Major Depressive Disorder: Diagnosis, Treatment & Impact on Rural Communities

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Major Depressive Disorder: Diagnosis, Treatment & Impact on Rural Communities

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Accreditation: Pharmacists 798-000-08-079-L01-P
Pharmacy Technicians 798-000-08-079-L01-T

Target Audience: Pharmacists & Technicians

CE Credits: 1.0 Credit hour or 0.1 CEU for pharmacists/technicians

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Program Overview: Major Depressive Disorder is a condition characterized by one or more Major Depressive Episodes without a history of manic, mixed, or hypomanic episodes. MDD is a major mental health condition, with statistics proving that completed suicide occurs in up to 15% of individuals with severe cases! Major Depressive Episode can be conquered! With correct intervention, up to two-thirds of these cases may completely recover. This program is designed to assist pharmacists review the facets of Major Depressive Disorder (MDD), especially in rural areas of the United States, as well as the benefits of managing this disorder with medications. Their knowledge of available treatment options for victims of MDD will be enhanced. The program includes information on pharmacologic treatments, drug interactions, patient counseling, and a question/answer period.

Objectives:
- To state the theories associated with the causes of MDD, as well as detrimental affects that this disorder may have on its victim’s lives, incorporating information on the prevalence of this predicament.
- To list therapeutic agents used in the treatment of MDD, and be able to state an agent’s dosage schedule, mechanism of action, and side effects.
- To explain the pharmacological and non-pharmacological options for patients suffering from MDD, to include their mechanisms of action, efficacy, dosing, safety, and tolerability profiles.
What is Major Depressive Disorder?

- Mary - 57 year old white female
- Long history of depressive episodes since teens
- Treatment resistant
- Comorbid anxiety
- Genetic predisposition
- Psychosocial stressors
What is a Major Depressive Episode?

- Depressed mood (irritable in children) and SIG-E-CAPS criteria
- S: suicidal ideation
- I: decreased interests
- G: excessive guilt (worthlessness, hopelessness)
- E: decreased energy
- C: decreased concentration
- A: appetite
- P: psychomotor retardation or agitation
- S: sleep disturbance
What is a Major Depressive Episode?

- Must last at least 2 weeks
- At least 5 of criteria with one including depressed mood or decreased interests
- Must causes clinically significant impairment
Features of MDD

- Multiple modifiers
- Single episode or recurrent
- Mild/moderate/severe
- Psychotic features
- Catatonia
- Melancholic features
- Atypical features
- Postpartum onset
- Seasonal pattern
Other Affective Illnesses

- Dysthymic disorder
- Part of bipolar disorder
- Cyclothymic disorder
- Substance-induced depression
- Due to general medical condition
- Depressive disorder NOS
Epidemiology

- 12 month prevalence: 6.6% (NCS-R) 9.6% (WHO); 1.7-3.4% (ECA)
- Lifetime prevalence: 16.2% (NCS-R), 5.8% (ECA)
- WHO ranks MDD as “one of most burdensome diseases in the world”
- Median age of onset: 32 years
- F:M 2:1
- High comorbidity (esp. anxiety and substance abuse)
- 1st degree relative: risk 1.5-3x
- Both parents: 50-75% chance for child to have MDD
Rural Population Differences

- No difference in prevalence of MDD in urban vs rural populations (NCS & NCS-R)
- Outcomes for MDD are worse
Rural Population

- Poor health
- Chronic disease
- Inactivity
- BMI > 30
- Unemployment
- Poverty
- High school drop out
- Alcohol consumption
- Fewer personal resources
Rural Living

- ↓ Access to primary health care providers
- ↓ Access to specialists
- ↓ Access to health related technologies
- ↓ Access to social services
- ↑ Distance to travel for care
- ↓ Confidentiality
- ↑↑ Stigma
MDD in Rural Population

- Most likely to see PCP
- Only recognized 50% of time
- “Minimally adequate” treatment 14% of time with PCP
- “Minimally adequate” treatment 50% of time with MH specialist
- Delay in diagnosis results in increased costs, need for higher level care
Role of Pharmacists in MDD with Rural Population

