PSYCHOPHARMACOLOGY UPDATE

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Emory University
Most Common Disorders in Older Adults

In order of prevalence:

- Anxiety
- Severe cognitive impairment
- Mood disorders

Am Assoc of Geriatric Psychiatry, 2011

- Growing number of older adults with Psychotic Disorders
Epidemiology – Depressive Syndromes

Community dwelling older adults
- 1%-4% Major Depressive Disorder
- 35% depressive symptoms

Long Term Care older adults
- 10-15% depressive syndromes

Impact

Increased health care costs

- Increased service utilization
  5.3 office visits for vs. 2.9/ per year without depression
- Less compliance with medical treatment
- Hospital readmissions

Medical Evaluation

- Medical History
- Psychosocial History (drug, etoh, marriages, work hx)
- Family Medical/ Psychiatric History
- Labs (CBC, Chem 7, B12 and Folate, TSH, vitamin D)
- CT scan (when there are concerns regarding memory or psychosis)
Depressive Disorders

DSM V
Major Depressive Disorder

- At least one of the two,
  1. depressed mood or
  2. loss of interest or pleasure

5+ symptoms, 2-week period, represent a change from previous functioning
Major Depressive Disorder

- Weight loss when not dieting or weight gain
- Insomnia or hypersomnia nearly
- Psychomotor agitation or retardation
- Fatigue or loss of energy
- Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional)
- Diminished ability to think or concentrate, or indecisiveness
- Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.
Others

- Unspecified Depressive Disorder
- Substance/Medication- Induced Depressive Disorder
- Depressive Disorder Due to Another Medical Condition
Geriatric Depression

- Cognitive changes
- Somatic symptoms
- Fatigue
- Loss of interest
- Depression without sadness

Depression and Dementia

- Over 50% of patients with dementia have depressive symptoms
- 20% meet major depressive criteria

Symptoms of Depression vs. Dementia

- Depression:
  - Impairment in attention
  - Psychomotor slowing
  - Slowed speed of information processing
  - Impaired executive functioning

- Dementia:
  - Global cognitive impairment
Dementia vs. Depressive Disorder

- Dementia Screening and/or neuropsychological test
  - Depressed - show poor effort, results inconsistent over time
  - Dementia - cover deficits with confabulations
Treatment
Mild Depression
Expert Consensus Guidelines

Preferred Treatment
- Antidepressant medication and psychotherapy
- SSRI, Venlafaxine XR

Alternate Treatment
- Antidepressant alone or psychotherapy alone
- Bupropion, Mirtazapine

Adapted from Alexopolus et al (2001) A postgraduate medicine special report
Severe Depression
Expert Consensus Guidelines

Preferred Treatment
- Antidepressant medication and psychotherapy OR antidepressant medication alone
- SSRI, Venlafaxine XR (SNRI)

Alternate Treatment
- Electroconvulsive Therapy
- Tricyclic antidepressants, Mirtazapine, Bupropion

Adapted from Alexopolus et al,
Pharmacotherapy

- 1\textsuperscript{st} choice - Selective serotonin reuptake inhibitors (SSRIs)

- 2\textsuperscript{nd} choice - Serotonin-Norepinephrine reuptake inhibitors (SNRIs)

Pharmacotherapy

Selective Serotonin Reuptake Inhibitors

- Fluoxetine (Prozac)
- Sertraline (Zoloft)
- Paroxetine (Paxil)
- Citalopram (Celexa)
- Escitalopram (Lexapro)
- Fluvoxamine (Luvox)
SSRIs Side Effects

- Headache
- GI side effects
- Hyponatremia
- Excessive activation
- Sleep disturbance
- Tremor
- Sexual dysfunction
- QT prolongation (Citalopram 20mg or less)
Pharmacokinetics

- Inhibition of CP450
  - Strongest - Fluoxetine (Prozac), flovoxamine, nefazodone
- Caution SSRIs and WARFARIN
# Inhibition of P450 cytochromes

