The Pharmacist's Role in Major Depressive Disorder: Optimizing Care

Welcome
We will begin shortly.
The Canadian Pharmacists Association is pleased to be partnering with Pfizer to highlight the role of pharmacists who are in the unique position to optimize patient care for MDD.
Today’s Speaker

Jamie Kellar, RPh, BSc.HK, BSc.Phm, Pharm.D
Acting Director Doctor of Pharmacy Program,
Assistant Professor – Teaching Stream
Leslie Dan Faculty of Pharmacy,
University of Toronto
Learning Objectives

By the end of this session participants will be able to:

• describe the clinical presentation
• list key diagnostic features of MDD
• demonstrate the importance of measurement-based practice in the management of patients with MDD
• identify first line treatments and common adverse effects
• describe an approach to antidepressant non-response
• recognize the key roles a pharmacist can play
Meet Cheryl

• 45 years old
• Low mood for over 6 months
• Taken an extended leave from work – cannot meet demands of job, calling in sick 6-10 days/month
• Cannot sleep
• No longer enjoys being with children
• No appetite – lost 20 lbs over 6 months

Source: http://www.istockphoto.com/stock-photos
What is Going on with Cheryl?
Major Depressive Disorder

A. 5 or more of the following symptoms, present during same 2-week period, must represent a change from previous functioning. At least one symptom must be depressed mood or loss of pleasure.
   - Depressed mood*
   - Markedly diminished interest or pleasure*
   - Significant weight loss or gain, increase or decrease in appetite
   - Insomnia or hypersomnia
   - Psychomotor agitation or retardation
   - Fatigue or loss of energy
   - Feelings of worthlessness or excessive guilt
   - Diminished ability to think or concentrate
   - Recurrent thoughts of death, suicidal ideation or suicide attempt

B. Symptoms cause clinically significant distress or impairment in social, occupational or other important areas of functioning.

C. Episode is not due to physiological effects of a substance or another medical condition.

D. Not better explained by schizophrenia or other psychotic disorder

E. There has never been a manic or hypomanic disorder

Adapted from DSM-5 2013
Clinical Presentation - SADAFACES

- **S** – sleep changes
- **A** – anhedonia
- **D** – depressed mood
- **A** – appetite disturbance
- **F** – fatigue
- **A** – agitation (psychomotor) or psychomotor retardation
- **C** – concentration
- **E** – esteem
- **S** – suicidal ideation

Source: https://quizlet.com/7250331/dsm-criteria-selected-for-osce-revision-flash-cards/
Back to Cheryl

• How severe are Cheryl’s symptoms?
• Would you treat her?
• What are the goals of therapy?
## Patient Health Questionnaire (PHQ 9)

1. Over the last 2 weeks, how often have you been bothered by any of the following problems?

<table>
<thead>
<tr>
<th></th>
<th>Not at all (0)</th>
<th>Several days (1)</th>
<th>More than half the days (2)</th>
<th>Nearly every day (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.</td>
<td>Little interest or pleasure in doing things.</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>b.</td>
<td>Feeling down, depressed, or hopeless.</td>
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<td>☐</td>
<td>☐</td>
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<tr>
<td>c.</td>
<td>Trouble falling/staying asleep, sleeping too much.</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>d.</td>
<td>Feeling tired or having little energy.</td>
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<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>e.</td>
<td>Poor appetite or overeating.</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>f.</td>
<td>Feeling bad about yourself, or that you are a failure, or have let yourself or your family down.</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>g.</td>
<td>Trouble concentrating on things, such as reading the newspaper or watching TV.</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
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<tr>
<td>h.</td>
<td>Moving or speaking so slowly that other people could have noticed. Or the opposite; being so fidgety or restless that you have been moving around more than usual.</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
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<tr>
<td>i.</td>
<td>Thoughts that you would be better off dead or of hurting yourself in some way.</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

2. If you checked off any problem on this questionnaire so far, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

- Not difficult at all
- Somewhat difficult
- Very difficult
- Extremely difficult

**TOTAL SCORE**

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## Guide for Interpreting the Score

<table>
<thead>
<tr>
<th>Score</th>
<th>Recommended Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>Normal range or full remission. The score suggests the patient may not need depression treatment.</td>
</tr>
<tr>
<td>5-9</td>
<td>Minimal depressive symptoms. Support, educate, call if feel worse, return in 1 month for reassessment.</td>
</tr>
<tr>
<td>10-14</td>
<td>Major depression, mild severity. Use clinical judgement about treatment, based on patient’s duration of symptoms and functional impairment. Treat with antidepressants or psychotherapy.</td>
</tr>
<tr>
<td>15-19</td>
<td>Major depression, moderate severity. Warrants treatment using antidepressant or psychotherapy or both.</td>
</tr>
<tr>
<td>20 or higher</td>
<td>Major depression, severe. Warrants treatment with antidepressant and psychotherapy</td>
</tr>
</tbody>
</table>
Treatments
General Treatment Options

