Interprofessional Webinar Series

MJHS

INSTITUTE FOR INNOVATION
IN PALLIATIVE CARE
Assessment and Management of Delirium

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Disclosure Slide

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Delirium

- Definition
- Prevalence
- Pathophysiology
- Etiology
- Diagnostic criteria (DSM-5)
- Clinical features
- Evaluation instruments
- Management
Definition

Transient organic brain syndrome characterized by the acute onset of disordered attention (arousal) and cognition, accompanied by disturbances of psychomotor behavior and perception.
Definition

• Syndrome composed of disturbances:
  ▪ consciousness
  ▪ attention (i.e., arousal)
  ▪ cognition

• Abrupt onset and fluctuating course

• Types: Hypoactive, Hyperactive, Mixed
Subsyndromal Delirium (SSD)

- Presence of any core delirium symptoms without presence of all diagnostic criteria
- Severity of scores on rating scales are below the diagnostic threshold
- Intermediate between full syndrome (FDS) and no delirium
Definition

- Very distressing for patients, family members, and staff
- Often misdiagnosed or unrecognized, poorly treated
- Predictor of:
  - increased morbidity/distress/mortality in patients, family, staff; (21 vs. 39 days survival) in cancer patients
  - increased risk of self-harm, harm to staff
  - longer hospitalization
- Interferes with symptom assessment and control

Prevalence

- All hospitalized patients 10%
- Hospitalized cancer patients 8 to 40%
- Terminally ill cancer patients 80%
- Elderly patients with medical illnesses, incidence is ranging from 25% to 41%
- Common neuropsychiatric complication of hospitalized AIDS patients (Tross)

Etiology

• Discovered in fewer than 50% terminal patients

• **Malignant causes:**
  - cancer related
    - brain tumor
    - metastases
  - cancer-treatment related
    - radiation therapy
    - chemotheraphy
  - paraneoplastic syndromes
Etiology

• Nonmalignant causes:
  - metabolic abnormalities (dehydration, electrolyte imbalance)
  - organ failure (liver, renal)
  - medications side effects (benzo, cortico, opioids)
  - infection/sepsis
  - nutritional deficiencies
  - hypoxia
Pathophysiology

• Numerous theories with support

• Different abnormalities of neurotransmitters of various areas of brain:
  ▪ Decreased oxidation metabolism
  ▪ Direct effect on neurotransmitters (acetyl choline, dopamine)
  ▪ Age-related neurotransmitter changes
  ▪ Increased inflammatory cytokines
  ▪ Stress reaction
  ▪ Changes in intraneural signals
    – Leading theory:
      • Decreased cholinergic activity
      • Increased dopaminergic activity

Clinical Features

• Recent onset

• fluctuation of signs, symptoms

• clinical variants:
  ▪ hypoalert/hypoactive
  ▪ hyperalert/hyperactive
  ▪ mixed

• Essential elements:
  ▪ impaired cognition
    • memory impairment
    • confusion
  ▪ impaired emotions
    • dysphoria
    • hypomania
  ▪ impaired perception
    • illusions
    • hallucinations
  ▪ impaired arousal
    • increased, decreased
    • less responsive, distractible
Delirium: DSM-5

Diagnostic Criteria

A. A disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment).

B. The disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day.

C. An additional disturbance in cognition (e.g., memory deficit, disorientation, language, visuospatial ability, or perception).

D. The disturbances in Criteria A and C are not better explained by another preexisting, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma.

E. There is evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e., due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies.

Behavioral Symptomatology

• Early symptoms

- Change in sleep patterns; restlessness and transient periods of disorientation
- Increased irritability
- Withdrawal; refusal to talk to staff or relatives
- Forgetfulness that was not previously present
Behavioral Symptomatology

• Late symptoms
  ▪ Refusal to cooperate with reasonable requests
  ▪ Anger, swearing, shouting, and abusive or physical outbursts
  ▪ Demanding to go home; pacing the corridor
  ▪ Illusions: misidentifying staff; visual and sensory clues
  ▪ Delusions: misinterpreting events, usually paranoid in nature; fears of being harmed or poisoned by chemotherapy
  ▪ Hallucinations: visual or auditory
Hypoactive Delirium

