More than Just the Blues: Major Depressive Disorder and Serotonin Syndrome in the Elderly

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Learning Objectives

1. Using definitions of major depressive disorder, differentiate depression from delirium and dementia in an older adult.
2. Review available treatment options for depression with a focus on use in the geriatric population.
3. Determine the risks associated with the development of serotonin syndrome in an older adult.
4. Describe the clinical presentation of and management strategies for serotonin syndrome.

Epidemiology

- One of the most common and serious health conditions in older adults
- Impaired functioning
- Increased health care expenditures
- Increased mortality
- Increasing prevalence with aging population
- Not a consequence of aging
- Higher rates of depression in older adults with co-morbidities including stroke, myocardial infarction (MI), cancer, and dementia

Risk Factors

- Family history
- Previous episode of depression
- Chronic medical conditions
  - Stroke, MI, diabetes
  - Alzheimer’s, Parkinson’s disease
  - Cancer
  - Rheumatoid arthritis
  - Insomnia
- Use of certain medications (e.g., beta-blockers, corticosteroids)
- Alcohol
- Female
- Single, widowed, divorced
- Social isolation
- Lower socioeconomic status
- Stressful life events
  - Loss of a loved one
  - Disease or injury
  - Disability
  - Functional impairment
  - Loneliness

Etiology and Pathogenesis

- Age-related decline in neurons and receptors in the central nervous system (CNS)
- Frontostriatal region
- Amygdala
- Hippocampus
- Cerebrovascular disease
- Cerebral atrophy and decrease in brain volume

Faculty Disclosure

Stephanie Sibicky has no actual or potential conflicts of interest to disclose pertaining to this presentation.
DSM-V Diagnostic Criteria

Major Depressive Episode
- ≥ 5 of the following during same 2-week period and represent a change from previous functioning
  - Must have either depressed mood or loss of interest/pleasure as a symptom
  - Significant weight loss without dieting or weight gain or decrease/increase in appetite
  - Insomnia or hypersomnia
  - Psychomotor agitation or retardation
  - Fatigue or loss of energy
  - Feelings of worthlessness or excessive/inappropriate guilt (may be delusional)
  - Diminished ability to think or concentrate, or indecisiveness
  - Recurrent thoughts of death (not just fear of death), suicidal ideation without a plan, or a suicide attempt or plan to commit suicide
- Symptoms cause distress or social, occupational, or other functional impairment
- Episode is not attributable to the effects of a substance or other medical condition

Clinical Presentation in Older Adults
- Often underdiagnosed or delayed diagnosis or treatment
- Older adults often present with more physical or somatic symptoms
  - Somatic complaints of pain, insomnia, fatigue, heart palpitations, headache, gastrointestinal distress, weight loss
  - Anxiousness, worry, or distress more than depressive symptoms
- Decreased concentration
  - Fear of Alzheimer’s disease and dementia
  - Pseudodementia
    - Cognitive impairment that develops after the onset of mood symptoms
    - Deficits in mental processing speed and executive function
    - Resolution of depression allows for normal thinking and memory returns

Impact of Depression for Older Adults
- Untreated depression
  - Decreased daily function
  - Poor quality of life
  - Increased rate of mortality with comorbid conditions
  - Increased rate of suicide
    - Older adults are one of the most affected populations
    - Possible mechanism includes loss of signaling in decision-making and reward centers leading to impulsive and/or careless behaviors

Check Point #1
Which of the following statements is TRUE regarding depression in older adults?
A. Most older adults experience depression as a consequence of aging.
B. Older adults complain of more psychiatric symptoms as opposed to physical (somatic) symptoms.
C. Certain medications, like corticosteroids and beta-blockers, may contribute to depressive symptoms.
D. The diagnosis of depression is different for older adults than younger adults.

Check Point #1
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D. The diagnosis of depression is different for older adults than younger adults.
Goals of Therapy

- Address comorbid conditions and underlying causes
- Select appropriate pharmacotherapy and other modalities
- Monitor therapy for effectiveness, adherence, complications
- Continual monitoring and close follow-up

Non-Pharmacologic Treatment

- Psychotherapy
  - As monotherapy or with pharmacotherapy
  - Cognitive behavioral therapy (CBT)
  - Interpersonal psychotherapy
  - Problem-solving therapy
- Neurostimulation
  - Electroconvulsive therapy (ECT)
  - Deep brain stimulation (DBS)
- Exercise
- Light therapy
- Collaborative care programs
  - Non-physician mental health professionals
  - Depression care managers
- Home-based care
- Family support

Pharmacologic Treatment

- First-line includes second generation antidepressants
  - Little difference in efficacy between classes
  - Consider side-effects and drug interactions
- Response to therapy
  - Typically 4-6 weeks in healthy, younger adults
  - Older adults may take 8, 12, or up to 16 weeks
- Dosing strategy
  - Start low and go slow
  - Titrate to adequate dosing
  - Assess adherence

Selective Serotonin Reuptake Inhibitors (SSRIs)

- Less side effects, safer in overdoses compared to other agents
- Concern for hyponatremia (SIADH), Parkinsonism, anorexia, bradycardia, bleeding
- Sertraline, citalopram, escitalopram
  - Less drug interactions and cognitive effects
  - Citalopram maximum dose 20 mg daily due to dose-dependent QTC prolongation
- Not recommended first-line
  - Paroxetine (sedation)
  - Fluoxetine (activating, long half-life with metabolites)

Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

- Beneficial in depression with neuropathic pain or fibromyalgia ( duloxetine FDA-approved)
- Can be excitatory – administer in the morning
- Monitor for blood pressure elevations and in patients with significant cardiac history
- Concern for SIADH and hyponatremia (especially with venlafaxine)

