DEPRESSION IN THE ELDERLY
Synergize
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OBJECTIVE 1:
EPIDEMIOLOGY OF DEPRESSION IN OLDER ADULTS

Objectives

1. Review the epidemiology of depression in older adults.
2. Describe the presentation of depression in older adults.
3. Develop an approach to the management of depression in older adults and review recent developments in treatment options.

Presenter disclosures

Faculty: Dallas Seitz
Relationships with commercial interests:
- NONE
Potential for conflict(s) of interest:
- NONE
Case presentation

Mrs. A presents to your clinic today with her daughter, who is worried her mother might be depressed:
- Mrs. A is 75 years old
- Retired Nurse
- Lives independently at home
- More details to come…

How common is depression?

- Prevalence:
  - Depressive symptoms in community up to 28.7%
  - Lifetime prevalence MDD in age >60 10.3%
  - 5-10% in primary care settings
  - 12-45% within hospitals
  - Up to 37% after hospitalization for critical illness
  - Up to 40% in LTC

Prevalence

- Depression is under reported
  - Considered a “normal” consequence of ageing
  - Stigma
  - Race

- Depression is under diagnosed
  - Co-morbid medical illness: symptom overlap
  - Not reported

- Depression is under treated

Risk factors

- Female gender
- Sleep disturbance
- Prior depression
- Cognitive impairment
- New medical illness
- Poor self-rated health
- Disability
- Stressful life events
- Bereavement
- Alcohol use

Conner 2010
Lyness 1995

Kessler 2005    Glismaer 2011
Taylor 2014 Lyness 1999
Jackson 2014 CCSMH 2006

Conner 2010
Lyness 1995

Cole 2003
Chang-Quan 2010
CCSMH guidelines
Medical comorbidity and depression

Medical conditions associated with MDD
- Ischemic Heart Disease
- Diabetes
- Arthritis/pain
- Stroke
- Parkinson's disease
- Dementia
- Hip fractures
- Respiratory disorders

Patten 2001

Impact of depression

- Health related consequences:
  - Increased perceived poor health
  - Poor function
  - Non-adherence to medical treatments
  - Cognitive decline
  - Increased mortality
- Health economic consequences:
  - Utilization of Medical Services
  - Increased health care costs

Beekman 2002

OBJECTIVE 2:
PRESENTATION OF DEPRESSION IN OLDER ADULTS

More on Mrs. A

- Her daughter tells you Mrs. A is:
  - Withdrawn and has stopped going to church
  - Spends much time in bed
  - Has lost weight
  - Has been more forgetful
  - Has been self-deprecating, and at times saying the “world would be a better place without me”
- Her past medical history is significant for DM II, HTN, and she was recently diagnosed with CHF and moderately severe CKD
- She also suffers from neuropathic pain
### Differential

- Delirium (especially hypoactive)
- Pain or discomfort
- Other medical causes
- Environmental causes
- Apathy associated with dementia

Sink, JAMA, 2005

### Medication use potentially related to depression:
- Methyldopa
- Beta-blockers
- Diuretics
- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Selective serotonin reuptake inhibitors (SSRIs)
- Serotonin-norepinephrine reuptake inhibitors (SNRIs)
- Tricyclic antidepressants
- Selective norepinephrine reuptake inhibitors
- Trazodone
- Buspirone
- Benzodiazepines
- Metoclopramide
- Donepezil

Alexopoulos, Lentin, 2005

### Medical conditions potentially related to depression:
- Endocrine disorders: hypothyroidism, hypoadrenalism, Cushing syndrome
- Infections: mononucleosis, tuberculosis
- Neurological disorders: Parkinson disease, epilepsy
- Cardiac disorders: myocardial infarction
- Hypertension
- Diabetes mellitus
- Gastrointestinal disorders: peptic ulcer disease

### Screening tools
DSM-5 criteria for MDD

- ≥ 5 of the following symptoms; same 2-week period; represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.
  - Depressed mood
  - Markedly diminished interest or pleasure
  - Significant weight loss or increase or decrease in appetite
  - Insomnia or hypersomnia
  - Psychomotor agitation or retardation
  - Fatigue or loss of energy
  - Feelings of worthlessness or inappropriate guilt
  - Decreased concentration, or indecisiveness
  - Recurrent thoughts of death (not just fear of dying) or suicidal ideation
Features of late life depression