- Also called hypoalert, hypoaroused

- Psychomotor retardation, lethargy, sedation, reduced awareness of surroundings

- Different from depression, sedation due to opioids, obtundation in last days of life

- Most common in palliative care setting

- Occurs most commonly with hypoxia, metabolic disturbances, and anticholinergic medications

- Higher mortality
Hyperactive Delirium

- Restlessness, agitation, hypervigilance, hallucinations and delusions

- 13% to 46% in palliative care setting

- Correlated with alcohol and drug withdrawal, drug intoxication, medication adverse effects
Assessment Instruments

• Diagnostic classification systems
  ▪ DSM-5
  ▪ ICD-9, ICD-10

• Diagnostic interview instruments
  ▪ Delirium symptom interview (DS)
  ▪ Confusion Assessment Method (CAM) - ICU & Peds versions
Assessment Instruments

• Delirium rating scales
  ▪ Delirium Rating Scale (DRS)
  ▪ Confusion Rating Scale (CRS)
  ▪ Memorial Delirium Assessment Scale (MDAS)

• Cognitive impairment screening scales
  ▪ Mini-Mental State Exam (MMSE)
  ▪ Short Portable Mental Status Questionnaire (SPMSQ)
  ▪ Cognitive Capacity Screening Examination Test (BOMC)
**Delirium and Dementia**
*(clinical features)*

<table>
<thead>
<tr>
<th>Feature</th>
<th>Delirium</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaired memory</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Impaired thinking</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Impaired judgment</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Clouding of consciousness</td>
<td>+++</td>
<td>--------</td>
</tr>
<tr>
<td>Major attention deficits</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Fluctuation over course of day</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Disorientation</td>
<td>+++</td>
<td>++</td>
</tr>
</tbody>
</table>

+++ = always present; ++ = usually present; + = present sometimes; ------ = usually absent

## Delirium and Dementia (clinical features)

<table>
<thead>
<tr>
<th>Feature</th>
<th>Delirium</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vivid perceptual disturbances</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Incoherent speech</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Disrupted sleep-wake cycle</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Nocturnal exacerbation</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Insight</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Acute or subacute onset</td>
<td>++</td>
<td>-------</td>
</tr>
</tbody>
</table>

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## Depression and Hypoactive Delirium

<table>
<thead>
<tr>
<th>Features</th>
<th>Hypoactive Delirium</th>
<th>Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arousal</td>
<td>hypoaroused</td>
<td>normal</td>
</tr>
<tr>
<td>Cognitive Changes</td>
<td>Memory, dysnomia, +++</td>
<td>Mild deficits, subjective</td>
</tr>
<tr>
<td>Temporal Onset</td>
<td>Abrupt</td>
<td>Slow</td>
</tr>
<tr>
<td>Perceptual Disturb</td>
<td>Up to 75% of patients</td>
<td>Rarely</td>
</tr>
<tr>
<td>Thought Content</td>
<td>Paranoid delusions</td>
<td>Guilt, hopelessness...</td>
</tr>
<tr>
<td>Mood Symptoms</td>
<td>Labile, disinhibition</td>
<td>Sad, depressed</td>
</tr>
<tr>
<td>Psychomotor Activity</td>
<td>Quiet, slowed</td>
<td>Slowed, quiet,</td>
</tr>
<tr>
<td>Family History</td>
<td>N/A</td>
<td>common</td>
</tr>
<tr>
<td>Neurological Exam</td>
<td>Asterixis, frontal release</td>
<td>Usually normal</td>
</tr>
<tr>
<td>Past Psychiatric History</td>
<td>May be present</td>
<td>Not uncommon</td>
</tr>
</tbody>
</table>

Breitbart W, Alici Y. Agitation and delirium at the end of life: "We couldn't manage him." *JAMA* 2008;300(24):2898-2910, E1
Delirium Management: Treatment of Underlying Cause(s)

- Evaluation is dependent on goals of care

- Reversibility:
  - reversible in 50%:
    - medications
    - hypercalcemia
    - metabolic abnormalities
    - infection
    - dehydration
  - irreversible:
    - metabolic derangements (renal, liver)
    - hypoxic encephalopathy
Delirium Management: Nonpharmacological Measures

