Pharmacological Treatment of Delirium

Where do drugs fit in the picture of delirium treatment?

Lisa Burry
Mount Sinai Hospital
University of Toronto
Meet Mrs. Anne H

- 79 YOF ICU day 5 for pneumonia.

- She lays in bed most of the day and is not interactive. Her eyes are closed, and she is hard to rouse. Her words are slurred & difficult to understand. She does not respond appropriately to questions; not oriented.

- RN reports she often appears to be picking at things on the bed.

- You are unable to assess her mood, but her affect is restricted. The daughter tells you is “not herself” - she seems sad.
  - High functioning prior to admission
  - Last MMSE @ GP’s office 30/30

- ICDSC = 4
NOW THAT YOU HIGHLY SUSPECT HYPOACTIVE DELIRIUM, WHAT SHOULD THE NEXT STEP BE?

Conduct a DELIRIUM “WORK UP” to determine reversible causes
ETIOLOGY MNEMONIC

- Infectious
- Withdrawal
- Acute metabolic
- Trauma
- Central nervous system pathology
- Hypoxia
- Deficiencies (nutritional)
- Endocrinopathies
- Acute vascular
- Toxins/drugs (includes polypharmacy)
- Heavy metals
## “WORK UP” RESULTS

### Non-Drug

- Mild dehydration
- Magnesium & potassium require replacement
- All other results normal

### Drug

1. Metoprolol 25 mg BID
2. Atorvastatin 20 mg OD
3. ECASA 81 mg OD
4. Ramipril 5 mg OD
5. Amitriptyline 25 mg HS
6. Multivitamin tab OD
7. Digoxin 0.125 mg OD*
8. Furosemide 20 mg IV TID*
9. Enoxaparin 40 mg SC OD*
10. Gravol 25-50 mg PO/IV PRN*
11. Ranitidine 150 mg OD*
12. Fentanyl 50-100 mcg IV q1h prn*
13. Lorazepam 1 mg IV q1h prn*

* New medications

Potentially cause delirium
Now that you have made a diagnosis of delirium and performed the appropriate “work-up”, you need to determine if additional [drug] intervention is required.

Does Anne need further drug intervention?
DELIRIUM

Evaluation

History (dementia?) and Physical Exam (head to toe)

FOCAL EXAM:
Do appropriate next step (e.g., fever → cx)
THEN, review meds & Order other tests

NON-FOCAL EXAM:
Review meds
Order add’l tests

Treat Findings & Manage symptoms

Management

NON-AGITATED PATIENT:
Non-Pharmacologic treatment

AGITATED PATIENT:
Non-Pharmacologic & Pharmacologic tx

Treat Findings & Manage symptoms

Canadian Coalition for Senior’s Mental Health - Delirium Guidelines
NON-PHARMACOLOGIC MANAGEMENT

• Mobilization

• Modifiable risk factors
  – Correct sensory deficits
  – Manage pain
  – Support normal sleep pattern

• Assess safety
  – Prevent harm to self or others
  – Try to avoid physical restraints

• Encourage self-care & promote meaningful activities

• Optimize communication
  – Provide education
  – Calm, supportive approach
  – Use re-orientation strategies
    • Clock, TV

• Optimize environment
  – Support routine (staff, familiar objects)
  – Avoid sensory deprivation or overload (Noise reduction)
  – Involve friends and family
Early Exercise in the ICU

Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial

William D Schweickert, Mark C Pohlman, Anne S Pohlman, Celerina Nigos, Amy J Pawlik, Cheryl L Esbrook, Linda Spears, Megan Miller, Mietka Franczyk, Deanna Deprizio, Gregory A Schmidt, Amy Bowman, Rhonda Barr, Kathryn E McCallister, Jesse B Hall, John P Kress

- Early exercise = progressive mobility
- Study design: paired SAT/SBT protocol with PT/OT from earliest days of mechanical ventilation

Wake Up, Breathe, and Move

EARLY MOBILIZATION DURING SEDATION INTERRUPTION

ABCs OF DRUG TREATMENT

- **A**ntipsychotics
- **B**enzodiazepines
- **C**holinesterase inhibitors
- **D**exmedetomidine
- **E**arly mobilization during DSI
**Question:** Does treatment with haloperidol reduce the duration of delirium in adult ICU patients?

**Answer:** There is no published evidence that treatment with haloperidol reduces the duration of delirium in adult ICU patients.

