Delirium: A Study of Difficult Cases

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Disclosures:
• No relevant financial relationships to disclose

Off-Labeled Medication

• We WILL be discussing off label use of various medications (anti-psychotics, benzodiazepines, anesthetics, anti-seizure)

Learning Objectives

Delirium Treatment
a. Hyperactive Reversible Delirium
b. Irreversible Delirium
c. Pediatric Delirium

Vignette 1

Reversible Delirium

• Key points
  ▪ Delirium can be reversed
  ▪ Opioids and benzo’s can cause and worsen delirium
  ▪ Dose anti-psychotics like pain medications

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Potential Reversibility of Delirium
Guides Work-up & Management…

Delirium has
Many, Many Causes…
Many are Discoverable and Reversible…

Potential Reversibility of Delirium
Potentially Reversible
Irreversible
- Patient is dying (terminal delirium)
- Goals of care
- Work-up / reversal unsuccessful

Most Common Causes…
- Medications
  - Anticholinergics
  - Benzodiazepines
  - Opioids
  - Steroids
- Fluid imbalance
- Infections
- Hepatic / renal failure
- Hypoxia
- Hematological disturbance

…Most Common Causes…
Hazard ratio of developing delirium (43 inpatients with cancer)
- Benzodiazepines
  2.04 if > 2 mg / day (1.05 – 3.97)
- Corticosteroids
  2.67 if > 15 mg / day (1.18 – 6.03)
- Morphine equivalents
  2.12 if > 90 mg / day (1.09 – 4.13)

Management Strategies…
Manage based on:
- potential reversibility
- goals of care
Ensure safety
Address environment
Consider 1st generation antipsychotics, avoid benzodiazepines


Available online at: http://wwwpsychorg/psych_pract/treatg/pg/prac_guidedfm

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...Management Strategies...

Reverse
  - Treat underlying causes
Relieve
  - Non-pharmacological
  - Pharmacological (time limited trials)
Consult psychiatry / mental health

Always Use Non-pharmacological Treatments...

Use Pharmacological Treatments when Appropriate...
& Appropriately...

Potentially Reversible, Hyperactive

context & reasonable goals of care

potentially reversible

hyperactive

reverse cause

antipsychotics

Treat reversible causes:

- Review medications (eliminate unnecessary and deliriumogenic)
- Rehydrate if indicated and desired
- Consider opioid rotation

Pharmacological Management

No medication is FDA approved for the treatment of delirium
No published double-blind, randomized, placebo controlled trials
No consensus among oncologists, geriatricians, psychiatrists, or palliative medicine specialists

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Antipsychotic Indications

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Anti-agitation</th>
<th>Sedation</th>
<th>Amnesia</th>
<th>Muscle relaxation</th>
<th>Anti-convulsant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td></td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td></td>
</tr>
<tr>
<td>Risperidone</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td></td>
</tr>
<tr>
<td>Olanzapine</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td></td>
</tr>
<tr>
<td>Quetiapine</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td></td>
</tr>
</tbody>
</table>

PEARL

Use 1st generation antipsychotics

Do Not Use Benzodiazepines

- Not first-line treatment
- Increase confusion, disinhibition, falls
- Necessary for alcohol or sedative withdrawal

APA Practice Guidelines 2004


Application of Pharmacological Principles Improves Management...

Sample Orders... For Agitation

Haloperidol – 1 mg SC q 30 min PRN or Chlorpromazine – 50 mg SC q 30 min PRN

- If not effective double the dose every 30 minutes until patient is calm and not agitated. Call MD if not effective after doubling the dose 3 times
- Do not exceed
  - 100 mg in 24 hr (haloperidal)
  - 2000mg in 24 hr (chlorpromazine)
- Schedule today’s PRNs tomorrow
  - 1 or 2 x / day + same PRN schedule

What about 2nd Generation Antipsychotics?

Haloperidol is EQUAL to:
- Olanzapine (Zyprexa)
- Risperidone (Risperdal)
- Aripiprazole (Abilify)

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## Comparisons

<table>
<thead>
<tr>
<th>Names</th>
<th>Relative Potency</th>
<th>Available Formulations</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol (Haldol)</td>
<td>1</td>
<td>tabs, liquid, IM / SQ</td>
<td>Gold standard, also anti-nausea</td>
</tr>
<tr>
<td>Chlorpromazine (Thorazine)</td>
<td>50</td>
<td>tabs, liquid, IM / SQ, PR</td>
<td>May be more effective for highly agitated patient, more anticholinergic, also helps with hiccups, SOB</td>
</tr>
<tr>
<td>Risperidone (Risperdal)</td>
<td>1.5</td>
<td>Tab, liquid, sublingual</td>
<td>Very similar to Haldol</td>
</tr>
<tr>
<td>Olanzapine (Zyprexa)</td>
<td>2.5</td>
<td>Tab, IM, sublingual</td>
<td>More sedating, more anticholinergic</td>
</tr>
<tr>
<td>Quetiapine (Seroquel)</td>
<td>50</td>
<td>Tabs</td>
<td>1st line in Parkinson's</td>
</tr>
</tbody>
</table>