• Pharmacotherapy
  • antidepressants

• Psychotherapy
  • Cognitive behavioural therapy (CBT)
  • Interpersonal therapy (IPT)

• Electroconvulsive therapy (ECT)

• Adjunctive or combined therapy

• Alternative therapy
  • Mindfulness meditation
  • Light therapy
  • Transmagnetic stimulation (r-TMS)
Pharmacotherapy

SSRIs
- citalopram (Celexa)
- escitalopram (Cipralex)
- fluoxetine (Prozac)
- fluvoxamine (Luvox)
- paroxetine (Paxil)
- sertraline (Zoloft)
- vortioxetine (Trintellix)

SNRIs
- venlafaxine (Effexor)
- desvanlafaxine (Pristiq)
- duloxetine (Cymbalta)

NDRIs
- bupropion (Wellbutrin)

SARI
- trazodone (Desryl)

NaSSRI
- mirtazapine (Remeron)

MAO-I
- moclobemide
- phenalzine
Cheryl comes to the pharmacy with the following prescription:

Escitalopram 10 mg po od x 1 month

What do you think?
How Do You Select Antidepressant Therapy for Patients?

- Evidence
- Severity of episode
- Drug interactions
- Age
- Accessibility
- Pharmacokinetics
- Patient preference
- Potential side effects

- Long term adherence
- Previous treatment response
- Comorbid psychiatric or medical disorders
- Suicide risk
- Clinician experience
Early improvement (defined as >20%–30% reduction from baseline in a depression rating scale after 2–4 weeks) is correlated with response and remission at 6 to 12 weeks.

CANMAT recommends increasing the antidepressant dose for non-improvers at 2 to 4 weeks if the medication is tolerated and switching to another antidepressant if tolerability is a problem.

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1. Monitor outcomes using measurement-based care.
2. Depending on tolerability, first optimize antidepressant by increasing dose.
3. For early treatment resistance, consider adjunctive use of psychological and neurostimulation treatments.
4. After failure of 1 or more antidepressants, consider switch to a second-line or third-line antidepressant.
5. For more resistant depressions, consider longer evaluation periods for improvement.
6. Depending on tolerability, increase dose if not at maximal doses.
7. For more chronic and resistant depressions, consider a chronic disease management approach, with less emphasis on symptom remission and more emphasis on improvement in functioning and quality of life.
# Antidepressants: Guidelines

<table>
<thead>
<tr>
<th>Class of Antidepressant</th>
<th>Adapted from CANMAT (1&lt;sup&gt;st&lt;/sup&gt; line recommendations)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selective Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)</td>
<td>Desvenlafaxine, duloxetine, venlafaxine</td>
</tr>
<tr>
<td>Selective Serotonin Reuptake Inhibitors (SSRIs)</td>
<td>Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline</td>
</tr>
<tr>
<td>Tricyclic Antidepressants (TCAs)</td>
<td>N/A</td>
</tr>
<tr>
<td>Serotonin-2 Antagonist/Reuptake Inhibitor (SARI)</td>
<td>N/A</td>
</tr>
<tr>
<td>Noradrenergic/Specific Serotonergic Antidepressant (NaSSA)</td>
<td>Mirtazapine</td>
</tr>
<tr>
<td>Monoamine Oxidase Inhibitors (MAOIs)</td>
<td>Moclobemide</td>
</tr>
<tr>
<td>Norepinephrine Dopamine Reuptake inhibitor NDRIs</td>
<td>Bupropion</td>
</tr>
</tbody>
</table>

Source: http://www.canmat.org/resources/canmat%20depression%20guidelines%202009.pdf
Cheryl’s Escitalopram prescription is deemed appropriate.

Cheryl has the following questions for you:
- When will I feel better?
- How long will I need to take this medication for?
When will I start to feel better?

• Important for clinicians to help their patients set **realistic goals** and **expectations** with respect to their antidepressant therapy.
Onset

• Many patients expect symptom relief immediately after starting an antidepressant.

• Onset of effects typically thought to be 2–4 weeks or longer.

• Some studies suggest that response may occur earlier in people that will eventually have a response to treatment (1-2 weeks).

• Physical symptoms usually improve first, followed by mood symptoms and then functional symptoms (i.e. work, activities of daily living).

How Long Will I Need to Take this Medication?