**Question:** Does treatment with atypical antipsychotics reduce the duration of delirium in adult ICU patients?

**Answer:** Atypical antipsychotics may reduce the duration of delirium in adult ICU patients.
HOPE-ICU RCT

• Single centre, double-blind, placebo-controlled RCT of 142 adult needing MV < 72 hrs of admission
  – regardless of delirium or coma status

• Methods:
  – haloperidol 2.5mg IV q8h or placebo x 14 days
  – Rx until ICU discharge or coma and delirium-free x 2 days
  – no titration or tapering of study drug
  – fentanyl + propofol infusions titrated to RASS -1 to 0
  – Weaning/SBT standardized; physiotherapy step-wise program
  – Acute agitation: reversible causes investigated by bedside team; PRN haloperidol 10 mg/24 hours

• Primary outcome: delirium-free & coma-free days in 1st 14 days post-randomization
# HOPE-ICU RCT OUTCOMES

<table>
<thead>
<tr>
<th></th>
<th>Haloperidol (N = 71)</th>
<th>Placebo (N = 70)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive, delirium-free &amp; coma-free days in 1st 14 days</td>
<td>5</td>
<td>6</td>
<td>0.53</td>
</tr>
<tr>
<td>Days in delirium in 1st 14 days</td>
<td>5</td>
<td>5</td>
<td>0.99</td>
</tr>
<tr>
<td>Days in coma in 1st 14 days</td>
<td>0</td>
<td>0.5</td>
<td>0.99</td>
</tr>
<tr>
<td>Ventilator-free days in 1st 28 days</td>
<td>21</td>
<td>17</td>
<td>0.88</td>
</tr>
<tr>
<td>Mortality at 28 days</td>
<td>28.2%</td>
<td>27.1%</td>
<td></td>
</tr>
<tr>
<td>Length of ICU stay, days</td>
<td>9.5</td>
<td>9</td>
<td>0.47</td>
</tr>
</tbody>
</table>
## OUTCOMES

<table>
<thead>
<tr>
<th></th>
<th>Haloperidol (N = 71)</th>
<th>Placebo (N = 70)</th>
<th>Difference (95% CI) or P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of any antipsychotic</td>
<td>11%</td>
<td>26%</td>
<td>RR 0.44 (0.2–0.94)</td>
</tr>
<tr>
<td>Open-label haloperidol, n</td>
<td>8%</td>
<td>21%</td>
<td>RR 0.39 (0.16–0.96)</td>
</tr>
<tr>
<td>Total dose of open-label</td>
<td>1.0</td>
<td>1.71</td>
<td>P 0.32</td>
</tr>
<tr>
<td>QTc prolongation &gt; 500 ms</td>
<td>10%</td>
<td>9%</td>
<td></td>
</tr>
<tr>
<td>Supraventricular tachycardia</td>
<td>6%</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>10%</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>Akathisia</td>
<td>1%</td>
<td>3%</td>
<td></td>
</tr>
</tbody>
</table>

MIND RCT

• Multi centre, double-blind, placebo-controlled feasibility RCT
  101 MV medical or surgical patients with delirium

• Methods:
  – Haloperidol 5mg po q6h or ziprasidone 40 mg or placebo up to 14 days
  – Taper off study drug
  – All other treatments, including sedation, determined by ICU team
  – Open label antipsychotics were strongly discouraged
  – No formalized non-pharmacologic intervention to prevent or treat delirium

• Primary outcome: # of days alive without delirium or coma
## OUTCOMES

<table>
<thead>
<tr>
<th></th>
<th>Haloperidol N = 35</th>
<th>Ziprasidone N = 30</th>
<th>Placebo N = 36</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delirium/coma-free days in 1st 21 days</td>
<td>14.0</td>
<td>15.0</td>
<td>12.5</td>
<td>0.66</td>
</tr>
<tr>
<td>Delirium days</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>0.93</td>
</tr>
<tr>
<td>Resolution of delirium on study drug</td>
<td>69%</td>
<td>77%</td>
<td>58%</td>
<td>0.28</td>
</tr>
<tr>
<td>Coma days</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>0.90</td>
</tr>
<tr>
<td>Ventilator-free days</td>
<td>7.8</td>
<td>12.0</td>
<td>12.5</td>
<td>0.25</td>
</tr>
<tr>
<td>ICU Length of stay, days</td>
<td>11.7</td>
<td>9.6</td>
<td>7.3</td>
<td>0.70</td>
</tr>
<tr>
<td>Akathisia QTc prolongation &gt; 500 ms</td>
<td>29% 6%</td>
<td>20% 17%</td>
<td>19% 8%</td>
<td>0.60 0.31</td>
</tr>
</tbody>
</table>
Patients requiring either MV, NPPV or in shock who are CAM-ICU+
N=876 patients at n=14 USA centers