Other Antidepressant Options

- Bupropion
  - Most activating (administer in the morning)
  - Contraindicated in seizure disorders
- Mirtazapine
  - Causes sedation and increases appetite
  - Sedating effects at lower doses but diminish when noradrenergic effects predominate anticholinergic
- Trazodone and Nefazodone
  - Trazodone: sedating at low doses, antidepressant at higher doses, priapism
  - Nefazodone: better gastrointestinal tolerance, caution with CYP 3A4 drug-drug interactions
  - Both: sedation and hyponatremia
Other Pharmacologic Options

- Tricyclic antidepressants (TCA)
  - Use if failure of other antidepressants
  - Caution in cardiovascular disease
  - Side effects: limit use
  - Beers criteria recommends these agents be avoided

- Monoamine oxidase inhibitors (MAOI)
  - Rarely used unless previously initiated and tolerated
  - Treatment resistant cases

Monoamine oxidase inhibitors (MAOI)
- Dietary restrictions and drug-drug interactions limit use

Check Points

Check Point #2

KL is an 84-year-old female with depression who was started on sertraline 25 mg daily 4 weeks ago. She presents to your clinic asking for another medication because she is still symptomatic. What is an appropriate response to her inquiry?

A. Let’s switch to bupropion since it is in another class
B. It can take up to 16 weeks for a full response, so let’s stay the course
C. Let’s increase your dose to 100 mg daily
D. Let’s add quetiapine to your regimen

Differentiating Depression, Delirium, and Dementia

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<th>Delirium</th>
<th>Dementia</th>
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<tbody>
<tr>
<td>Chronic, gradual onset</td>
<td>Acute development, can fluctuate</td>
<td>Progressive decline, often difficult to pinpoint start</td>
</tr>
<tr>
<td>Depressed mood, apathy, anhedonia, normal attention</td>
<td>Irritability, can have impaired cognition, disorientation, delusions</td>
<td>Primary defect in short term memory, difficulty finding words or naming items</td>
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Adjunctive Therapies

- Methylphenidate
- Aripiprazole
- Lithium
- Liothyronine
- Buspirone
- Quetiapine

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Serotonin Syndrome
Serotonin Syndrome

- Potentially life-threatening
- Associated with medication use, drug-drug interactions, and intentional self-poisoning
- Occurs in all age groups, but elderly specifically susceptible
- Incidence is often under-reported due to clinical diagnosis
- Caused by stimulation of post-synaptic serotonin receptors by excess serotonin in the CNS

Clinical Features

Changes in Mental Status
- Anxiety
- Agitation
- Restlessness
- Disorientation

Autonomic Hyperactivity
- Diaphoresis
- Tachycardia
- Hyperthermia
- Hypertension
- Vomiting
- Diarrhea

Neuromuscular Abnormalities
- Tremor
- Rigidity
- Myoclonus
- Hyperreflexia
- Ocular clonus

Diagnosis

- Recent history including medication use, additions, changes to doses and schedules
- Hunter Toxicity Criteria Decision Rules (84% sensitive, 97% specific)
- Laboratory tests to rule out other causes (infection, electrolyte abnormalities)
- Differential include neuroleptic malignant syndrome, malignant hyperthermia, anticholinergic toxicity, meningitis/encephalitis

Check Point #3: Patient AP

- AP is an 80-year-old male admitted to short-term rehab after falling and suffering a right thalamic hemorrhage
- His PMH is significant for major depressive disorder, TIA, CAD, BPH, asthma, atrial fibrillation, and hypertension
- His SH and FH are unremarkable
- He is currently hemodynamically stable and his only abnormal laboratory value is a hemoglobin of 11.6 (low)

Check Point #3: AP’s Medication List

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Evidence of taking a serotonergic agent + ONE of the following:
- Spontaneous clonus, inducible clonus + agitation or diaphoresis
- Ocular clonus + agitation or diaphoresis
- Tremor + hyperreflexia
- Hypertonia + temperature > 38°C + ocular clonus or inducible clonus

Check Point #3: Which medications put AP at risk for serotonin syndrome?

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Management of Serotonin Syndrome

Discontinuation of Serotonergic Agent

Supportive Care

Administration of Serotonin Antagonist

Prevention, Monitoring, Follow-up

• Cyproheptadine (available in tablets and oral solution)
• Side effects include sedation, hypotension
• Efficacy is lacking, mostly from case reports

• Mainstay of therapy
• Oxygen, intravenous fluids, continuous cardiac monitoring, correction of vital signs
• Use of chemical > physical, if necessary
• Can use benzodiazepines
• Avoid haloperidol due to anticholinergic properties

• Mild (4-6 hours observation), moderate (cardiac monitoring), severe (ICU admission)
• Avoid multi-drug regimens
Check Point #4
Which of the following treatment strategies can be employed for a patient experiencing severe serotonin syndrome?

A. Oxygen and intravenous fluids  
B. Benzodiazepines  
C. Cyproheptadine  
D. Vasopressors, if hemodynamically unstable  
E. Call poison control/toxicologist  
F. All of the above

Key Points

• Depression in late life is a common and serious condition that requires appropriate assessment and treatment
• It is important for geriatric pharmacists to evaluate for concurrent conditions such as delirium and dementia, as these can make the diagnosis of depression difficult
• Medication selection and appropriate monitoring is essential to increase the patient’s chance for remission
• Pharmacists play a key role in identifying risk factors for serotonin syndrome in older adults including therapeutic duplications and drug-drug interactions

Check Point #4
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Questions?
Thank you!
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References


References, cont.