Psychosis in the Elderly - Differentiating Delirium, Dementia, Drug and Disease State Causes

Christina Ward, PharmD, BCPS
Deaconess Health System
September 29, 2017

Learning Objectives

- Discuss methods of identifying and treating multiple causes of psychosis in elderly patients.
- Describe potential adverse effects of antipsychotic use in the elderly population.

<table>
<thead>
<tr>
<th>Delirium</th>
<th>Dementia</th>
<th>Drugs</th>
<th>Disease States</th>
<th>Antipsychotics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
What is the most commonly used ICU delirium assessment tool?

Answer - CAM-ICU or ICDSC

- Delirium
- Attentional deficits
  - Cardinal feature of delirium vs dementia
  - Usually reversible
  - Temporary confusion
  - Fluctuates throughout the day
- Acute onset
- Disorganized thinking
- Altered level of consciousness
- Sleep-wake cycle disturbances
- Perceptual disturbances/hallucinations

What is an essential piece of diagnostic work-up for patients with altered mental status or psychosis but often difficult to obtain?
Answer - Patient History

- Patient work-up/diagnosis
  - History
  - Physical examination
    - Fever, hypertension, tachycardia, Cushingoid appearance
  - Laboratory testing
    - CBC, CMP, thyroid function, urine drug screen, vitamin B₁₂ and folate levels, UA/cultures, NH₃
  - Medication history
    - Imaging
      - Brain CT/MRI, CXR, abdominal CT

Am Fam Physician 2015;91(12):856-863

Answer

- Which of the following is the most common risk factor for delirium in elderly patients?
  A. Surgery
  B. Medications
  C. Dementia
  D. Sleep deprivation

Answer - C (Dementia)

- Potentially modifiable risk factors
  - Immobilization (restraints)
  - Medications
  - Infections/disease states
  - Surgery
  - Environment (ICU)
  - Uncontrolled pain
  - Sleep deprivation
  - Hearing/vision impairment

- Nonmodifiable risk factors
  - Age > 65 years
  - Dementia/cognitive impairment
  - Male
  - Renal/hepatic disease and multiple comorbidities
  - History of stroke, delirium, neurological disease

Nat Rev Neurol 2009;5(4):210-220
True or False?

All causes of dementia are progressive and irreversible.

Answer - False

- Dementia is persistent memory loss and impaired function in one of the following:
  - Aphasia
  - Apraxia
  - Visuospatial function
  - Executive function

- Reversible causes of dementia
  - Pseudodementia
  - Dementia resulting from depression
  - Normal pressure hydrocephalus
  - Vitamin deficiencies
    - Vitamin B₁₂ (cyanocobalamin)
    - Vitamin B₁ (thiamine)
    - Vitamin B₃ (niacin)

How many people in the United States currently have Alzheimer’s Disease?

A. 1 million
B. 5 million
C. 20 million
D. 500,000
Answer - B (5 million)

- Warning signs of Alzheimer’s Disease
  - Memory loss affecting job
  - Language problems
  - Difficulty performing familiar tasks
  - Disorientation to time/place
  - Poor/decreased judgment
  - Problems with abstract thinking
  - Misplacing items
  - Changes in mood/behavior
  - Personality changes
  - Loss of initiative
- Severity assessment
  - Mini mental state exam
  - Clock drawing
  - Clinical dementia rating scale
  - Alzheimer’s Disease Assessment Scale (ADAS)

Name 2 of the 5 currently available FDA-approved medications for Alzheimer’s disease.

Answers

- Current pharmacologic treatments
  - Donepezil
  - Galantamine
  - Memantine
  - Rivastigmine
  - Donepezil/memantine
- Non-pharmacologic treatments
  - Memory/orientation exercises
  - Art/music therapy
  - Exercise programs
  - Validation/reminiscence therapy
- Upcoming potential treatments
  - Solanezumab - targets beta-amyloid
  - Verubecestat - targets beta-secretase
  - AβVact - targets tau protein
  - Intepirdine - targets acetylcholine
Which anti-epileptic medication can cause increased ammonia levels, resulting in altered mental status?

**Answer - Valproic acid/ Divalproex**

- Elevated ammonia levels can occur at any time during treatment.
- Caused by interference with an enzyme that helps clear ammonia via the urea cycle.
- Typical presentation includes confusion, lethargy, vomiting, increased seizure frequency but can progress to death in rare cases.
- Valproic acid should be discontinued in patients with hyperammonemia-related encephalopathy.
  - Consider risk vs benefit of resuming - can add carnitine supplementation and lactulose to medication regimen to help control ammonia.

A 69 yom visits his doctor for a 3 day history of runny nose, cough and chills. His physician diagnoses him with pneumonia and prescribes azithromycin and a prednisone taper and recommends he take diphenhydramine OTC.

His family brings him to the ER 2 days later for confusion and agitation. What is/are the most likely medication-related culprit(s)?
Answer - diphenhydramine + prednisone

- Medications most likely to cause delirium
  - POLYPHARMACY
  - Opioids
  - Meperidine
  - Benzodiazepines/hypnotics
  - Muscle relaxers
  - Anticholinergic agents
    - Diphenhydramine, promethazine, hydroxyzine, meclizine, amitriptyline, scopolamine
  - Antipsychotics
  - Corticosteroids
  - H2-receptor antagonists
    - Famotidine, ranitidine
  - Substance abuse/withdrawal

What is the name of the American Geriatrics society list of potentially inappropriate medications that should be avoided or carefully monitored in older adults?

