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

Elizabeth Montagnese, M.D.
Adult, Child and Adolescent Psychiatrist

This program has been supported by an educational grant from Bristol-Myers Squibb

Legal Disclaimer: The material presented here does not necessarily reflect the views of Pharmaceutical Education Consultants (PharmCon) or the companies that support educational programming. A qualified healthcare professional should always be consulted before using any therapeutic product discussed. Participants should verify all information and data before treating patients or employing any therapies described in this educational activity.

PharmCon is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education

Speaker: Dr. Montagnese is board certified in adult, child, and adolescent psychiatry by the American Board of Psychiatry and Neurology. Dr. Montagnese provides comprehensive psychiatric evaluation and treatment for individuals, couples, and families. Her primary area of focus is working with children and adolescents, but she also treats adults. Dr. Montagnese received her medical degree at Wayne State University in Detroit, Michigan. She completed her general psychiatry and child psychiatry training at the Penn State University Milton S. Hershey Medical Center. Dr. Montagnese is the medical director of Family and Children Services of Central Pennsylvania. This is a United Way funded nonprofit agency that serves the greater Harrisburg, York, and Lancaster areas. To contact her at this agency please call 717-238-8118.

Speaker Disclosure: Dr. Montagnese has no actual or potential conflicts of interest in relation to this program.

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

Target Audience: Pharmacists & Technicians

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 effects 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)

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

25% relapse w/i 2 mos if meds stopped
- Maintenance psychotherapy

If no improvements after 6-8 weeks, reassess
- Maximize meds
- Change in meds, augmentation
- Change in therapeutic approach

Course of Disease - Continuation Phase
**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
Conquering Major Depressive Disorder in Rural Communities – The Pharmacist’s Role

© 2010 Pharmaceutical Education Consultants, Inc. unless otherwise noted. All rights reserved. Reproduction in whole or in part without permission is prohibited.

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-Is

Tricyclics

- Older medications
- Most often used: imipramine, desipramine, doxepin, nortriptyline, amitriptyline
- 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

SNRIs
- Duloxetine (Cymbalta):
  - Usual dose is 60-120mg/day
  - Targets physical symptoms
  - Chronic pain
  - Fibromyalgia

SNRIs
- 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
Conquering Major Depressive Disorder in Rural Communities – The Pharmacist’s Role

© 2010 Pharmaceutical Education Consultants, Inc. unless otherwise noted. All rights reserved. Reproduction in whole or in part without permission is prohibited.

Norepinephrine-Serotonin Modulator
- Mirtazapine (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

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