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<tr>
<th>Drug Name</th>
<th>CYP1A2</th>
<th>CYP2C9</th>
<th>CYP2C19</th>
<th>CYP2D6</th>
<th>CYP3A4</th>
<th>CYP2B6</th>
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<tr>
<td>Fluoxetine</td>
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<tr>
<td>Fluvoxamine</td>
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<tr>
<td>Sertraline</td>
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<td>+</td>
<td>+/-+</td>
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</table>
Pharmacotherapy

Serotonin and Norepinephrine Reuptake Inhibitors

Venlafaxine (Effexor, Effexor XR)
Duloxetine (Cymbalta)
Desvenlafaxine (Pristiq)
Milnacipran (Ixel, Savella)
Levomilnacipran (Fetzima)
Tofenacin (Elamol, Tofacine)
SNRI Side Effects

- Most common:
  - loss of appetite, weight loss, and sleep disturbance.

- Possible:
  - drowsiness, dizziness, fatigue, headache, increase in suicidal thoughts, nausea/vomiting, sexual dysfunction (less than in SSRIs), and urinary retention.
SNRI Side Effects

- Increased Norepinephrine:
  - anxiety, mildly elevated pulse, and elevated blood pressure – usually dose related
  - Cymbalta – Monitor liver function tests and creatinine
Serotonin and Psychiatric Symptoms

- Mood
- Anxiety: OCD, GAD, PTSD, Social Phobia & Panic Disorder
- Impulsivity
- Aggression
- Eating Disorders: Bulimia, Anorexia
Pharmacotherapy

Others

- Mirtazapine (Remeron) – Noradrenergic and specific serotonergic

- Bupropion (Wellbutrin) (SR/XL) – Norepinephrine Reuptake Inhibitor and non-competitive antagonist of multiple neuronal n ACH receptors
Mirtazapine (Remeron)

- Helpful when do not tolerate SSRIs
  - Sedating at low dosage
  - Stimulates appetite
  - Minimal warfarin interaction

- Could exacerbate REM sleep behavior in PD
- Neutropenia, agranulocytosis

Bupropion

- CYP2D6 inhibitor
  - ↑ paroxetine, sertraline, fluoxetine, diazepam
  - ↑ bupropion blood levels
- CYP2B6 inducers, such as carbamazepine, clotrimazole, rifampicin, ritonavir, St John's Wort, phenobarbital, phenytoin and others
  - ↓ bupropion
- Bupropion lowers the threshold for epileptic seizures
Bupropion

- No sexual dysfunction
- Smoking cessation
- Activating (will cause sleep disturbance if given late in day)
- Asthenia
- Alopecia
Pharmacotherapy

Older Medications

Tricyclics

- Nortriptyline (Pamelor)
- Amitriptyline (Elavil)
- Desipramine (Norpramin)
- Imipramine (Tofranil)
- Doxepin (Adapin, Sinequan)
- Clomipramine (Anafranil)
- etc

MAOIs

- Isocarboxazid (Marplan)
- Phenalzine (Nardil)
- Tranylcypromine (Parnate)
- Selegiline (EMSAME) patch
- etc
Table 1. Daily dosages for various antidepressants

<table>
<thead>
<tr>
<th>Antidepressant</th>
<th>Target daily dosage or plasma concentration*</th>
<th>Maximum daily dosage or plasma concentration</th>
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<tbody>
<tr>
<td>Citalopram</td>
<td>30 mg</td>
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<td>Fluoxetine</td>
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<td>Fluvoxamine</td>
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<td>40 mg</td>
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<tr>
<td>Sertraline</td>
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<td>200 mg</td>
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<td>Trazodone</td>
<td>300 mg</td>
<td>600 mg</td>
</tr>
<tr>
<td>Nefazodone</td>
<td>200 mg</td>
<td>400 mg</td>
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<tr>
<td>Bupropion</td>
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<td>400 mg</td>
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<tr>
<td>Mirtazapine</td>
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<td>45 mg</td>
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<tr>
<td>Venlafaxine</td>
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<td>300 mg</td>
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<td>Phencelzine</td>
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<td>Tranzylcypromine</td>
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<td>Nortriptyline</td>
<td>plasma concentration ≥50 ng/ml</td>
<td>plasma concentration 120 ng/ml</td>
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<tr>
<td>Desipramine</td>
<td>plasma concentration ≥100 ng/ml</td>
<td>plasma concentration 150 ng/ml</td>
</tr>
</tbody>
</table>