## Vignette 1: Summary

- **Hyperactive Delirium**
- Likely drug induced and reversible
- Delirium workup, reverse suspected etiology, use 1st gen antipsychotics for safety/distress then taper when done
- Outcome: Patient clears in 3 days and antipsychotics stopped

## Vignette 2

### Irreversible delirium

- **Key points**
  - Define terminal delirium
  - Treatment strategies for irreversible delirium

## Terminal Delirium

- Delirium during dying process
- Prospective, irreversible
- Altered level of consciousness
- Tachycardia
- Abnormal breathing patterns
- Loss of swallow / gag
- Oral / tracheal secretions
- Loss of sphincter control

## Irreversible Terminal, Hyperactive

- Signs of Active Dying
  - Irreversible
  - Hyperactive
  - Support
  - Benzodiazepines, Barbiturates, Propofol

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**Benzodiazepine Indications**

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<tr>
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<th>Sedation</th>
<th>Amnesia</th>
<th>Muscle relaxation</th>
<th>Anti-convulsant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorazepam</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Midazolam</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

**Antipsychotics**
- ✓
- / ✓
- ✓
- ✓
- –

**Opioids**
- ✓
- ✓
- ✓
- ✓
- –

**Sample Orders... For Agitation**

With signs of the dying process:

- Lorazepam – 1 mg PO q 60 min PRN
- If 3 doses not effective, call MD
- Do not exceed 40 mg in 24 hr
- Schedule today’s PRNs tomorrow
- 3 x / day + same PRN schedule

**Benzodiazepines**

**Lethal Doses**
- Lorazepam LD₅₀ = 5,000 mg
- Midazolam LD₅₀ = 10,000 mg

**Not concerned about**
- Amnesia, confusion, restlessness
- Hypotension
- Respiratory depression

**When Benzodiazepines Fail**

- Propofol
- Phenobarbital

**PEARL**

- Treat agitation like a breakthrough symptom, e.g., pain
- Provide breakthrough (PRN) doses on the Time to maximum concentration (T_cmax)
- If 3 doses not effective, call MD (time-limited trials)
- Provide routine doses once every Half-life (t½)

Lundström S, et al. (2005) JPSM 30: 570
Vignette 2 Summary

- Hyperactive Irreversible Delirium
- Agitation control is medical goal
- Rapid titration to effect, as with pain
- May need other agents besides antipsychotics and benzodiazepines
- Outcome: Patient (and family) comfortable after 6mg of lorazepam

Vignette 3

Pediatric Delirium . . .

- Key Points
  - Delirium is under recognized in children
  - Mixed type can be challenging to assess
  - Principles of treatment are similar to adults

.Pediatric Delirium . . .

- Occurs in Children
  - ICU: 3-20%
  - Under-recognized

Pediatric Delirium: Assessment

- Few tools available: pCAM-ICU
- Presentation is confusing
- Ask the parents

Pediatric Delirium: Treatment

- Extremely limited data
- Similar to adults
- Base treatment on reasonable goals
- Reverse cause if consistent with reasonable goals
Always Use Non-pharmacological Treatments…

<table>
<thead>
<tr>
<th>Non-Pharmacological Treatments Can Address</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disordered thinking</td>
</tr>
<tr>
<td>Risk of falls / injury</td>
</tr>
<tr>
<td>Disorientation</td>
</tr>
<tr>
<td>Sensory deprivation</td>
</tr>
<tr>
<td>Sleep disturbance</td>
</tr>
<tr>
<td>Dehydration</td>
</tr>
<tr>
<td>Environmental factors</td>
</tr>
<tr>
<td>Immobility</td>
</tr>
</tbody>
</table>

Pediatric Delirium: Non-Pharm Tx

- Orient frequently
- Appropriate stimulation
- Familiar objects and people
- Educated constant companion
- Avoid restraints
- Relaxation techniques

Use Pharmacological Treatments when Appropriate…

& Appropriately…

Pediatric Delirium: Pharmacology

- Haloperidol
  - Infants
  - Multiple routes
- Risperidone
- Benzodiazepines

Pediatric Delirium: Pharmacology

- Haloperidol
  - Young child: 0.05 – 0.5mg / kg / day
    - Max: 10mg / day
  - Adolescent: 0.5 – 10mg / day
    - Max: 100mg / day
  - Divided 1 - 2 times per day
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Pediatric Delirium: Pharmacology

- Risperidone
  - Young child: 0.01 – 0.06 mg / kg / day
    - Max: 2mg / day
  - Adolescent: 0.5 – 6 mg / day
    - Max 8 mg / day
    - Divided 1 - 2 times per day

Vignette 3: Summary

- Recognition is key
- Mixed type can have a variable and challenging presentation
- Antipsychotics are safe
- Non-pharmacologic treatments
- Outcome: patient and family settle and delirium resolves with haloperidol and medication simplification

Wrap Up

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- Lori Montross, PhD

Discussion

www.palliativemed.org  www.IPCRC.net

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