Answer - Beers Criteria/List

- Annual outpatient polypharmacy visits in adults ≥ 65 years increased from 1.5 to 3.68 million between 2004-2013
- Polypharmacy = 3+ Beers List medications
Diagnose me - 81 yof presenting with confusion, agitation, and decreased appetite. Her Urinalysis resulted:

WBC = 24
Leukocyte esterase = +
Nitrite = +
Bacteria = Many

Answer - Urinary tract infection

- Infections that can cause altered mental status:
  - Urinary tract infection
  - Pneumonia
  - Meningitis/encephalitis
  - Neurosyphilis
  - Human Immunodeficiency virus
  - Brain abscess
    - Toxoplasmosis
    - Neurocysticercosis

Diagnose me - 45 yom presenting with altered mental status. Family reports he drinks a fifth of vodka daily. Pertinent labs include NH₃ 115 µg/dL, Na 124 mEq/L.
Answer - Hepatic Encephalopathy + Hyponatremia

- Metabolic disorders that can cause altered mental status:
  - Hypo/hypernatremia
  - Hypo/hypercalcemia
  - Hepatic/renal failure (esp accumulation of medications)
  - Thiamine deficiency (Wernicke’s encephalopathy)
  - Hypo/hyperglycemia

Diagnose me - a 72 yof presenting with vision loss, auditory hallucinations, dry skin and hair, TSH 45 mlU/L, T4 <1µg/dL, T3 24 ng/dL.

Answer - Myxedema Madness

- Endocrine disorders that can cause altered mental status:
  - Hyperthyroidism/hypothyroidism
  - Cushing disease
    - Adrenal tumor that produces excessive ACTH, stimulating excessive cortisol production
  - Insulinomas
    - Pancreatic tumor that produces excessive amounts of insulin
  - Pheochromocytoma
    - Adrenal tumor that produces excessive epinephrine, norepinephrine, dopamine
Other disease state causes of psychosis

- Cerebrovascular accident
- Subarachnoid/intraventricular hemorrhage
- Brain tumors
- Hypertensive encephalopathy
- Congestive heart failure/acute myocardial infarction
- Hypoxemia
- ICU delirium
- Hypo/hyperthermia
- Narcolepsy
- Epilepsy
- Trauma

True or false?

There is a black box warning for an increased risk of death when antipsychotics are used to treat elderly patients with dementia-related psychosis.

Answer - True

- 1.5-1.7x increased risk of mortality when atypical antipsychotics are used in dementia
- 2-3x increased risk of cerebrovascular events for those on atypical antipsychotics
- Increased risk of preventable adverse events (adjusted OR = 3.4)
- American Geriatrics Society recommends only using antipsychotics to treat neuropsychiatric symptoms of dementia if the patient is a threat to self or others and has failed non-pharmacological options
The Centers for Medicare and Medicaid services require pharmacists to review nursing home residents’ antipsychotic regimens how often?

Answer - Monthly

- Psychotropic drugs (antipsychotics, antidepressants, anti-anxiety, hypnotics, opioids) reviewed monthly for:
  - Excessive dose or duration
  - Inadequate monitoring
  - Inadequate indication for use
  - Need for dose reduction/discontinuation due to adverse effects
- PRN orders for antipsychotics or psychotropic agents limited to 14 days
Name at least 2 major adverse effects associated with antipsychotics.

**Answers**
- Sedation
- QTc prolongation
- Metabolic syndrome
  - Weight gain
  - Diabetes mellitus
  - Dyslipidemia
- Extra pyramidal symptoms (EPS)
  - Dystonia
  - Akathisia
  - Pseudoparkinsonism
  - Tardive dyskinesia
- Valbenazine (Ingrezza®) - new treatment
- Hyperprolactinemia

**Atypical antipsychotic comparison**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Metabolic</th>
<th>QTc prolongation</th>
<th>Sedation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Wt. gain</td>
<td>Diabetes</td>
<td>Dyslipidemia</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Clozapine</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Lurasidone</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Paliperidone</td>
<td>Low-mod</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Mod</td>
<td>Mod</td>
<td>Mod</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
</tbody>
</table>
New antipsychotics

- Cariprazine (Vraylar®)
  - Treatment of schizophrenia/bipolar disorder
  - Improved control of negative symptoms (apathy, flat affect, decreased expressiveness)
- Brexpiprazole (Rexulti®)
  - Concurrent treatment of depression and schizophrenia
- Pimavanserin (Nuplazid®)
  - Hallucinations/delusions associated with Parkinson’s disease psychosis

![Psychosis in the Elderly - Differentiating Delirium, Dementia, Drug and Disease State Causes](image)

Christina Ward, PharmD, BCPS
Deaconess Health System
September 29, 2017

---

FINAL JEOPARDY

What 3 words did I have you memorize at the beginning of this presentation?