Improving Clinical Outcomes in Depressed Older Adults

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Learning Objectives

• Competence:
  • Increased knowledge of issues affecting prognosis in depressed geriatric patients
  • Increased knowledge of treatment options in depressed geriatric patients

• Performance:
  • Improved outcomes by applying new knowledge of assessment and treatment planning for older adults with depression and related conditions

Terminology

• Response: 50% reduction in symptoms
• Remission: 80% reduction in symptoms
• “Treatment resistant” or “treatment refractory”: lack of response to several (2 to 4 depending on CPG) adequate (dose, duration, adherence) trial of antidepressant medication
• Augmentation: adding second medication or therapeutic intervention to primary antidepressant or psychotherapy

Limited Literature

• Most of the published literature (prospective trials, cohort-controlled observation studies, etc.) include young-old subjects (average age 70)
• Outcome data from younger adult trials (often with average age 40-50) might be safely extrapolated to young-old (65-80), independently living patients but not to old-old (>80) or disabled elderly

Systems Issues

• 80% of depressed elderly are treated only by their primary care provider: stigma, lack of mental health resources in the community
• Old-old and those with more than one co-morbid condition are not likely to be diagnosed: atypical presentation, co-morbid condition becomes the primary focus, atypical presentation, therapeutic nihilism
• Many are undertreated and have poor outcomes: wrong diagnosis, under dosing, wrong medication, lack of interdisciplinary team involvement

Prevalence Rates in Old Age

• Prevalence rates vary widely depending on general health and functional status and screening criteria
• Physically healthy independent elderly: 2-4% for major depression
• General adult population: 5%
• Older adult w/acute illness in hospital: 30%
• Chronic illness (no dementia) in long term care: 50%
• Prevalence of depressive symptoms (subsyndromal) are higher
## Risk Factors

<table>
<thead>
<tr>
<th>Early vs. Late Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Late onset</strong>: less genetic loading, more medical co-morbidity, higher suicide risk, higher risk for vascular dementia</td>
</tr>
<tr>
<td><strong>Early onset</strong>: higher genetic risk, higher psychosocial stressors, more recurrences and residual symptoms, higher risk for Alzheimer’s disease (?)</td>
</tr>
</tbody>
</table>

## Critical Biomedical Factors Affecting Prognosis

- Chronic pain
- Loss of function
- Early age of onset
- Small-vessel disease
- Multiple previous episodes
- Neurodegenerative disease

## Critical Psychosocial Factors Affecting Prognosis

- Early onset
- Bereavement
- Demoralization
- Lack of purpose
- Substance abuse
- Loss of independent living

## Consequences of Poor Outcomes

- Decreased quality of life, prolonged suffering in patients and family
- Much higher health care utilization
- Mortality rates increase by factor of 3 to 4
- Neurodegeneration
- Medical risk increases: diabetes, vascular disease
- Suicide (elderly white males highest rates)

## Making the Diagnosis

- DSM IV-TR criteria for major depression: “Loss of interest” more sensitive criterion than “persistent sadness” in old-old (>80)
- Neurovegetative symptoms less specific in older adults (fatigue, insomnia, anorexia, libido, memory)
- Persistent anger and irritability may be masking depression
- Late onset alcohol or over-use of prescribed and OTC medications may be masking depression
Validated Rating Scales

- Improve diagnostic sensitivity two-fold
- Geriatric Rating Scale (5, 15, 30-item forms)
- Cornell Scale for Depression in Dementia
- Center for Epidemiologic Studies of Depression Scale
- Patient Health Questionnaire-9

Simple Screens

- 2-Question Screen
  - To the last month have you mostly:
  - Been down, depressed, hopeless
  - Had little interest or pleasure in things?
  - Positive screens if both are answered yes.

