USE OF ANTIPSYCHOTICS FOR THE MANAGEMENT OF DELIRIUM

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Delirium

- Confusion (time, space, recent memory)
- Hallucinations – tactile!
- Delusions
- Agitation
- Disinhibition: symptoms or emotions!!
2 MAJOR DISORDERS OF COGNITION
DELIRIUM AND DEMENTIA

DELIRIUM:
- Usually acute in onset
- Relatively brief in duration
- Fluctuating level of consciousness
- Can be reversible

DEMENTIA:
- Intellectual deterioration of protracted & usually irreversible nature

- Delirium reported to be most common OMS in Cancer PTS
Differential diagnosis

- Dementia (easy from history)
- Sedation (opioids)
- Obstructive sleep apnea (Reddy 2008)
- Depression (60% delirium referrals)
- Anxiety/ manic episode
- Akathisia
Delirium

- 85% cancer pts before death
- Multicausal
- 80% of brain is GABA
- Disinhibition: expression of symptoms and emotions
Delirium

- Tumor byproducts and host cytokines
- Metabolic Na, Ca, Creat
- OPIOIDS and other drugs (psych!!)
- Chemo
- Sepsis
- Dehydration
- CNS Involvement
Opioid induced neurotoxicity (OIN)

- severe sedation
- cognitive failure
- hallucinosis/delirium
- myoclonus/grand mal seizures
- hyperalgesia/allodynia
Risk Factors for OIN

- High opioid dose
- Prolonged opioid exposure
- Pre-existing borderline cognition/delirium
- Dehydration
- Renal failure
- Other psychoactive drugs
- Opioids with mixed agonist/antagonist activity
Delirium management

1. Screening/ early (or late) diagnosis
2. Look for reversible causes
3. Pharmacological treatment
4. Environmental control
5. Bedside nurse/ referring MD education
6. Family education/ counseling
MDAS
Memorial Delirium Assessment Scale

ITEM 1 – REDUCED LEVEL OF CONSCIOUSNESS (AWARENESS):
- 0: none
- 1: mild
- 2: moderate
- 3: severe

ITEM 2 – DISORIENTATION:
- 0: none
- 1: mild
- 2: moderate
- 3: severe

ITEM 3 – SHORT-TERM MEMORY IMPAIRMENT:
- 0: none
- 1: mild
- 2: moderate
- 3: severe

ITEM 4 – IMPAIRED DIGIT SPAN:
- 0: none
- 1: mild
- 2: moderate
- 3: severe

ITEM 5 – REDUCED ABILITY TO MAINTAIN AND SHIFT ATTENTION
- 0: none
- 1: mild
- 2: moderate
- 3: severe
ITEM 6 – DISORGANIZED THINKING
- 0: none
- 1: mild
- 2: moderate
- 3: severe

ITEM 7 – PERCEPTUAL DISTURBANCE:
- 0: none
- 1: mild
- 2: moderate
- 3: severe

ITEM 8 – DELUSIONS:
- 0: none
- 1: mild
- 2: moderate
- 3: severe

ITEM 9 – DECREASED OR INCREASED PSYCHOMOTOR ACTIVITY:
- 0: none
- 1: mild
- 2: moderate
- 3: severe

ITEM 10 – SLEEP-WAKE CYCLE DISTURBANCE (DISORDER OR AROUSAL):
- 0: none
- 1: mild
- 2: moderate
- 3: severe

TOTAL __________
Other tools

- CAM
- DRS
- DSM TN criteria interview
- MMSE
THE MANAGEMENT OF DELIRIUM

1. Assessment
   - Hypoactive
   - Hyperactive
   - Mixed (80 % !!!!)

2. Pharmacological Interventions
   - Haloperidol
   - Other neuroleptics
   - Lorazepam-midazolam

3. Counseling
   - Patient
   - Family
   - Staff

4. Prevention of Delirium
   - Screening- MDAS
   - Opioid rotation
   - Hydration
COUNSELING

1. Patient
   - Brief conversations
   - Avoid Confrontation – Avoid stimulation (hyperactivity)
   - Reassurance: familiar objects, people and sounds
   - Monitor behavior regularly

2. Family
   - Explain the mechanism of delirium
   - Reassure regarding physical suffering
   - Major cause of conflict!!

3. Staff
   - Difference between pain and agitated delirium
   - Aggressive behavior by patient
   - Family distress and dissatisfaction
   - Importance of consistent behavior! team approach!!
Environment control

1. Excessive or NO light
2. Loud noises (TV, sitter on cell phone)
3. Stimulation (visitors, consultants, family)
4. Large clock/ calendar
5. Familiar objects, sounds smells
6. Do not ask for consent/ debate
Family

- Global brain dysfunction (blood products, poor quality fuel)
- Very common and poor prognosis
- Disinhibition of symptoms and emotions
- Environmental control
- Expressive/supportive counseling!!! High distress
Pharmacological Management

- Haloperidol IV/ SC/ PO. Dose: ???.
- “loading (up to 5 mg/dose q1h) and maintenance”
- “regular (2mg q 6h, etc) and breakthrough (q1-2h)”
Haloperidol

- Onset: 30-60 min; dose 0.5-5 mg, half life 18 hs, metabolized and into urine.
- Time to peak: oral 2-6hs; IM 20 min
- DPM blocker
- Extrapyramidal (less in autonomic neuropathy?), tardive diskynesia, NMS
- Q-T prolongation, more IV
Should every delirium be on regular haloperidol?