- “Depressed mood” may be less prominent
- More anxiety
- More likely to express somatic complaints
  - 65% have hypochondriacal symptoms
- Cognitive impairment
- Psychosis more common
- Less likely to have family history of depression

Alexopoulos, 2005

Depression and cognition

- Relationship to dementia: each increases risk of the other
- Concept of “vascular depression”
  - Greater disability
  - More cognitive impairment
- Brain imaging:
  - Lateral ventricles more enlarged
  - More white matter intensities
  - Temporal lobe atrophy
- Effect of depression on cognition
  - Memory, verbal learning
  - Especially on tasks involving focused attention, verbal learning, working memory

Beekman 2013
Saczynski 2010
Bayer 2011
Olesen 2010

OBJECTIVE 3: DEVELOP AN APPROACH TO MANAGEMENT

Mrs. A?

- Anything else you want to know?
- Any tests you would order?
Assessment

- Past psychiatric history
  - Depression, bipolar disorder (or history of manic type episodes), anxiety, suicide attempts
  - History of treatment response
- Past Medical History:
  - Screen for diseases that may increase risk of depression (e.g. Parkinson’s disease, stroke) or that may be affected by treatment
  - Review medications for potential contributing causes and potential drug interactions if treatment is initiated
- Screen for cognitive impairment
  - What type of problems, if any?
  - Clarify timeline
- In theory, cognitive changes associated with depression are reversible but…
- Obtain collateral

Management

Guidelines

- Nonpharmacological
- Pharmacological

Management: what do guidelines say?

- Non-pharmacological
  - Supportive care should be offered to all
  - Psychotherapy is a first line option alone or in combination
    - Based on type of depression (and severity), coping style, cognition
- Pharmacological
  - Mild-moderate: antidepressants, psychotherapy or combo
  - Severe: combination; consider ECT

Blazer, 2003
Non-pharmacological treatments

Psychotherapy
- Strongest evidence for Cognitive Behavioural Therapy (CBT) and Problem Solving Therapy (PST)
- Interpersonal Therapy (IPT)
- Usually weekly visits for 8-12 weeks
- Access, presence of cognitive impairment, patient motivation all potential barriers

Evidence for PST
- PATH (problem solving approach + caregiver participation) in older adults with cognitive impairment ranging from mild deficits to moderate dementia
  - 37.8% vs. 13.5% remission rate compared to supportive therapy in a RCT
  - 66.7% vs. 32.3% response rate
- Dementia or depression severity at baseline not significant moderators

Non-pharmacological Treatments

Electroconvulsive Therapy (ECT)
- Consider if:
  - Medical refractory/resistant/intolerant
  - Severe suicidal risk
  - Food/fluid refusal
  - Psychotic depression
  - Depression with motor symptoms (e.g. catatonia)
- Good response rates in older adults, as well tolerated as in younger adults
- Transcranial Magnetic Stimulation
  - Conflicting evidence re: age influence on response

Pharmacological treatments

General principles:
- Start lower (usually half of dose used in younger adults)
- Go slower (but go!)
- Aim to reach target dose in one month
- Use lower max dose in most cases
- Monitor treatment response and do not continue ineffective medications

CCSMH, 2006
Pharmacological Treatments

- **First line: SSRIs**
  - Effective in some but not all trials
  - Generally effective in larger trials
    - Response rates 35-60% vs. 26-40% with placebo
  - Paroxetine effective in trials but usually avoided due to increased anticholinergic side effects
  - Citalopram, escitalopram, sertraline generally used first due to tolerability
    - Check sodium
- **Second line: SNRIs**
  - Venlafaxine and duloxetine

Response rates


Remission rates


Pharmacological treatments

- Other options (3rd line, or augmentation)
  - Bupropion XL
  - Mirtazapine
- TCAs
  - As effective as SSRIs, but more side effects
  - Nortriptyline

NEJM 2014
Mulsant, Am J Geriatr Psychiatr, 2001
Pharmacological treatments

Other
- Atypical antipsychotics
  - Augmentation not monotherapy
  - Aripiprazole and quetiapine
- Stimulants
  - Few high quality or large controlled trials
- Lithium
  - Supported by evidence in older adults but can be difficult to initiate due to side effects and need for monitoring

Treatment: how long?