- GDS-5
  - In the last 2 weeks, have you mostly:
  - Been satisfied with your life?
  - Felt very tired?
  - Felt happy?
  - Felt like wasting time?
  - Felt pretty worthless?
  - Positive screens if 2 of the 5 are endorsed (no for #1, yes for others)

The Basics: Screening
From Randall Espinoza, MD, MPH at UCLA

<table>
<thead>
<tr>
<th>2-Question Screen</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Inpatient</th>
<th>Cognitive Impairment</th>
<th>Physically Ill</th>
<th>Cognitive Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>GDS 5-item</td>
<td>94%</td>
<td>81%</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Unknown</td>
</tr>
<tr>
<td>CSDD (19-item)</td>
<td>90%</td>
<td>75%</td>
<td>Yes</td>
<td>Yes</td>
<td>Unknown</td>
<td>Yes</td>
</tr>
<tr>
<td>CES-D (20-item)</td>
<td>93%</td>
<td>73%</td>
<td>No</td>
<td>Yes</td>
<td>Unknown</td>
<td>No</td>
</tr>
<tr>
<td>PHQ-9</td>
<td>88%</td>
<td>88%</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

Assessment

- History from patient and family/caregivers
- Use cognitive instruments and Epworth Sleepiness Scale to quantify cognitive impairment and sleepiness
- Neurobehavioral neurologic exam
- Functional status assessment, timed Up and Go
- Detailed medication review
- Basic labs, vitamin D, TSH, testosterone?

Basically, a good geriatric assessment

Neurobehavioral Neurologic Exam

- Cranial nerves
- Muscle strength (esp. hip extendors), tone
- Overall animation, motor speed, dexterity, praxis (Luria maneuver, etc.)
- Tremor, ataxia, dyskinesia
- Gait, balance, postural control
- Timed Up and Go, Tinetti Balance
- Imaging studies as indicated by cognitive and motor findings

Subtypes Depression

- Bereavement
- Dysthymia
- Minor depression/Adjustment disorder
- Major depression
- Dysphoric mania
- Vascular depression
- Psychotic depression
- Mood disorder associated with primary neurodegenerative disease
Initiating Treatment

- Admit to hospital: high suicide risk, unable to maintain hydration, unable to do ADLs and no assistance available
- Medication targets: sleep, anxiety, anorexia, anhedonia, severe depression, delusional thinking
- Psychotherapy targets: bereavement, low self-esteem, pessimism, mild cognitive distortions

Choosing Antidepressants

- SSRIs: Generally first choice, start low, titrate every few days to standard dose in young-old, half that in old-old and frail. Target mood, anxiety.
  - Risks: Hyponatremia, bleeding, falls, CVA, MI, QTc prolongation (citalopram)
- NSRI: Titration same as above. May be better for co-morbid pain.
- NE/DRI: Titration same as above. Target apathy, mood.
- Mirtazepine: Target appetite, sleep, mood, anxiety. Start at 7.5 mg at bedtime, increase to 15 mg, then 30 mg.

Response Rates

- Meta-analysis of 15 RCT of antidepressants in older patients (> 55, mean 70 yrs., N=4756), 30% better response rate compared to placebo (Tedeschini et al. 2011)
- Meta-analysis of 6 trials (N=1840) with older subjects (mean 74 yrs.) showed comparable, placebo and active drug effects
- Responses may be better in more severely depressed
- People with co-morbidities generally excluded from these trials

What to Expect

- Some response within one or two weeks
- Affect, appetite, sleep may be early response indicators; mood itself is slow to change
- Remission may take 3 months: neuroplastic remodeling?
- 70% response rate for initial episode
- 40-50% response rates for recurrent episodes

Dialectical Behavioral Therapy

- Lynch TR et al. 2003
  - 34 subjects (mean age 66, range 60-80)
  - Randomized to medication or med + DBT
  - DBT: weekly group, phone coaching 30 minutes/wk
  - Remission rates at 28 wks.:
    - Medication alone = 47%
    - Medication plus DBT = 71%
  - Remission rate at 26 wks.: 31% vs. 75%

