Medication management and psychopharmacology

Learning objectives

- Recognize common psychotropics used to manage depression and anxiety.
- Discuss how to assess for medication adherence and side effects.

Case presentation

Dr. Kim refers a patient to you:

Mr. M. is an 80-year-old man with hypertension (HTN) and coronary artery disease (CAD), recently moved to assisted care facility. Family says he isn't like himself anymore, doesn't want to do anything. They think he's depressed. He's not sure.

Should he be started on an antidepressant?

Medication assessment

1. Diagnostic assessment
2. Contraindications and cautions
3. Medication selection
4. Patient education

Diagnostic assessment

Clinical History

- Does the chief complaint and history suggest a primary depressive or anxiety disorder according to DSM-5 criteria?
- Are there any features suggestive of another disorder, either somatic or psychiatric?

Symptom measures (PHQ-9, GAD-7, PCL-5)

- Increases diagnostic efficiency and thoroughness
- Include DSM-5 symptoms for making diagnosis
- Establishes severity
- Allows tracking of treatment response

Causes of “secondary” depression

Psychiatric

- Nearly any psychiatric disorder could present with depression
- Not necessary or feasible to screen for all disorders
- After assessing for MDD, GAD, PTSD and substance use, base additional screening on initial complaints and any other symptoms patient mentions (e.g., paranoia, mood swings)

Medical/Neurologic Causes

These should be assessed by PCP and reviewed by Psychiatric Consultant:

- Obstructive sleep apnea
- Chronic pain
- Hypothyroidism, endocrine disorders
- Anemia
- Infectious disease: HIV, TB, Mono
- Cancer
- Neurologic disorders (e.g., dementia, stroke, Parkinson’s)
- Autoimmune disorders (e.g., lupus)
- Medications: beta blockers, interferon, steroids, hormones, antibiotics, statins, anticonvulsants

Case follow up

- His PHQ-9 is 14, loss of interest started 1 month ago after moving
- GAD-7 is 9, no history trauma, no substance use
- Medical history positive for a heart attack 10 years ago with bypass surgery, has hypertension and high cholesterol, treated with medications (beta blocker, ace inhibitor, statin, and aspirin)
- PCP notes indicate no new medical complaints, no abnormal physical exam findings, no medication changes in past 6 months
- All lab work is normal

Contraindications and cautions

Only in rare cases are SSRIs absolutely contraindicated

Relative contraindication: Bipolar Disorder

- Risk of causing mania
- Risk is reduced by mood stabilizers
- May still be effective for comorbid anxiety disorder with mood stabilizer
- Screen all patients for bipolar before starting antidepressant

Caution with:

- Pregnancy
- Other serotonin-related medications
- Certain medical conditions (e.g., seizures, bleeding, liver, or kidney disease)
- Certain medications (e.g., for HIV or anticoagulants)
- Psychiatric consultant should review these cautions

Serotonin Syndrome

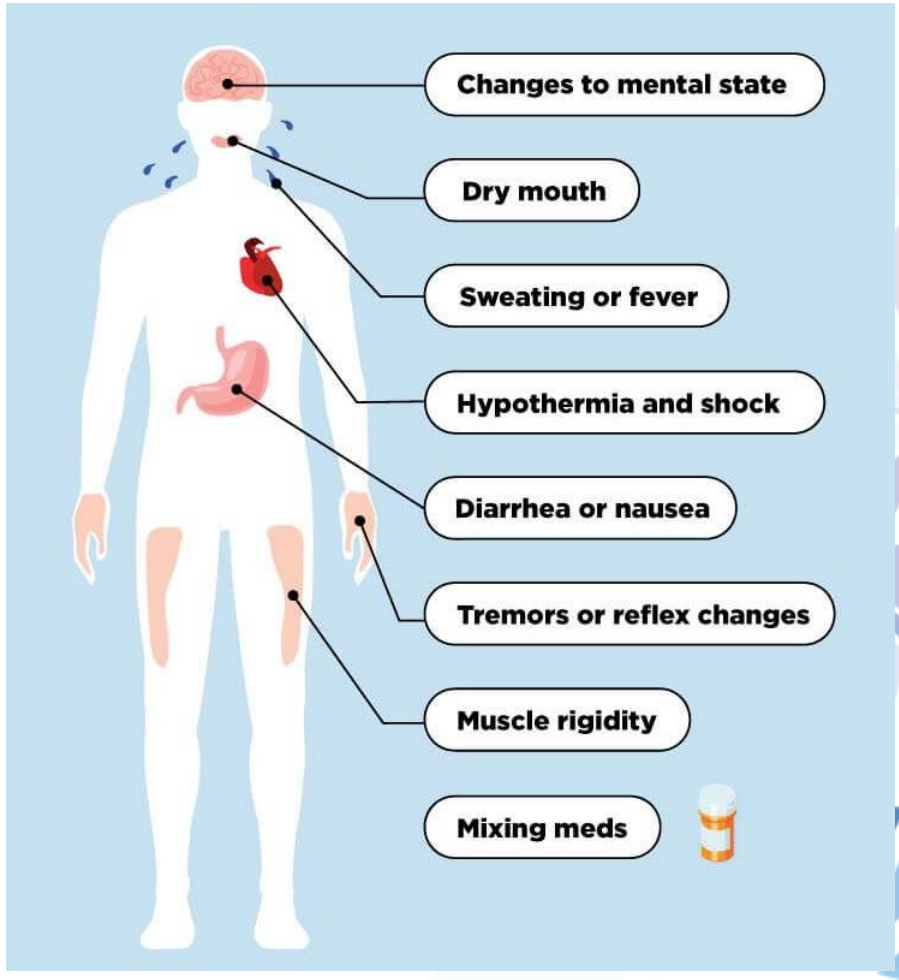
- **Rare but dangerous consequence of excessive serotonin activity**