- Frontline providers
- Communicate with PCPs/Psychiatrists
- Patient Education
- Simplify dosing regimens/medication reminders
- Monitor for polypharmacy
- May be first to see side effects
- Case management/benefits management
Course of Disease-Acute Phase

- Diagnostic evaluation, physical exam, labs
- Assure safety
- Determine treatment setting
- Evaluate functional impairments
- Develop therapeutic alliance
- Educate patient and family
- Decide on treatment modality
- Goal is remission
Treatment- Acute Phase

- Medication: moderate or severe cases
- Education: patient and family
- Psychotherapy: insight oriented, interpersonal, supportive, group therapy
- CBT
- ECT: severe, resistant, psychotic, catatonic
Treatment-Acute Phase

- Alternative treatments: exercise, yoga, acupuncture, herbal
- Newer/experimental: deep brain stimulation (DBS), vagal nerve stimulation (VNS), transcranial magnetic stimulation (TMS)
Treatment-Acute Phase

- If no improvements after 6-8 weeks, reassess
- Maximize meds
- Change in meds, augmentation
- Change in therapeutic approach
Course of Disease-Continuation Phase

- Patient in remission 4-5 months
- Goal is to prevent relapse
- Continue treatment
- Medication: at least 6 -9 months after remission
- 25% relapse w/i 2 mos if meds stopped
- Maintenance psychotherapy
Course of Disease-Maintenance Phase

- 50-80% have at least one recurrence
- Most often in first 2-3 years after remission
- Maintenance meds most studied
- Maintenance psychotherapy
- Combo maintenance therapy
- ECT
- 2 or more episodes: life long prophylaxis
Course of Disease

- Depression as part of bipolar increased if:
  - Earlier onset < 25 y. o.
  - 5 or more spells of MDD
  - Family hx of bipolar
  - Atypical depressive symptoms
Cost of Depressive Disorders

- 2000- $83.1 billion in US (total costs)
- $26.1 billion in direct costs
- $5.4 billion in suicide-related costs
- $51.5 billion in workplace costs
- Unemployed are 2X as likely to have MDD
- Leading cause of disability in US
- 75% of those with MDD report moderate to severe symptoms
Morbidity and Mortality

- 15% complete suicide
- Severe role impairment: 60% of MDD
- Prognosis worse for general medical conditions when MDD present
- Nursing home residents with MDD: more likely to die in 1st year
Causal Theories

- Bio-psycho-social model
- Genetic vulnerability
- Brain disorder: structural differences
- Neurotransmitter dysfunction: NE, DA, 5-HT
- Hypothalamic-pituitary axis dysfunction
Comorbid Conditions

- Substance abuse
- Anxiety disorders: OCD and Panic Disorder
- ADHD
General Medical Conditions
Associated with MDD

- Hypothyroidism
- Cardiovascular disease (MI)
- Stroke
- Chronic pain syndromes
- Cancer
- Diabetes
- HIV
- Neurological disorders: MS, Parkinson’s, spinal cord injuries
Treatment Goals

- Assess and treat acute exacerbations
- Decrease distress
- Improve functioning between episodes
- Prevent recurrences
- Provide support and insight to patient and family
STEPS in Pharmacotherapy

S: Safety
T: Tolerability
E: Efficacy
P: Payment
S: Simplicity
Pharmacotherapy for MDD

- Tricyclics and tetracyclics
- SSRIs
- Dopamine/norepinephrine reuptake inhibitors
- Serotonin/norepinephrine reuptake inhibitors
- Serotonin modulators
- Norepinephrine modulator
- MAO-Iso
Tricyclics

- Older medications
- Most often used: imipramine, desipramine, doxepin, nortriptyline, amitryptiline
- Starting doses: 25-50 mg/day
- Usual doses: 100-300 mg/day
- Generics available: CHEAP!!
- Not generally first line
- Narrow therapeutic index: lethal in overdose
- Sedation, orthostatic hypotension, anticholinergic, arrhythmias, weight gain, sexual dysfunction
- Can get blood levels
SSRIs