- Hyperactive and mixed YES!!
- In cancer 80% are MIXED!!
- In PURE hypo no evidence, prn needed in case of change to mixed
There is limited evidence from clinical trials on the role of drug therapy for the treatment of delirium in terminally ill patients. The key feature of delirium is a decreased level of consciousness (awareness). People may experience impaired memory, thinking and judgement, and become disoriented. They may experience distressing hallucinations or delusions. It occurs frequently in patients with terminal illness, and may be caused by the illness itself or occur as a side effect of drug treatments for symptom management. Our search of the international literature for trials of drug therapies for the treatment of delirium in patients with terminal illness yielded one small study, and therefore it was not possible to assess the effectiveness of drug treatment options. It is hoped that this review will provide an incentive for further research.
Haloperidol vs. Chlorpromazine vs. Lorazepam: HIV Patients

Double-blind, randomized controlled trial

30 HIV patients with delirium (mean KPS 52%)

- Haloperidol x6d, N=11
- Chlorpromazine x6d, N=14
- Lorazepam x6d, N=6

Outcomes
- Delirium Rating Scale
- Mini-Mental State Examination
- Extrapyramidal Symptom Rating Scale
- Other Side Effects
- Karnofsky Performance Status
- Medical Status Profile

**Haloperidol vs. Chlorpromazine vs. Lorazepam: HIV Patients**

- **Mean drug doses in first 24 h**
  - Haloperidol 3.8 (2.4) mg
  - Chlorpromazine 50 (23.1) mg
  - Lorazepam 3 (3.6) mg

- **Mean maintenance drug doses**
  - Haloperidol 1.4 (1.2) mg
  - Chlorpromazine 36 (18.4) mg
  - Lorazepam 4.6 (4.7) mg

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**TABLE 1. Drug Dosing Protocol for Treatment of Delirium in Hospitalized AIDS Patients**

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>Haloperidol Oral (mg/hour)</th>
<th>Haloperidol Intramuscular (mg/hour)</th>
<th>Chlorpromazine Oral (mg/hour)</th>
<th>Chlorpromazine Intramuscular (mg/hour)</th>
<th>Lorazepam Oral (mg/hour)</th>
<th>Lorazepam Intramuscular (mg/hour)</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>0.25</td>
<td>0.125</td>
<td>10</td>
<td>5</td>
<td>0.50</td>
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<tr>
<td>2</td>
<td>0.50</td>
<td>0.50</td>
<td>20</td>
<td>10</td>
<td>1.00</td>
<td>0.50</td>
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<tr>
<td>3</td>
<td>1.00</td>
<td>0.50</td>
<td>40</td>
<td>20</td>
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<td>0.70</td>
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<tr>
<td>4</td>
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<td>40</td>
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<tr>
<td>5</td>
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<tr>
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<td>3.00</td>
<td>200</td>
<td>100</td>
<td>4.00</td>
<td>2.00</td>
</tr>
</tbody>
</table>

Day 1: Increase dose to next level every hour if DRS >13
Day 2-6: Give total dose from day 1, div BID

Haloperidol vs. Chlorpromazine vs. Lorazepam: HIV Patients

- Improvement seen within 24 hours of treatment in haloperidol and chlorpromazine arms
- All 6 patients on lorazepam arm developed treatment limiting side effects (sedation, disinhibition, ataxia, increased confusion)

# Delirium RCTs

## At a Glance

<table>
<thead>
<tr>
<th>Study</th>
<th>Setting</th>
<th>Design</th>
<th>Findings</th>
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</thead>
<tbody>
<tr>
<td>Breitbart 1996</td>
<td>HIV</td>
<td>DB-RCT H/C/L; N=30</td>
<td>H~C&gt;L</td>
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<tr>
<td>Hu 2004</td>
<td>Med</td>
<td>OL-RCT H/O/X; N=175</td>
<td>H=O&gt;X</td>
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<td>Han 2004</td>
<td>Med</td>
<td>DB-RCT H/R; N=28</td>
<td>H~R</td>
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<td>Kim 2010</td>
<td>Med</td>
<td>DB-RCT O/R; N=32</td>
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<td>Tahir 2010</td>
<td>Med/Surg</td>
<td>DB-RCT Q/P; N=42</td>
<td>Q~P (AstraZeneca IIS)</td>
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<td>O~H (Eli-Lilly IIS)</td>
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<td>D&gt;L (Hospira IIS)</td>
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<td>D&gt;H (Hospira, drug)</td>
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<td>Devlin 2010</td>
<td>ICU</td>
<td>DB-RCT Q/P; N=36</td>
<td>Q&gt;P (AstraZeneca IIS)</td>
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</table>
Onset of delirium

?Preventative measures, proactive management

Worsening delirium symptoms

Delirium related distress

Delirium related distress

Patients and caregivers

Administration of neuroleptics

RNs and PC specialists