- **Causes**: overdose of antidepressants, combination of medications that affect serotonin

Other pro-serotonin drugs include:

- Tramadol and other opiates
- Triptans for migraine headaches
- Stimulants and drugs of abuse: cocaine, ecstasy (MDMA)
- Anti-nausea medications, some antibiotics
- St. John's Wort

Which symptoms are most concerning?



Antidepressant medication selection

- Selective serotonin reuptake inhibitors (SSRIs)
- Serotonin and norepinephrine reuptake inhibitors (SNRIs)
- Atypical antidepressants
  - Bupropion (Wellbutrin)
  - Mirtazapine (Remeron)
- Tricyclic antidepressants (TCAs)
- Other/new

Selective serotonin reuptake inhibitors (SSRIs)

- All FDA approved for major depressive disorder
- Some also FDA approved for anxiety disorders
  - All considered effective for anxiety
- What is the relationship between Celexa and Lexapro?

Fluoxetine (Prozac)

Sertraline (Zoloft)

Paroxetine (Paxil)

Citalopram (Celexa) &
Escitalopram (Lexapro)

SSRIs: common side effects

- **Gastrointestinal**: nausea, diarrhea, constipation, loss of appetite, vomiting (infrequent)
- **Sexual Dysfunction**: impaired libido or orgasm
- **Sleep & Energy**: Insomnia, somnolence, drowsiness, fatigue, lightheaded, weak
- **Nervousness** and **Agitation**
- **Dry Mouth**
- **Less Common (<10%)**: sweating, tremor, dry eyes

Which side effects can be symptoms of depression or anxiety?

Addressing side effects

Assess side effects to:

- Determine if related to antidepressant or another medical cause
- Decide to continue or stop medication

Care Manager should:

- Ask routinely if any side effects
- If side effects present, assess:
  - Timing—was it clearly after the medication?
  - Severity and frequency—getting better, worse, or staying the same?
  - Patient distress—do they want to stop the medication or give it more time?

Referring provider or psychiatric consultant should be made aware of all side effects in case further assessment is needed

Sample questions to identify side effects

- *Are you having any side effects to the medication?*

- *There is the possibility of side effects and some people may experience 1 or more of the following. Some side effects improve on their own after a few days, others can often be managed by dosage adjustment or by switching to another medication. Are you experiencing any of the following?*
  - Dry Mouth? yes/no
  - Gastrointestinal symptoms? yes/no
  - Drowsiness? yes/no
  - Headache? yes/no
  - Sexual Problems? yes/no

Sample questions to explore a specific side effect

Patient started Zoloft last week and reports side effect of headaches.

Onset:	Two days after starting Zoloft
Frequency:	Every day
Duration:	3-4 hours
Severity/Intensity:	Patient reports inability to work with headache.
Last time it occurred:	Today
What makes it better:	Patient reports taking Tylenol to manage headaches and finds it helpful.
What makes it worse:	Nothing
What does the patient want to do:	Give it a couple more days

Assessing for medication adherence[1]

Screening questions:

How many days over the past week did you not take your medication? (Preferred)

Vs.

Are you having any problems taking your medication?

Follow-up questions:

1. Do you **have** all the medications you were prescribed?
2. Do you **understand** why you are taking them?
3. Do you ever **forget** to take your medications?
4. Do any of your medications **make you sick**?
5. If you **feel worse**, do you **stop taking** them?
6. If you **feel better**, do you **stop taking** them?
7. Have you ever **intentionally taken too much or too little** medication?

