Maine Medical Center  
Department of Emergency Medicine  

Journal Club / Research Article Summary - (Adapted from Schultz Table)  

date: 11/28/2012  
Presenter: Lo Klouda  

Article:  
- Country: Australia  
- Funding Sources: NSW Health Drug and Alcohol Research grants Program 2007/2008, Australia. Dr Isbister is funded by NHMRC Clinical Career Development Award.  

Purpose:  
- Research question(s): Is IM midazolam, droperidol, or the combination of the two more effective for controlling agitation in the ED, and is there a difference in adverse effects between the groups?  

Design:  
- Study Design: blinded, randomized controlled trial from Aug 2008-July 2009. 91 out of 223 violent/disturbing pts received IM sedation. 33 received droperidol, 29 midazolam, and 29 combination droperidol/midazolam. They recorded the duration of violence/disturbance, reported whether pts needed more sedation, staff or pt injuries, and whether adverse events such as respiratory depression, injuries, or an abnormal QT developed.  

Setting / Subjects:  
- Research Setting: Urban ED with 27,000 annual visits with approx 5.2 per 1000 with violence or behavioral issues  
- Subjects:  
  - Study population: Pts 18 yrs or older with violent and acute behavioral disturbance, irrespective of cause, that required both physical restraint and parenteral sedation.  
  - Inclusion / Exclusion criteria: Inclusion criteria as above. Exclusion criteria—successful de-escalation of behavior whether by verbal means or presence of security, agreed to oral/IV sedation, other sedatives on board, the pt did not remain in the ED, or had a seizure.
Number (control / intervention groups): 91

Demographics:

<table>
<thead>
<tr>
<th></th>
<th>Droperidol 10mg</th>
<th>Midazolam 10mg</th>
<th>Droper 5mg/Midaz 5mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age</td>
<td>37</td>
<td>35</td>
<td>30</td>
</tr>
<tr>
<td>% male</td>
<td>36</td>
<td>62</td>
<td>52</td>
</tr>
<tr>
<td>Clinical assessment of agitation (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>70</td>
<td>76</td>
<td>66</td>
</tr>
<tr>
<td>Self-harm</td>
<td>48</td>
<td>41</td>
<td>45</td>
</tr>
<tr>
<td>Drug-induced</td>
<td>6</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Acute psychosis</td>
<td>6</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

Attrition: N/A

METHODS:
- Interventions: ECGs were obtained at 30min, 1hr and 4hrs after drug administration (when practical). 10mg IM midazolam vs 10mg droperidol vs combo of the two (5mg/5mg)
- Data Collection: Data recorded on clinical research forms and then entered into a relational database using Microsoft Access. Pulse, blood pressure, SaO2, respiratory rate, and the Altered Mental Status Scale were recorded every 5 min for first 30min, then every 15min for the next 90min, and then hourly until the study was completed at the 6hr mark.

DATA ANALYSIS:
- Level of Data: Categorical  Ordinal  Interval
- Statistics Used: ANOVA, Kaplan-Meier plots, graphs were made with a GraphPad Prism version 5.03 for Windows, Bayesian analysis with WinBUGS.

What, if any, confounding variables were controlled for / adjusted for: age, sex, and alcohol consumption

RESULTS:
- Brief answers to research questions: 223 pts presented to the ED with violence or behavioral disturbance in a 1yr period. Of those, 91 were treated with IM sedation. Of those 91, 79 stayed in the ED for the full 6hr duration (12 d/c’d prior to 6hr mark because of transfer to psych or awoke with no further disturbance). There was no significant difference in time to sedation between any of the medications (see below). Pts who received droperidol did not require as much additional sedation. The number of adverse events was greater with midazolam or after additional sedation was administered or associated with alcohol intoxication. The number of pts who developed an abnormal QT was not significantly different among the different groups (see below).
Time to sedation:
Droperidol—median duration of disturbance was 20min
Midazolam—24min
Droperidol/midazolam—25min

# of QT prolongations:
Droperidol—2/31
Midazolam—2/29
Droperidol/midazolam—4/29

• Additional findings:
  1. Midazolam proved to be unpredictable for them where pts were either over-sedated with more adverse events or under-sedated and requiring more sedation.
  2. See table 2 on pg 398 for secondary outcomes.
  3. With respect to QT interval, there was no significant difference between the 3 groups, however, the rate of abnormal QT is higher than the general population. They speculate that this may be due to pre-existing illness in this population or drugs they may have ingested prior to arrival.

• Limitations?:
  1. Possibility of interaction between drugs administered and any drugs/alcohol the pt already ingested. Alcohol is associated with a larger # of adverse drug effects, mainly with administration of midazolam, resulting in oversedation.
  2. Meds not dosed according to pt weight.
  3. Primary outcome was duration of unacceptable behavior as opposed to time to sedation using the Altered Mental Status Scale(AMSS). The believed the duration of behavior disturbance was a more objective measure and more clinically appropriate for the ED. But then say that using the AMSS may have been a better primary outcome.
  4. Possible inter-observer differences in using the AMSS because it was not possible for one person to be there for the duration of every pt’s 6hr window.
  5. Unstructured administration of further sedation.

IMPLICATIONS FOR PRACTICE:
• Applicable to this clinical practice: Yes

• Feasibility (cost, resources, etc): Minimal. We already use various means of sedation and it would not require any additional staff to use droperidol in lieu of haldol.

• Clinically Relevant: Yes

LEVEL OF EVIDENCE / DECISION FOR USE:
• Background Consider Replication Ready for use
Level of Evidence:

- **Ia** Evidence obtained from meta-analysis of randomized controlled trials
- **Ib** Evidence obtained from at least one RCT
- **IIa** Evidence obtained from at least one well-designed controlled study without randomization
- **IIb** Evidence obtained from at least one other type of well-designed quasi-experimental study
- **III** Well-designed non-experimental studies
- **IV** Expert committee reports, opinions of experts