Guidelines:
- In remission after first episode: treat minimum 1 and up to 2 years from time of improvement
- Recurrent episodes: indefinite maintenance treatment
- LTC: ?, evaluate regularly
- Psychotherapy
  - Not clear
  - Some evidence to support decreased risk of relapse (check for PST)

Treatment: partial or no response?

Guidelines
- If no improvement after 2 weeks at average dose, increase further until there is some improvement, max dose reached, or limited by side effects
  *Controversial*
- Change if, at max tolerated or recommended dose:
  - No improvement at 4 weeks
  - OR insufficient improvement at 8 weeks
  - In general: optimize, augment or switch, augment or switch
Summary

- Treatment often guided by practices in younger populations
- Limited data on efficacy and safety in older adults
- Little data on long-term treatment or maintenance strategies
- Little evidence to support practice of individualizing treatment/matching side effect profile to symptoms
- Comparable efficacy of all antidepressants across the lifespan
  
  “Approach with therapeutic optimism”

Blazer, 2004

Update on recent evidence

**Impact**

- Antidepressant or PST \(\rightarrow\) switch \(\rightarrow\) combine antidepressant and PST

**Prospect**

- Optimize dose \(\rightarrow\) switch to citalopram \(\rightarrow\) augment with bupropion \(\rightarrow\) switch to venlafaxine \(\rightarrow\) augment with mirtazapine, nortriptyline

*Same eligibility criteria in study and usual care groups


**Combined citalopram and methylphenidate improved treatment response compared to either drug alone in geriatric depression: a randomized double-blind, placebo-controlled trial**

- 16 week RCT in 143 geriatric outpatients with major depression \((N = 143)\)
- 3 treatment groups:
  - Citalopram 20-60mg
  - Methylphenidate 5-40mg
  - Methylphenidate + citalopram
- Depression significantly improved in all groups
  - Greater and faster improvement in combination group
  - No differences in cognitive outcomes

Am J Psychiatry, 2015
Efficacy, safety, and tolerability of augmentation pharmacotherapy with aripiprazole for treatment-resistant depression in late life: a randomised, double-blind, placebo-controlled trial

- 12-week RCT of aripiprazole augmentation of venlafaxine in depressed adults >60 years old (N = 181)
- Pre-trial treatment (N = 468) with at least 12 weeks of venlafaxine (150-300mg/day)
- Patients who did not achieve remission randomized to aripiprazole (10-15mg/day) or placebo
- Greater proportion achieved remission in aripiprazole group: 44% vs. 29% (p=0.03)
- Akathisia (26%) and Parkinsonism (17%) most common side effects

Depression in Dementia (DpD)

- NIMH provisional criteria
- Two week period of three or more symptoms:
  - Depressed mood
  - Decreased positive affect or pleasure in response to social contacts and usual activities
  - Disruption of sleep and/or appetite
  - Psychomotor changes
  - Irritability
  - Fatigue or loss of energy
  - Feelings of worthlessness, hopelessness, or excessive guilt
  - Recurrent thoughts of death, suicidal ideation or plan

Psychological Treatments for DpD

- 6 randomized controlled trials
  - Based on various models (CBT, IPT, counseling)
  - No effect on secondary outcomes, such as ADLs, quality of life, cognition, or caregiver depression

Antidepressants for DpD

- 2 meta-analyses of antidepressants for depression in dementia failed to find statistically significant benefits over placebo:
  - Nelson et al (N=7 studies):
    - Response OR: 2.12 (0.95 – 4.70)
    - Remission OR: 1.97 (0.85 – 4.55)
    - Adverse event rates relatively low: 9% vs. 6% with placebo
  - Bains et al (N=4 studies):
    - Weak support for efficacy of antidepressants
- 11 RCTs
  - 5 positive, 6 negative studies

1. Omega, B J Psychiat, 2015
Bains et al., Cochrane Syst Rev, 2002
Enach, Car Op in Psychiat, 2011
Challenges: DpD

- Can be difficult to assess and diagnose
- Overlap between symptoms of dementia and depression
- Limited role for psychological therapies in individuals with cognitive impairment
- Inconsistent evidence for pharmacological treatments

Thanks

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References

Selected references:
- CCSMH National Guidelines for Seniors Mental Health: Assessment and Treatment of Depression, May 2006 (available at ccsmh.ca)