*Patients are considered to have failed an adequate trial if they have received this dosage for ≥6 weeks with no or minimal improvement.

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Dosing guidelines

Depression with Psychosis

- Depression with psychotic symptoms is common among elderly patients.

- Somatic delusions, nihilism, persecution and jealousy are common psychotic features.

- Treatment should include the association of antidepressants and antipsychotics to improve treatment efficacy.

Adjunctive treatments

- Atypical antipsychotics
  - Aripiprazole (Abilify)
  - Lurasidone (Latuda)
  - Olanzapine (Zyprexa)
  - Quetiapine (Seroquel)
  - Risperidone (Risperdal)
  - Ziprasidone (Geodon)

- Others
  - Buspirone (Buspar)
  - Lithium (Eskalith, Lithobid)
  - Thyroid hormone
Electroconvulsive Therapy (ECT)

- 80% response rate
- When do not respond to medications, psychotic, not eating or drinking or actively suicidal

Non-pharmacological treatments

- Cognitive Behavioral Therapy
- Interpersonal Therapy
- Problem Solving Therapy
- Behavioral Activation

ReCap/ Recommendations

- Use SSRI’s/ SNRI’s in the elderly
  - Will also treat Anxiety
- May need comparable doses as younger patients
- 10-12 weeks to get full effect
- Psychotherapy is important!
Anxiety Disorders
Generalized Anxiety Disorder (GAD)

- Excessive anxiety and worry (apprehensive expectation) regarding a number of issues
- The individual finds it difficult to control the worry
Generalized Anxiety Disorder

- The anxiety and worry are associated with three (or more) of the following six symptoms:
  - Restlessness or feeling keyed up or on edge.
  - Being easily fatigued.
  - Difficulty concentrating or mind going blank.
  - Irritability.
  - Muscle tension.
  - Sleep disturbance (difficulty falling or staying asleep, or restless, unsatisfying sleep).
Prevalence of Anxiety Disorders

- Community dwelling older adults
  - Disorders 1 - 15%
  - Symptoms 15 – 52%
- Primary care patients 14 – 20%

Bryant et al, *Jrnl of Affective Disorders*, 2008;
Nonpharmacological Treatment

- Cognitive Behavioral Therapy
- Relaxation training
- No systematic studies in older adults.

Pharmacotherapy

- Antidepressants
- Benzodiazepines
- Buspirone
- Beta-blockers
- Antihistaminic
- Neuroleptics
Antidepressants

- SSRI’s
  - Sertraline (Zoloft)
  - Escitaolpram (Lexapro)

- Mirtazapine (Remeron)
  - Helpful with nauseated, losing weight and trouble sleeping
Benzodiazepines

- Indicated in Panic Attacks
- Short term use while maximizing treatment with SSRIs
Buspirone (Buspar)

- High affinity for serotonin 1A receptors enhancing brain dopaminergic and noradrenergic activity.
- Clinical trials found it effective for GAD but not for panic disorder
Others

Usually not used in Older Adults

- Beta Blockers
- Antihistamines
Evidence-Based Clinical Treatment Models for Older Adults with Depression

- **Key Components:** Screening, patient education, close monitoring, therapy offered (Cognitive Behavioral Therapy or Problem Solving Therapy)
  - **IMPACT**
  - **PROSPECT**
    - Bruce et al, JAMA 2004: 291(9), 1081-1091