SCHIZOPHRENIA IN OLD AGE

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Objectives

- Understand common causes of psychosis in the elderly.
  - Differentiate types of psychosis within the geriatric population.
- Understand appropriate treatment of psychosis in the elderly according to evidence based medicine.
- Understand the functional differences in treating elderly patients with schizophrenia.

Test your knowledge Q1

- What is the most common cause of psychosis in the elderly?
  - A. Infection
  - B. Schizophrenia
  - C. Dementia
  - D. Delirium

Test your knowledge Q2

- What is the most common presentation of psychosis in the elderly?
  - A. Hallucinations (auditory, visual or tactile)
  - B. Delusions
  - C. Negative symptoms
  - D. Paranoia

Test your knowledge Q3

- What is the preferred treatment (according to EBM) of acute agitation in elderly patients with delirium?
  - A. Benzodiazepines
  - B. High-potency antipsychotics (haloperidol)
  - C. Second generation antipsychotics
  - D. Combination antipsychotics and benzodiazepines

Test your knowledge Q4

- What is the most effective treatment for depression with psychotic features in the elderly population?
  - A. Selective serotonin reuptake inhibitor (SSRI) antidepressants
  - B. Antipsychotic medications
  - C. Electroconvulsive therapy (ECT)
  - D. Combination antidepressant and antipsychotic therapy
  - E. Tricyclic (TCA) antidepressants

Psychosis in Old Age

- Prevalence not well studied, but not uncommon.
- Challenging to diagnose.
- Multiple causes:
  - Delirium
  - Medication side effects
  - Medical illnesses
  - Schizophrenia
  - Dementia
  - Mood disorders
  - Substance abuse disorders
  - Metabolic derangements

Etiology of Psychosis in Elderly

- Dementia 40%
- Major depression 33%
- Delirium 7%
- Medical conditions 7%
- Mania 5%
- Substance-induced 4%
- Delusional disorder 2%
- Schizophrenia 1%

Holroyd and Laurie, 1999

Psychosis in Old Age

- In young/middle age adults most common cause for psychosis is schizophrenia or substance abuse disorders.
- Psychosis in old age is most commonly related to dementia.
  - Delusional based rather than auditory hallucinations
  - Alzheimer's #1
  - Lewy body dementia #2
    - Prominent visual hallucinations.

Alzheimer's Dementia and Psychosis

- ~30-50% of AD patients have psychotic symptoms.
  - Subtype of AD based on genetic testing and neuropathological testing
    - Genetic variation in dopamine receptor 1 and 3.
    - Increased densities of senile plaques and neurofibrillary tangles in the prosubiculum and middle frontal cortex.
    - Hypometabolism in the prefrontal cortex—correlated with delusions in AD patients.
- Most common in intermediate stage of dementia rather than early or late stages.

(Jeste & Finkel, 2000 Sweet et al., 1998; Zubenko et al., 1991; Mega et al., 2000; Sultzer et al., 2003)

Psychosis due to AD Diagnostic Criteria According to Jeste and Finkel

1. Patients must meet all criteria for the diagnosis of Alzheimer's-type dementia.
2. They must have visual or auditory hallucinations or delusions at least intermittently for one month of longer, and the psychosis must NOT have been present continuously prior to the onset of the symptoms of dementia.
3. The psychotic symptoms must be severe enough to cause some disruption in patients' or others' functioning and cannot be better accounted for by another general medical condition, substanceoinduced psychosis, nor occur exclusively in the course of delirium.
4. Criteria for schizophrenia, schizoaffective disorder, delusional disorder, or mood disorder with psychotic features must never have been met.

Jeste and Finkel, 2000

Treatment of Psychosis in AD

- Antipsychotics beneficial in treating AD with psychosis and/or behavioral disturbances—demonstrated in several studies.
- Lower doses recommended d/t FDA warnings of increased risk of stroke or MI in AD patients with antipsychotic use.
- According to the The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE-AD trial) elderly patients with AD were noted to benefit from symptom improvement, declines in hostility, aggression, mistrust and uncooperativeness with antipsychotic use.
  - However, no improved functional capacity or quality of life noted.
  - Need to take into account risks vs. benefits on an individual basis.

