THE SILENT SCREAM OF DELIRIUM

Improving Prevention, Diagnosis, and Management in Palliative Care

MN Rural Palliative Care Networking Group
Quarterly Education Session
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Edvard Munch – “The Scream” 1863
Disclosures

- I have no relevant financial disclosures related to this presentation

- All medications discussed in this presentation are technically Off-Label as currently there are no FDA-approved drugs for delirium management

Educational Objectives

1. Describe the impact of delirium on patient and family suffering, morbidity, mortality, and health care costs.

2. Outline data supporting current inadequate recognition and ineffective management of delirium.

3. Perform a diagnosis of delirium and understand delirium subtypes.

4. Discuss differences in management of potentially reversible versus terminal delirium states.
Delirium Is......

**ACUTE & FLUCTUATING BRAIN DYSFUNCTION SYNDROME**

- Disordered CONSCIOUSNESS
  - Hypo-vigilant, hyper-vigilant
  - Motor changes, involuntary movements
- Impaired ATTENTION
  - Distractibility, perseveration, inconsistency
- Altered COGNITION
  - Memory & language impairment, disorientation
- Abnormal PERCEPTION
  - Delusions, hallucinations, vivid dreams

Why Should We Care?

- High prevalence in serious illness
  - 70% of delirium cases may be either misdiagnosed, diagnosed late, or completely unrecognized!
- Under-treated, even when recognized,
- Long-term suffering occurs after delirium resolves, especially caregivers of dying patients
- Increases in patient morbidity, mortality & healthcare utilization & costs
Scope of Problem

- General medicine inpatients
  - Prevalence on admission - 11-33%
  - Incidence - subsequent development during course - 3-56%
  - Advanced cancer - 24-44%
  - EOL - >80%
- ICU cases - 50-80%
- Postoperative patients – up to 60% - usually resolves within shorter time

Delirium Experience

- Dream-like - “Trapped in incomprehensible experiences”
- Visual hallucinations of people & animals
- “Wide-open senses” → misinterpretation of stimuli → fear, paranoia, sense of threat
- Bustle on unit => “wild parties”
*...Delirium Experience*

- Humiliation
  - Unable to understand what was wanted from those talking to patient
  - Awareness of staff irritation or lack of patience
- Hopelessness, loneliness, depression
- Detachment - as “if in a mist”
- Comfort & reassurance when feeling understood or valued

*...Adverse Outcomes*

**Existential suffering**

- 74% of 99 cancer pts recalled delirium experience
- 81% patients & caregivers rated distress as severe (3.2-3.7/4 scale)
- Similar experience for staff distress
- Delusions associated with ↑ distress
- Decisional caregiver burden
- Bereavement complicated
- Increased risk of PTSD, cognitive decline, or other psychological complications

Bruera. JPM, 2009, 25:164-171
#### Adverse Outcomes

**Physical suffering**
- Increased co-morbid complications
- Decline in functional status
- Decline in cognitive status
- Increased healthcare utilization & costs
- Prolonged hospitalizations
- Increased level of facility care dispositions
- Total cost of care: $200 billion/year (2008)

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**Increased Mortality:**
- 14-37% mortality during admission
- Related to length of delirium
- Persistent delirium: (>2 weeks)
  - 5.2x increase in death at 6 months
  - 3x more likely to die at 1 year (39%)
  - Adjusted for confounding effects
  - 1/3 of cohort delirious at 6 months
- May be independent mortality risk not just marker for death from underlying disease

Marcantonio et al. JAGS, 53:963-969, 2005
Kiely et al. JAGS, 57:55-61, 2008
**Diagnostic Challenges**

- Fluctuating nature
- Overlap with other neuropsychiatric disorders
  - Concurrent association with these disorders
  - Confusion with depression, anxiety, failure to thrive, dementia
  - 42% cases referred to psychiatry = delirium

(Farrell & Ganzini 1995)