Maintenance

- Reynolds C et al. 1999
  - Relapse rates within 3 years:
    - Placebo: 90%
    - Interpersonal Therapy: 65%
    - Nortryptiline: 45%
    - IPT plus nortryptiline: 20%
Summary of Trial Data

- Few trials to review, especially for older patients
- Medications may be less effective in older adults, particularly >80 yrs.
- Psychotherapy works well, especially when combined with medications
- Interdisciplinary, integrated treatment works better than isolated treatment (Hunkeler EM et al. BMJ 2006; 332:259)
- Drop-out rates from medication trials very high, classes of meds equally effective (Cochrane 2009).

Inadequate Response?

- Monitor treatment adherence
- Ensure optimal dosing and duration
- Treat comorbid conditions (especially pain, anxiety, sleep)
- See more frequently
- Refer for psychotherapy if necessary: tele-mental health an option in rural areas
- Prescribe exercise, scheduled activities

Medical Augmentation

- No specific data other than case reports, small series
- Extrapolated from younger adult literature and clinical practice
- Equal efficacy: switch antidepressant classes, add antidepressant of synergistic effect (eg mirtazapine, TCA or buproprion to SSRI)
- Add mood stabilizer: olanzapine, quetiapine, aripiprazole
- Consider psychostimulant, MAOI
- Consider lithium, thyroid, testosterone

Brain Stimulation

- Electroconvulsive Therapy
  - 50-80% response rates; treatment of choice for delusional depression, catatonia
  - Acute cognitive side effects may limit initial series
  - Generally will need maintenance
  - Tolerance can develop
  - Long-term cognitive effects probably benign and much more favorable than depression itself
  - Risks of general anesthesia, CVA, MI
- Transcranial Magnetism (very few data for older adults)
- Deep Brain Stimulation (not yet a consideration)

Rethinking Diagnosis and Prognosis

- R/O Primary Apathy
  - Underlying neurodegenerative condition
  - Not distressed or anxious
  - Executive dysfunction
- R/O Vascular depression
  - Cognitive and motor slowing
  - Executive dysfunction
- R/O Dysphoric Mania
  - Agitated, talkative, intrusive, disinhibited

Depression Dementia vs. AD

<table>
<thead>
<tr>
<th>Depression</th>
<th>Alzheimer’s Disease</th>
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</thead>
<tbody>
<tr>
<td>I don’t know answers</td>
<td>Confabulation</td>
</tr>
<tr>
<td>Mixed recent and remote memory problems</td>
<td>Recent memory impairment</td>
</tr>
<tr>
<td>Slowed cognition</td>
<td>More aphasia, visuospatial impairment</td>
</tr>
<tr>
<td>Motor slowing</td>
<td>Less insight</td>
</tr>
<tr>
<td>Waxing/waning symptoms</td>
<td>More disorientation</td>
</tr>
<tr>
<td>Less disorientation</td>
<td>More praxis problems</td>
</tr>
</tbody>
</table>

Co-exist more often than not!
**Vascular Depression**

- Late life onset
- Mostly male
- Marked executive impairment more than memory
- Evidence of subcortical small vessel disease: motor and cognitive slowing, impoverished and perseverative thinking
- Poor response to treatment

**Palliative Care**

- There is such a thing as “end-stage” depression
- Generally due to severe, multiple recurrences
- Remissions may occur, but are brief
- Very high incident rates of dementia
- Supportive, palliative measures indicated to maintain comfort and function

**Summary**

- Relatively healthy young-old patients generally respond as younger adults do.
- Older and frail patients do not respond as well to treatment, require more comprehensive geriatric assessment and interdisciplinary intervention.
- While we should avoid therapeutic nihilism, prognostic implications of chronic, recurrent disease and neurodegeneration need to be kept in mind.

**References**

- Hunkeler EM et al. BMJ 2006; 332:259
- Reynolds C et al. JAMA 1999; 281:39