Sultzer et al., 2008

Treatment of Psychosis in AD continued

- "Go to" antipsychotics prescribed in the elderly in clinic:
  - Risperidone: 0.25 mg- 1mg BID or HS dosing
  - Olanzapine: 2.5-5 mg HS dosing
  - Quetiapine: 25-100 mg divided or HS dosing
  - Avoid antipsychotics with higher degree of anticholinergic side effects due to increased sensitivity in elderly patients.
- Avoid benzodiazepines for related agitation/aggression where possible d/t increased side effects in this population.
  - Increased risk for falls.
  - Worsened cognition.
  - Respiratory depression.

Major Depression and Psychosis in the Elderly

- 2nd most common cause of psychosis in the elderly.
- Late-onset depression (>50 y.o.) more commonly associated with psychosis.
  - F>M
  - Associated with more severe depression.
- Delusions frequent in elderly patients hospitalized for depression.
- Treat depression first with typical antidepressant therapy (SSRI, SNRI, TCA, etc).
- Combination therapy (antidepressant + antipsychotic) may be necessary.
  - Jury is still out as to if combination is really more effective.
- ECT
  - Most data supporting efficacy .

Sulzter et al., 2008; Kessing, 2006; Dombrovski et al., 2005; Dombrovski & Mulsant, 2007

Delirium in Old Age

- Third most common cause of psychosis in old age.
- Visual hallucinations most common.
- Frequent confusion, reactivity to hallucinations and disorientation leads to increased aggressive behaviors.
- Paranoia common.

Treatment Recommendations for Delirium in the Elderly

- Low-dose high potency antipsychotics most effective (ie; haloperidol).
  - Oral, IM, or IV.
    - Ability to use IV or IM allows for quick action to allow for appropriate treatment and testing of underlying causes of delirium.
  - Haloperidol has the most evidence supporting efficacy.
  - Theoretically 2nd generation antipsychotics could also be used, but research is very limited.
- Short duration of use
  - Increased mortality with chronic use.
- Ultimately need to determine and treat the cause of delirium.
  - UTI's most common medical cause of delirium in this age population.

Common Medical Causes of Psychosis in Old Age

- Nutritional deficiencies:
  - Folate, niacin, thiamin, vitamin B12.
- Space-occupying lesions of the brain:
  - Abscess, neoplasm, subdural hematoma.
- Neurological disorders:
  - Cerebrovascular disease, Huntington's disease, epliepsy, migraines, multiple sclerosis, Parkinson's disease, normal pressure hydrocephalus, Wilson's disease, Hearing or visual impairment.
- Metabolic and endocrine disorders:
  - Addison's disease, Cushing's disease, electrolyte imbalances, hepatic disease, hyper- or hypothyroidism, hyper- or hypoglycemia, pituitary insufficiency, porphyrias, renal disease.
- Infections:
  - Encephalitis, meningitis, human immunodeficiency virus (HIV), subacute bacterial endocarditis, syphylis.
- Autoimmune disorders:
  - Systemic lupus erythematosus.

Miller and Solai, 2013

DSM-5 Diagnostic Criteria for Schizophrenia

A. Two or more of the following must be present for a significant amount of time during a month long period (or less if treated accordingly). At least one of these must be either item 1, 2, or 3.
   1. Delusions.
   2. Hallucinations.
   3. Disorganized speech.
   4. Grossly disorganized or catatonic behavior.
   5. Negative symptoms.

B. For a large portion of the time since onset there needs to be significant impairment in ability to function in one or more major areas (ie; social, self-care, work, etc).

C. Continuous signs of disturbance need to be present for at least 6 months (unless successfully treated). This may include prodromal and residual periods.