- **Haloperidol**
  - up to 10mg IV q12h

- **Ziprasidone**
  - up to 20mg IV q12h

- **Placebo**
  - 10ml IV q12h

Treated until delirium has resolved x 48 hours or to 14 days
(whichever occurs first) and followed for 1 year

Period spent delirium-free and coma-free 14 days after randomization
### ADDITIONAL ATYPICAL ANTI-PSYCHOTIC RCTs

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Control</th>
<th>Population</th>
<th>Outcomes</th>
<th>ADRs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olanzapine PO 5 mg daily (n = 28)</td>
<td>haloperidol PO 2.5 mg q8h (n = 45)</td>
<td>SICU &gt; MICU Delirium +</td>
<td>- No difference in delirium index scores @ day 5 &lt;br&gt;- No difference in benzodiazepine use</td>
<td>13% mild EPS in haloperidol group</td>
</tr>
<tr>
<td>Quetiapine 50 mg PO q12h + titration (max 200 mg) (n = 18)</td>
<td>Placebo (n = 18)</td>
<td>MICU &gt; SICU Delirium +</td>
<td>- Time to 1st resolution: quetiapine 1.0 vs. 4.5 days placebo p = 0.001 &lt;br&gt;- Reduced duration of delirium: quetiapine 36h vs. 120 h placebo, P=0.006</td>
<td>0% EPS No diff in QTc</td>
</tr>
</tbody>
</table>

BLACK BOX WARNING

– Schneeweiss S. Risk of death associated with the use of conventional versus atypical antipsychotic drugs among elderly patients. CMAJ 2007;176(5):627-32

– Wang PS. Ventricular arrhythmias and cerebrovascular events in the elderly using conventional and atypical antipsychotics.

  • Atypical antipsychotic users had a dose-related increased risk for sudden cardiac death

  • Magnitude of increased risk not different from that of typical antipsychotics

BENZODIAZEPINES

• Generally avoided as may WORSEN delirium

• Adjunct to antipsychotics in treatment of severe agitation

• Primarily indicated in withdrawal associated delirium
**Question:** For mechanically ventilated, adult ICU patients with delirium who require continuous IV infusions of sedative medications, is dexmedetomidine preferred over benzodiazepines to reduce the duration of delirium?

**Answer:** We suggest that in adult ICU patients with delirium which is not related to withdrawal, continuous intravenous infusions of dexmedetomidine rather than benzodiazepine infusions be administered for sedation in order to reduce the duration of delirium in these patients.

Dexmedetomidine vs Midazolam for Sedation of Critically Ill Patients
A Randomized Trial

Delirium on study enrollment:
60.3% dex vs. 59.3% midaz, p=0.82

Prevalence of delirium during treatment:
54% dex vs. 76.6% midaz, p<0.001

Delirium-free days:
2.5 dex vs. 1.7 midaz, p =0.002

Bradycardia:
42.2% dex vs. 18.9% midaz, p <0.001
DEXMEDETO MIDINE vs. HALOPERIDOL

- Single centre, open-label RCT of 20 adult undergoing MV in whom extubation was not possible solely because of agitated delirium

- Methods:
  - Dexmedetomidine 0.2-0.7 mcg/kg/hr vs. haloperidol 0.5-2 mg/hr
  - All other treatments, including sedation & management of acute agitation, determined by ICU team

- Primary outcome: time from commencement of study drug to extubation
## OUTCOMES