- Reassuring: presence of person at bedside
- Orienting
- Massage
- Limit number of people in room
- Oxygen delivery
- Well-lit room
- Environment: calm, familiar objects
- Support to patient and family
Delirium Management: Pharmacological Measures

- Limited trials to evaluate the management of delirium
- Fewer trials to compare regimens in controlled fashion
- Treatment controversial
Delirium Management: Pharmacological Measures

- neuroleptics
- benzodiazepines
### Drugs

<table>
<thead>
<tr>
<th>Neuroleptics</th>
<th>Approximate daily dosage range (mg)</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol (Haldol)</td>
<td>0.5-5mg q2-12h</td>
<td>PO, IV, SC, IM</td>
</tr>
<tr>
<td>Quetiapine (Seroquel)</td>
<td>25-150mg q12</td>
<td>PO</td>
</tr>
<tr>
<td>Chlorpromazine (Thorazine)</td>
<td>12.5-50mg q4-12h</td>
<td>PO, IV, IM</td>
</tr>
<tr>
<td>Droperidol (Inapsine)</td>
<td>0.5-5mg q12h</td>
<td>IM, IV</td>
</tr>
<tr>
<td>Olanzapine (Zyprexa)</td>
<td>5-10mg bid</td>
<td>PO</td>
</tr>
<tr>
<td>Risperidone (Risperdal)</td>
<td>1-3mg bid</td>
<td>PO</td>
</tr>
</tbody>
</table>

### Benzodiazepines

<table>
<thead>
<tr>
<th></th>
<th>Approximate daily dosage range (mg)</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorazepam</td>
<td>0.5-2.0mg q1-4h</td>
<td>PO, IV, IM</td>
</tr>
<tr>
<td>Midazolam</td>
<td>30-100mg per 24h</td>
<td>IV,SC</td>
</tr>
</tbody>
</table>

- PO= orally, IV= intravenously, SC= subcutaneously, IM= intramuscularly
- Benzodiazepines can cause or increase delirium. Use short acting if sedation is needed and with caution
Pharmacological Management

• Typical antipsychotics:

  ▪ **Haloperidol** → first line / practice standard

    ▪ (few anticholinergic effects, minimal cardiovascular adverse effect, lack of active metabolites, different routes of administration)

• 1-2 mg po every 4 hours. Not to exceed 20 mg in 24 hours

• QTc prolongation and torsades de pointes

• Add lorazepam for severe agitation (help sedate, minimize extrapyramidal effects)
Pharmacological Management

- **Atypical antipsychotics** (risperidone, olanzepine, quietapine, ziprasidone, aripiprazole):
  - No statistically significant difference than Haldol
  - No difference in toxicity (except in high dose of Haldol (6.5mg))
  - Efficacy is equivalent to Haldol, suggestion of fewer EPS

Pharmacological Management

• Sedative agents: Benzodiazepines
  ▪ 30% of patients do not have symptoms controlled by antipsychotics
  ▪ Role unclear
  ▪ Not first line (unless benzo withdrawal)
  ▪ Use in combination with antipsychotics
  ▪ Can cause and increase delirium (caution)
  ▪ Use of lorazepam, midazolam (shorter acting)
Pharmacological Management

- **Psychostimulants**
  - For hypoactive delirium
  - Only case reports and one open-label study
“Terminal” Delirium / Sedation

• Most common symptoms requiring sedation

• Rates of sedation 10%-52%

• Controversial topic

• Indication: intractable delirium

• Drugs of choice: midazolam, lorazepam

Pharmacological Prevention of Delirium

• Prophylactic use of pharmacologic agents in the prevention of delirium have had mixed results at best

• Prophylactic neuroleptics do not prevent delirium in palliative care settings
Conclusion

- Delirium is a frequent, devastating complication of advanced disease

- Pathophysiology is related to neurotransmitters: decrease in cholinergic activity, increase in dopaminergic activity

- Work-up and treatment should be in accord with GOC

- Treatment with neuroleptics is the treatment of choice

- Haldol is the best and most practical drug

- Benzos need to be used with caution; they can increase delirium
Assessment and Management of Delirium

Q/A
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