Practical barriers to medication adherence[2]

- **Financial:** Cost of medication or getting to pharmacy
- **Issues with remembering:** Difficulty establishing routine
- **Formulation**: Taste, shape, size of tablets; difficulty swallowing
- **Instructions for use**: Dosing frequency or variation, storage, administration requirements, restrictions while taking, total number of medications
- **Capability**: Reading and understanding labels, difficulty opening container, cutting pills to get correct dose
- **Supply**: Pharmacy does not have supply, ran out of medication, need to obtain new script
- **Social environment**: Reluctance to take around friends or family, stigma associated with certain medications

Serotonin and norepinephrine reuptake inhibitors (SNRIs)

- **Efficacy and side effects similar to SSRIs**
- **Advantage vs. SSRIs**: also effective for neuropathic pain (e.g. from diabetes, fibromyalgia)
- **Disadvantage vs. SSRIs**: greater hypertensive effects (mild)
- **Mechanism**: Blocks reuptake of norepinephrine and serotonin

Venlafaxine (Effexor) &
Desvenlafaxine (Pristiq)

Duloxetine (Cymbalta)

Atypical antidepressants

Bupropion (Wellbutrin)

- **Advantage vs. SSRIs**: Suppresses appetite, less sexual dysfunction, stimulant-like
- **Disadvantage vs. SSRIs**: not effective for anxiety disorders
- **Mechanism**: stimulates release of dopamine and norepinephrine
  - Also effective for smoking cessation
  - Caution in patients with seizure history

Mirtazapine (Remeron)

- **Advantage vs. SSRIs**: Sedating and stimulates appetite, useful for insomnia and weight loss
- **Disadvantage vs. SSRIs**: Sedation and weight gain
- **Mechanism**: blocks serotonin receptors, increases serotonin and norepinephrine release

Tricyclic antidepressants (TCAs)

- Older generation, replaced by SSRIs
  - Significant **anticholinergic side effects**
  - **Dangerous in overdose (cardiac arrythmias)**
- Still used for migraine headaches, nerve pain, sleep
- **Should not be first choice for depression or anxiety**

Nortriptyline

Amitriptyline

Choice of initial antidepressant

25-year-old woman with depression, no other psychiatric or medical history

- Which antidepressant should be started?
- What if she has comorbid PTSD?
  - Sertraline
  - Venlafaxine
  - Bupropion
  - Mirtazapine

- **What about Mr. M**, who is 80-year-old with hypertension and coronary artery disease, and no significant pain/neuropathy, no separate anxiety disorder?
- What if Mr. M has severe insomnia and weight loss?

If initial treatment fails

Options for the next step include:

- Increase dose
- Switch to another antidepressant
  - SSRI to other SSRI is as good as switching to SNRI/bupropion/mirtazapine
- Add a second “augmenting” antidepressant from other class
  - SSRI + bupropion or mirtazapine are common choices
- Augment with an antipsychotic or other medication
  - VA trial found augmentation with aripiprazole (Abilify) was more effective than switch to bupropion

After 2 failures: scrutinize diagnosis, consider intensifying treatment

Patient education

- Antidepressants need to be **taken daily, not as needed**
- All antidepressants take **2-4 weeks to see a benefit**
- Most side effects resolve in a few days, serious side effects are rare
- Antidepressant should be **continued for at least 6 months**
- If the first antidepressant doesn’t work out, there are many other options

What would you say? (1 of 6)

I don’t want to feel like a zombie.

Most are not sedating nor cause problematic slowing of cognition. Some report emotional flattening. Patients often have a friend/relative that “acts like a zombie” but this could be due to depression itself or other medications. Antidepressants do not cause loss of insight or awareness.

What would you say? (2 of 6)

Am I going to be on this medication forever?

Recommend at least 6 months after achieving remission to avoid relapse, indefinite treatment if multiple prior episodes.

It’s up to you how long you take this medication and whether you find the benefits outweigh the costs.

What would you say? (3 of 6)

Are antidepressants addictive? Can I stop them any time?

Very rarely abused, not considered addictive, and no dangerous withdrawal syndromes.

Discontinuation syndrome may occur, “brain zaps,” malaise, can last a few days and can be addressed by slower taper.

What would you say? (4 of 6)

How do these medications work?

Brain cells communicate with one another through chemicals that go between them. These medications affect the activity of those chemicals.

What would you say? (5 of 6)

Do antidepressants cause suicide?

FDA warning—increase in suicidal thoughts and behaviors in those under 24 years old, no established increase in suicide death. Risk not shown in older patients.

What would you say? (6 of 6)

Are antidepressants just a placebo?

Antidepressant trials consistently show superiority to placebo. About 30% will get better with a placebo compared to 40% with an antidepressant.

Placebo response is high with depression, some consider this part of antidepressant treatment.

Resources

- NIMH Depression Patient Handout
- AIMS Center Common Questions & Answers about Treatments for Depression
- AIMS Center Commonly Prescribed Psychotropic Medications
- AIMS Center Brief Medication Prescribing Directions
- Antidepressant Treatment Algorithm

References

1. Apgar, T., & Nunlist, M. M. (2016). Practical Ways to Improve Medication Adherence. Family Practice Management, 23(5), 52.

2. Chan, A. H. Y., Cooper, V., Lycett, H., & Horne, R. (2020). Practical Barriers to Medication Adherence: What Do Current Self- or Observer-Reported Instruments Assess? Frontiers in Pharmacology, 11, 572. https://doi.org/10.3389/fphar.2020.00572