<table>
<thead>
<tr>
<th></th>
<th>Dexmedetomidine (n = 10)</th>
<th>Haloperidol (n = 10)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median time to extubation, hours</td>
<td>19.9</td>
<td>42.2</td>
<td>0.016</td>
</tr>
<tr>
<td>Time to ICU discharge post-randomization, days</td>
<td>1.5</td>
<td>6.5</td>
<td>0.004</td>
</tr>
<tr>
<td>Time to achieve RASS score (-2 to 1), hours</td>
<td>4</td>
<td>18</td>
<td>0.071</td>
</tr>
<tr>
<td>Proportion of time with ICDSC &lt; 4</td>
<td>95.5</td>
<td>31.5</td>
<td>0.122</td>
</tr>
<tr>
<td>Proportion of time with ICDSC &lt; 1</td>
<td>61.0</td>
<td>0.0</td>
<td>0.134</td>
</tr>
<tr>
<td>Any adverse event Arrhythmias</td>
<td>0%</td>
<td>10%**</td>
<td>0.31</td>
</tr>
<tr>
<td></td>
<td>20%</td>
<td>20%</td>
<td>1.00</td>
</tr>
</tbody>
</table>

**Nearly all QTc prolongation**
GENERAL PRINCIPLES FOR PHARMACOLOGICAL TREATMENT OF DELIRIUM

• Non-pharmacological interventions should be used for all patients with delirium (although most not studies in ICU)

• Treatments should include modifying existing drug regimen that includes ‘risky’ drugs & correcting reversible causes (e.g. lytes, infection)

• Pharmacological interventions should be reserved for patients in distress due to agitation or psychotic symptoms

• If pharmacological intervention is warranted, attempt monotherapy & the lowest effective dose. Re-evaluate need for therapy frequently.
Troubled in my sleep
In and out on repeat
Faces trading faces
Places trading places
Nothing makes sense
My mind is in a mess
In a state of delirium
I Find myself to be...
MEDICATIONS

Sedative/hypnotics
  – Benzodiazepines
  – Barbituates
  – Antihistamines

Opioids

Corticosteroids

Anticholinergic activity
  – oxybutynin
  – tricyclic antidepressants
  – Antipsychotics

Antiarrhythmics (digoxin)

Furosemide

Histamine blocking agents
  – ranitidine

Anticonvulsants (phenytoin)

Antiparkinsonian medications
  – Dopamine agonists
  – levodopa-carbidopa
  – Benztropine

Consider withdrawal reactions.
Polypharmacy is an issue!
HOPE-ICU RCT

Daily rate of recovery from delirium and coma over 28 days

Proportion of patients delirium and coma-free x 2 days

P=0.53

Figure 2: Proportion of study patients with resolution of delirium over time

RIVASTIGMINE vs. PLACEBO RCT
Greater mortality & lower delirium resolution with rivastigmine

Mortality during rivastigmine administration: 22% vs. 8%, p = 0.07

Van Eijk, MMJ et al Lancet 2010; 376:1829
**Use of dexmedetomidine as a sedative and analgesic agent in critically ill adult patients: a meta-analysis**