Diagnostic and statistical manual of mental disorders (5th ed.), 2014

Epidemiology

- Worldwide prevalence = 0.5%-1%
- Age of onset typically 18-25 y.o. for males and 21-30 y.o. for females
- Frequently remain single
- Less likely to have children
- Increased risk for suicidal behavior
  - 1/3 attempt
  - 1/10 eventually complete

Late-Onset Schizophrenia

- Late-onset (>40-65 years) represents ~15-20% of all patients with schizophrenia, according to several estimates.
- ~4% develop symptoms after age 60.
- F>M
- More often presents with visual tactile and olfactory hallucinations
  - Earlier onset more often presents with auditory hallucinations.
- Paranoid subtype more common
- Less likely to exhibit formal thought disorder and/or observed affective flattening.
- Better prognosis, requires lower daily doses of antipsychotics.

Harris and Jeste, 1998; Howard et al., 2000; Howard et al., 2000; Pearlson et al., 1989; Jeste and Maglione, 2913

Aging and Schizophrenia

- Patients with schizophrenia have been shown to have accelerated physical aging.
  - Premature morbidity and mortality compared to general population.
  - Average life span is 20-23 years shorter.
  - Mean standard all cause mortality rate = 2.58.
- Aging in schizophrenic patients associated with improved psychosocial function, less substance abuse, and decreased psychotic symptoms, reduced risk of hospitalization, and improved mental health related quality of life.

Tiihonen et al., 2009; Saha et al., 2007; Jeste and Maglione 2013

Pertinent Pharmacodynamic Changes Observed in the Elderly

- Must take into account functional and structural anatomical differences in older populations in regards to prescribing.
  - Hepatic synthesis declines with age.
  - Antipsychotic medication largely hepatically cleared.
    - Increased % of biologically active drug in the blood.
    - Increased volume of distribution.
    - Increased half-life.
  - Permeability of BBB also affected by aging.
    - Increased concentrations of antipsychotic medication in the brain?
  - Decreased # of DA neurons and decreased density of D_2 receptors with increasing age.
    - Increased EPS, parkinsonism, falls and metabolic syndrome.

Treating Schizophrenia in the Elderly

- Historically not many studies on treatment in this population.
- More recent studies have been on olanzapine and risperidone.
  - Well tolerated (drop out rates not statistically significant)
  - Effective
- Theoretically atypical antipsychotics preferred over typicals due to less EPS and other side effects.
- Use lowest dose effective—frequently dose will be lower than what may have been used when patient was younger.
- For many, reduction in dose or gradual taper with eventual discontinuation of antipsychotic medication may be possible for some.
- Weigh risks vs. benefits.

Jeste and Maglione, 2013

EPS and other AP Side Effects in the Elderly

- Extrapyramidal symptoms common with antipsychotic therapy (1st gen>2nd gen).
  - Frequently dose related and chronicity of treatment related.
- Commonly treated with benztropine, diphenhydramine or propranolol.
  - Caution with benztropine and diphenhydramine in elderly population due to anticholinergic properties→increased confusion, delirium and other side effects.
- Risperidone most likely to cause EPS, Clozapine least likely.
- TD also common with antipsychotic therapy.
  - 24% prevalent in those on chronic antipsychotic therapy, compared to 4-5% in younger adults.
- Akithesia does not appear to be age related.
- Neuroleptic Malignant Syndrome (NMS), rare but fatal.
  - Characterized by: high fever, muscular rigidity, confusion, autonomic instability, and elevated CPK (creatinine phosphokinase).
    - No data exists suggesting increased risk of NMS in the elderly.

Psychosocial Interventions

- Cognitive Behavioral Social Skills Training
  - Improved insight, frequency of social activities, and overall functioning in adults with schizophrenia >45 y.o.
- Functional Adaptation Skills Training
  - Enhances everyday living skills and social skills in schizophrenic patients >40 y.o.
- Social Rehabilitation and Integrated Health Care Program
  - Improvement in social skills measures as well as improved psychosocial and community functioning, improved negative symptoms and self-efficacy.

Granholm et al., 2007; Patterson et al., 2006; Mueser et al., 2010

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Test your knowledge Q4

- What treatment has the most research behind it suggesting efficacy in treating major depression and related psychosis in the elderly population?
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  - B. Antipsychotic medications
  - C. Electroconvulsive therapy (ECT)
  - D. Combination antidepressant and antipsychotic therapy
  - E. Tricyclic (TCA) antidepressants

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