**Delirium Subtypes**

- Hypoactive
  - More prevalent in ICU (43-64%)
- Hyperactive
- Mixed
- Sub-syndromal
  - Outcomes appear to be the same
  - Hypoactive form may have less existential distress
  - All respond equally to pharmacologic management – doses required to treat will vary by subtype
**Delirium Assessment Tools**

- Mini Mental Status Exam
  - Does not differentiate delirium & dementia
- Delirium Rating Scale
  - Not designed for diagnosis
- Memorial Delirium Assessment Scale
  - Not designed for diagnosis
- Confusion Assessment Method (CAM)
  - Some special training needed
  - CAM-ICU available
  - 94% sensitive; 89% specific
- Nursing Delirium Screening Scale (NuDSS)
  - 86% sensitive; 87% specific

**Confusion Assessment Method**

**Acute Onset of Mental Status Changes or a Fluctuating Course**

**AND**

- Inattention

**AND**

- Disorganized Thinking **OR**

- Altered Level of Consciousness
### Nursing Delirium Screening Scale

**Symptom Description**

<table>
<thead>
<tr>
<th>Symptom Description</th>
<th>12MN -</th>
<th>8 AM -</th>
<th>4 PM -</th>
<th>12 MN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disorientation</td>
<td></td>
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<tr>
<td>Inappropriate Behavior</td>
<td></td>
<td></td>
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<tr>
<td>Inappropriate communication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illusions or Hallucinations</td>
<td></td>
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<tr>
<td>Psychomotor Retardation</td>
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</tbody>
</table>

**TOTAL SCORE**

- Symptoms scored 0-2
- Score ≥ 2/10 => delirium present

### Delirium Risk Factors

- **Age**
- **Drugs:**
  - Benzodiazepines
  - Opioids
  - Corticosteroids
  - Anticholinergics
  - Poly-pharmacy
  - Sensory impairment
- **Dementia or prior impaired cognition**
- **Severity of illness**
- **Metabolic abnormalities**
- **Metastatic cancer**
- **Infection**
- **Severity of illness**
- **Poly-pharmacy**
- **Sensory impairment**
Delirium Pathophysiology

- Not fully elucidated
- Brainstem reticular formation
  - Hypothalamus, thalamus, & cortex links regulating sleep-awake cycle

- Important neurotransmitters/receptors:
  - **Acetylcholine A
  - Dopamine A
  - Norepinephrine A
  - Serotonin A
  - Histamine A
  - Hypocretin (orexin) A
  - GABA S

Pathophysiology: Final Common Pathway

- Oxidative Stress
- Dopaminergic Excess
- Cholinergic Deficiency
- Agitation
- Hallucinations
- Decreased Consciousness
- Inattention
- Agitation
- Hallucinations
**Prevention of Delirium**

**Multidisciplinary team interventions**

- Identify at risk patients - screening
- Manipulate environmental factors
  - Safety, companionship, reducing overstimulation, correcting sensory deficits, emotional support, avoid sleep interruptions or deprivation (Inouye, 1999; Marcantonio et al, 2001)
- Provide decisional support for avoidance of drug interactions & toxicities

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**Prevention of Delirium**

- Some evidence for proactive use of antipsychotics pre-hip surgery or immediately post cardiac surgery (Kalisvaart et al, 2005; Prakanrattana & Prapaitrakool, 2007)
  
  Other drugs tried with some effects: odansetron, cholinesterase inhibitors
  - Delirium not prevented
  - Delirium severity & duration significantly decreased
  - Hospital LOS reduced
Treatment of Delirium

- ≠ antipsychotics
- Correction of underlying etiologies
  - As possible or feasible
  - As consistent with patient's goals of care
- Removal of potential offending existing medications
  - Especially benzodiazepines & agents with anticholinergic effects
- Rotation of opioids if neurotoxicity is suspected

