ideal’ patients?
Example #1

- Slightly hemodynamically unstable (but not so much that they can’t be awake)
- Trying to wean
- Emerging agitated from other sedation
- Oversedated when given antipsychotics
Example #2

- Elderly/fragile – (you know they are a setup for delirium)
- Mild respiratory distress but not needing intubation
  - Trying to tolerate BIPAP
- Moderately anxious, starting to get sleep deprived
# Prevention of Shivering During Therapeutic Temperature Modulation: The Columbia Anti-Shivering Protocol

H. Alex Choi · Sang-Bae Ko · Mary Presciutti · Luis Fernandez · Amanda M. Carpenter · Christine Lesch · Emily Gilmore · Rishi Mallotra · Stephan A. Mayer · Kiwon Lee · Jan Claassen · J. Michael Schmidt · Neeraj Badjatia

<table>
<thead>
<tr>
<th>Step</th>
<th>Intervention</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Baseline</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Acetaminophen</td>
<td>650–1000 mg Q 4–6 h</td>
</tr>
<tr>
<td></td>
<td>Buspirone</td>
<td>30 mg Q 8 h</td>
</tr>
<tr>
<td></td>
<td>Magnesium sulfate</td>
<td>0.5–1 mg/h IV Goal (3–4 mg/dL)</td>
</tr>
<tr>
<td></td>
<td>Skin counterwarming</td>
<td>43°C/MAX Temp</td>
</tr>
<tr>
<td>1</td>
<td>Mild sedation</td>
<td>Dexmedetomidine</td>
</tr>
<tr>
<td></td>
<td>or</td>
<td>0.2–1.5 mcg/kg/h</td>
</tr>
<tr>
<td></td>
<td>Opioid</td>
<td>Fentanyl starting dose 25 mcg/h</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Meperidine 50–100 mg IM or IV</td>
</tr>
<tr>
<td>2</td>
<td>Moderate sedation</td>
<td>Dexmedetomidine and Opioid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Doses as above</td>
</tr>
<tr>
<td>3</td>
<td>Deep sedation</td>
<td>Propofol</td>
</tr>
<tr>
<td>4</td>
<td>Neuromuscular blockade</td>
<td>Vecuronium</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50–75 mcg/kg/min</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.1 mg/kg IV</td>
</tr>
</tbody>
</table>
Etoh withdrawal

- Adjunct to benzodiazepines
- Case reports only
“In mechanically ventilated patients, nighttime infusions of dexmedetomidine preserved the day-night cycle of sleep but induced severely disturbed sleep architecture without evidence of [slow wave sleep] or REM sleep”
Other options...

- No sedation
- Opiate-based sedation
- Antipsychotic medications
  - Haloperidol
  - Atypicals
- Ketamine infusion
- (Inhaled anesthetic)
- (New formulation of etomidate)
Summary

- Dexmedetomidine is another tool
- Greatest benefits
  - Lack of respiratory depression
  - Hard(er) to over-sedate
  - May help with delirium
- Downsides
  - Cost
  - Bradycardia
  - Lack of deep sedation
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