- Newer, first choice
- Safe and more tolerable
- Some can induce cytochrome P450 enzyme system: drug-drug interactions
- FDA approval for treatment of several disorders
- Nausea, headache, diarrhea, sedation (less), sexual dysfunction
- Serious side effect: Serotonin Syndrome
## SSRIs

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose mg/day</th>
<th>CYP450 effect</th>
<th>Generic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine (Prozac)</td>
<td>20-60</td>
<td>2D6, 2C19</td>
<td>Yes</td>
</tr>
<tr>
<td>Citalopram (Celexa)</td>
<td>20-60</td>
<td>Weak</td>
<td>Yes</td>
</tr>
<tr>
<td>Escitalopram (Lexapro)</td>
<td>10-30</td>
<td>3A4, Weak</td>
<td>No</td>
</tr>
<tr>
<td>Sertraline (Zoloft)</td>
<td>50-200</td>
<td>2D6, Weak</td>
<td>Yes</td>
</tr>
<tr>
<td>Paroxetine (Paxil)</td>
<td>20-60</td>
<td>2D6</td>
<td>Yes</td>
</tr>
<tr>
<td>Fluvoxamine (Luvox)</td>
<td>50-300</td>
<td>2C19, 1A2</td>
<td>No</td>
</tr>
</tbody>
</table>
Dopamine-Norepinephrine Reuptake Inhibitors

- Bupropion (Wellbutrin, Zyban)
- Usual dose is 150-450 mg/day
- Contraindicated with eating disorder or seizures
- Can increase anxiety at first
- Generic available
- Smoking cessation agent
SNRIss

Duloxetine (Cymbalta):

- Usual dose is 60-120mg/day
- Targets physical symptoms
- Chronic pain
- Fibromyalgia
SNRIss

Venlafaxine (Effexor):

- Usual dose is 75-225 mg/day
- Same side effect profile as SSRIs
- In higher doses, can cause hypertension, tachycardia, diaphoresis, anxiety
Serotonin Modulators

Nefazadone (Serzone):
- Usual dose is 150-300 mg/day
- Life-threatening hepatic failure (black box warning)
- Effects CYP450 3A
- Improves sleep

Trazadone (Desyrel):
- Mostly used as nonaddictive sleep aid
Norepinephrine-Serotonin Modulator

- **Mirtazipine** (Remeron):
  - Usual dose is 15-45 mg/day
  - Less GI upset
  - Helps sleep
  - Less sedating at higher doses
  - Less sexual dysfunction
  - Rare agranulocytosis
  - Not as popular
Monoamine Oxidase Inhibitors (MAO-I)

- Phenelzine: 15-90 mg/day
- Tranylcypromine: 30-60 mg/day
- Particular efficacy in atypical depression
- Not first line
- Dietary restrictions: hypertensive crisis
- Many drug-drug interactions
Augmentation Strategies

- What is treatment resistant depression?
- Fails to respond to 2-4 or more trials of monotherapy (controversial)
- Traditional augmentation: lithium and T3 (thyroid hormone)
Augmentation Strategies

- Buspirone
- Stimulants
- Bupropion
- Dopamine agonists (amantadine)
Augmentation with Atypicals

- Affect multiple neurotransmitters
- Norepinephrine, dopamine and serotonin
- Aripiprazole recently approved by the FDA for augmentation therapy
- Dosing 2-20 mg/day along with antidepressant
- Olanzapine/fluoxetine combination pill (Symbyax)
- Other atypicals effective as well
General Side Effects of Atypicals

- Less likely to cause EPS or TD
- Prolactin elevation-galactorhea, gynecomastia
- Sedation
- Anticholinergic
- Weight gain

(EPS: extra pyramidal symptoms; TD: tardive dyskinesia)
Conclusions

- MDD is common
- MDD is debilitating
- MDD is treatable and relapses can be prevented.
References

- Diagnostic and Statistical Manual of Mental Disorders, fourth edition, Text Revision, American Psychiatric Association, 2000
- Physicians Desk Reference, 2008