Pharmacologic Management of Delirium

- Dearth of well-established, evidence-based guidelines
- Haloperidol use
  - Supported by years of experiential data & >30 published studies (25-60% improved)
  - Recommended drug by APA, SCCM, & ACCCM Guidelines for treatment
- Atypical AP use – 3 controlled trials of risperidone & olanzapine (Cochrane 2009)
  - Atypicals may be 1st line when higher haloperidol doses needed or pt at increased risk of EPS or cardio-toxicity
- No FDA-approved medications
Antipsychotics

- **Haloperidol** = drug of choice
- 0.25-0.5mg IV q30 minutes until calm >65yo
- 1-2mg IV q30 minutes until calm <65yo
- Use for 3 doses then double if not effective

- Schedule previous day’s dose with continued prn doses
- May want to double dose each 30 minutes in severe cases
- May be combined with atypical antipsychotic
- 60% in case series managed with titrated haloperidol alone

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**Comparative Pharmacologic Actions of Antipsychotics**

<table>
<thead>
<tr>
<th>Antipsychotic Agent</th>
<th>Sedation</th>
<th>Extrapyramidal Signs</th>
<th>Anticholinergic</th>
<th>Orthostatic Hypotension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol</td>
<td>+</td>
<td>++++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Risperidone (&gt;6mg/d)</td>
<td>+</td>
<td>++</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>+++</td>
<td>0</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
### Parenteral Haldol Equivalents / Comparisons

<table>
<thead>
<tr>
<th>Drug</th>
<th>Relative Potency</th>
<th>Available Formulations</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol (Haldol)</td>
<td>1</td>
<td>Tabs/solution/parenteral</td>
<td>Gold standard antiemetic</td>
</tr>
<tr>
<td>Chlorpromazine (Thorazine)</td>
<td>50</td>
<td>Tabs/solution/parenteral/suppository</td>
<td>Most anticholinergic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>More sedating</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hiccups/SOB mgmt</td>
</tr>
<tr>
<td>Risperidone (Risperdal)</td>
<td>1.5</td>
<td>Tabs/ solution/sublingual</td>
<td>Very similar to haldol</td>
</tr>
<tr>
<td>Olanzapine (Zyprexa)</td>
<td>2.5</td>
<td>Tabs/ parenteral/sublingual</td>
<td>Medium sedation &amp; anticholinergic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Antiemetic, appetite stimulant</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>50</td>
<td>Tabs</td>
<td>Most sedating, less</td>
</tr>
</tbody>
</table>

### Haloperidol Equivalent Daily Dose (HEDD)

- **Median Range needed to manage**
  - 1-4.7mg/day HEDD
  - Hyperactive subtype up to 9mg/d
- **Did not prevent distress experienced by patients at recall even though physical signs controlled**

Hui et al. JPSM 39: 186-196, 2010
Key Points: Management of Delirium

- Further research on optimal dosing is required
  - Different targeted outcomes may require different dose ranges of antipsychotics
  - Larger doses may be needed than currently recommended to reduce distress in addition to physical symptoms
  - Combination antipsychotics may be more efficacious with fewer adverse side effects

...Key Points: Management of Delirium

- Management may need to be proactive not reactive using higher doses at lower level of symptoms or preemptively
- Role of non-pharmacologic approaches in preventing subsequent distress needs further evaluation
- Without altering causal factors, antipsychotics may not improve delirium outcomes
- Prevention has greatest impact on reducing incidence of delirium
Persistent Irreversible Delirium

- Poor prognostic sign
- Marker of limited survival
- Consideration should be made for
  - Transition to Hospice Care
  - Management with Palliative Sedation if not responsive to reasonable use of antipsychotics

3-Pronged Approach - Protocol Based

Prevention
- Environmental
- Pharmacologic

Detection
- Target Risk Population
- Apply Validated Screening Tools

Management
- Reverse or Avoid Offending Factors
- Aggressive Antipsychotic Intervention
- Post-Resolution Distress Intervention
Contact Information

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