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Dexmedetomidine n/N</th>
<th>Control n/N</th>
<th>RR (random) 95% CI</th>
<th>Weight %</th>
<th>RR (random) 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elective postoperative patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Herr [19]</td>
<td>5/148</td>
<td>1/147</td>
<td>2.36 [0.59, 41.99]</td>
<td>2003</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Martin [20]</td>
<td>2/203</td>
<td>6/198</td>
<td>4.00 [0.07, 1.59]</td>
<td>2003</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corbett [23]</td>
<td>1/43</td>
<td>1/46</td>
<td>1.48 [0.07, 16.57]</td>
<td>2005</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maldonado [32]</td>
<td>4/40</td>
<td>33/76</td>
<td>8.78 [0.09, 0.60]</td>
<td>2009</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shehabi [17]</td>
<td>13/152</td>
<td>22/147</td>
<td>14.25 [0.30, 1.09]</td>
<td>2009</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>586</td>
<td>614</td>
<td></td>
<td></td>
<td></td>
<td>30.88</td>
</tr>
<tr>
<td>Total events: 25 (Dexmedetomidine), 63 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: Chi² = 7.66, df = 4 (P = 0.10), I² = 47.8%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.49 (P = 0.14)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-elective critically ill patients</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pandharipande [34]</td>
<td>41/52</td>
<td>42/51</td>
<td>26.69 [0.79, 1.16]</td>
<td>2007</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Riker [33]</td>
<td>132/244</td>
<td>93/122</td>
<td>27.50 [0.61, 0.83]</td>
<td>2009</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>337</td>
<td>217</td>
<td></td>
<td></td>
<td></td>
<td>69.12</td>
</tr>
<tr>
<td>Total events: 191 (Dexmedetomidine), 146 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: Chi² = 11.91, df = 2 (P = 0.003), I² = 83.2%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Test for overall effect: Z = 0.32 (P = 0.75)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>923</td>
<td>831</td>
<td></td>
<td></td>
<td></td>
<td>100.00</td>
</tr>
<tr>
<td>Total events: 216 (Dexmedetomidine), 209 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: Chi² = 24.61, df = 7 (P = 0.0009), I² = 71.6%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.36 (P = 0.18)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**Fig. 6. Effect of dexmedetomidine on risk of delirium**
<table>
<thead>
<tr>
<th>User Status</th>
<th>No. of Person-Years</th>
<th>No. of Sudden Deaths</th>
<th>Incidence-Rate Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonuser</td>
<td>624,591</td>
<td>895</td>
<td>Reference group</td>
<td></td>
</tr>
<tr>
<td>Former user</td>
<td>189,981</td>
<td>311</td>
<td>1.13 (0.98–1.30)</td>
<td>0.08</td>
</tr>
<tr>
<td>Current user†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Typical agent</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>86,735</td>
<td>255</td>
<td>1.99 (1.68–2.34)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>21,728</td>
<td>58</td>
<td>1.61 (1.16–2.24)</td>
<td>0.005</td>
</tr>
<tr>
<td>Thioridazine</td>
<td>15,715</td>
<td>65</td>
<td>3.19 (2.41–4.21)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Atypical agent</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>79,589</td>
<td>223</td>
<td>2.26 (1.88–2.72)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clozapine</td>
<td>4,654</td>
<td>19</td>
<td>3.67 (1.94–6.94)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>27,257</td>
<td>75</td>
<td>2.04 (1.52–2.74)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>17,355</td>
<td>40</td>
<td>1.88 (1.30–2.71)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Risperidone</td>
<td>24,589</td>
<td>85</td>
<td>2.91 (2.26–3.76)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Sudden Cardiac Death IRRs: Antipsychotic Type and Dose

![Bar chart showing incidence rate ratios for typical and atypical antipsychotic agents at different dose levels.]

- **Typical Antipsychotic Agent**
  - Low dose: 1.31 (0.97–1.77)
  - Moderate dose: 2.01 (1.62–2.50)
  - High dose: 2.42 (1.91–3.06)

- **Atypical Antipsychotic Agent**
  - Low dose: 1.59 (1.03–2.46)
  - Moderate dose: 2.13 (1.70–2.65)
  - High dose: 2.86 (2.25–3.65)

**P-values**
- Typical Antipsychotic Agent: P < 0.001
- Atypical Antipsychotic Agent: P = 0.01
• MIDEX: N=233 midazolam, N= 227 dex
• PRODEX: N=214 propofol, N= 223 dex
• “In both studies, there were no differences between [groups]... in delirium assessed using the Confusion Assessment Method for ICU Patients (CAM-ICU) at 48 hours after stopping study sedation”
Other RCTs showing NO reduction in delirium (CAM ICU) with Dexmedetomidine

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients</th>
<th>Delirium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pandharipande</td>
<td>106 med-surg ICU</td>
<td>Dexmedetomidine 79%</td>
</tr>
<tr>
<td>MENDS JAMA 2007</td>
<td></td>
<td>Lorazepam 82%, p=.71</td>
</tr>
<tr>
<td>Shehabi</td>
<td>N = 306, &gt;60 yrs, post cardiac surgery</td>
<td>Dexmedetomidine 8.6%</td>
</tr>
<tr>
<td>Anesthesiology 2009</td>
<td></td>
<td>Morphine 15%, p=.088</td>
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<tr>
<td>Ruokonen Int Care Med 2009</td>
<td>85 med-surg ICU</td>
<td>Dexmedetomidine 43.9%</td>
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<td></td>
<td></td>
<td>Propofol/midazolam 25%, p=.035</td>
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</tbody>
</table>
RCTs showing reduction in delirium (CAM ICU) with Dexmedetomidine

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<tr>
<td>Riker SEDCOM JAMA 2009</td>
<td>375 med/surg; 68 centers, 5 countries</td>
<td>Dexmedetomidine 54% Midazolam 77%, p&lt;.001</td>
</tr>
<tr>
<td>Pandharipande MENDS sepsis subgroup Crit Care 2010</td>
<td>103 pts 63 sepsis, 40 no sepsis</td>
<td>Dexmedetomidine 79% Lorazepam 82%, p=.71</td>
</tr>
</tbody>
</table>