• No clear answer – generally thought that patients should be maintained for 9-12 months if first episode

• If patient has risk factors (older age, recurrent episodes, chronic or severe episodes, psychotic features etc.) then therapy should be 2 years to lifetime

Source: http://www.canmat.org/resources/canmat%20depression%20guidelines%202009.pdf
Other Key Issues with Antidepressants

• Adverse Effects
• Withdrawal/Discontinuation symptoms
• Adherence issues
• Treatment refractory depression
• Suicide/self-harm
• Efficacy controversies
Potential Adverse Effects

• GI upset
• Headache
• Sexual dysfunction
• Weight gain
• Increased suicidal thoughts
• Sedation
• Activation
• Serotonin Syndrome
• QTc Prolongation
Suicidal Risk

• Increasing concern that newer antidepressants may cause “worsening or emergent suicidal ideas and attempts.”

• Resulted in black box warnings for all antidepressants.

• In adults, RCTs have not shown any increased risk of completed suicide or increased suicidality with SSRIs and newer antidepressants.

• Data is less clear for adolescence – family should be encouraged to monitor for worsening or new onset of suicidal thoughts.

Serotonin Syndrome

• Occurs when central and peripheral serotonin receptors are over-stimulated through the action of medications or drugs of abuse

• Clinical presentation is likely a spectrum; ranging from mild to life-threatening

• Incidence is unknown; reports have increased as availability of serotonergic medications increase

Source: Canadian Pharmacist’s Letter. “Facts About Serotonin Syndrome.”
Clinical Presentation

• **Hallmark sign**: clonus (i.e. involuntary, rapid muscle contractions and relaxation) or tremor.

• **Mental status changes**: agitation, confusion, delirium, hallucinations, hyperactivity, hypomania, pressured speech.

• **Autonomic changes**: diarrhea, fever, flushing, increased bowel sounds, increased RR, hypo- or hypertension, sweating, etc.

• **Neuromuscular changes**: hyper-reflexia, increased muscle tone, restlessness, rhabdomyolysis, rigidity, shivering, tremor, etc.

Discontinuation Syndromes

• Most common with abrupt discontinuation of SSRIs and SNRIs
• Can be very distressing to patients – work with them to slowly taper medications

Clinical Presentation of Discontinuation Syndromes

• Symptoms are fairly non-specific – has been mistaken for other illnesses in ER or relapse of depression:
  • **Somatic:** Fatigue, N/V, diarrhea, fever, sweating, chills, malaise, insomnia
  • **Neurological:** myalgia, dyskinesia, paresthesias
  • **Psychological:** anxiety, agitation, crying, irritability, confusion, disoriented

Onset and Duration

• Typically begins 1-7 days after stopping or greatly reducing dose of an SSRI or SNRI with a short half-life (i.e. paroxetine)
• Less likely to occur in drugs with longer half-life
• Reactions less likely to occur in patients taking SSRIs for a short period of time
• Typically resolves within 3 weeks

Cheryl come back 4 weeks later – she reports no major improvement but also no adverse effects.

She wants to know why she is not better – what could be going on?
ANTIDEPRESSANTS DON'T WORK
THE DEBATE OVER THE NATION'S MOST POPULAR PILLS
BY SHARON BEGLEY

Overall Response Rates: Antidepressants

Meta-analysis including 262 drug-placebo comparisons from 182 clinical trials (n=36,385)

Slide created by Adil Virani for Pharmacy U Presentation 2016
Cheryl’s MD increases her escitalopram dose to 20 mg po od – but after another 4 weeks she is still not better.

What do you do next?
## Non or Incomplete Response to Initial Antidepressant

### 1st line options

<table>
<thead>
<tr>
<th>Switch to an agent with evidence for superiority</th>
<th>Add-on another agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escitalopram</td>
<td>Aripiprazole</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>Lithium</td>
</tr>
<tr>
<td>Sertraline</td>
<td>Olanzapine</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>Risperidone</td>
</tr>
<tr>
<td>Duloxetine</td>
<td></td>
</tr>
</tbody>
</table>

### 2nd line options

<table>
<thead>
<tr>
<th>Switch to an agent with evidence for superiority but with side effect limitations</th>
<th>Add-on another agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline</td>
<td>Bupropion</td>
</tr>
<tr>
<td>Clomipramine</td>
<td>Mirtazapine</td>
</tr>
<tr>
<td>MAO inhibitors</td>
<td>Quetiapine</td>
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<tr>
<td></td>
<td>Triiodothyronine</td>
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<tr>
<td></td>
<td>Other antidepressant</td>
</tr>
</tbody>
</table>

Slide adapted from CANMAT
Role of the Pharmacist

• Build rapport
• Provide medication education – determine what individual patients would like to know
• Learn about the patients medication experience – their perceptions about taking antidepressants, what they hope the medication will do for them
• Help set realistic goals
• Monitor adherence – work with patients to keep them on the antidepressant therapy
• Use the PHQ-9 for screening and to assess response to therapy
References


Questions

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Thank you!

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http://www.pharmacists.ca/index.cfm/education-practice-resources/professional-development/pharmacy-practice-webinars/