Managing Depression and Anxiety in Primary Care

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Objectives

1. Differentiate depression and anxiety from other mood disorders
2. Analyze choices in pharmacotherapy
3. Evaluate outcomes to determine when to escalate therapy vs when to refer

Financial Disclosure

• I have no financial relationships to disclose
• I have no real or potential conflicts of interest
Making the Diagnosis

• Screening for depression has become a common mandate in primary care
  – Most compelling for those with chronic disease, history of depression, and the elderly
• Conventional screening and diagnostic tools are based upon DSM-V domains to establish diagnosis

DSM-V Criteria for MDD
(present nearly every day for at least 2 weeks)

• Depressed mood or irritability*
• Decreased interest or pleasure*
• Change in weight (> 5%) or appetite
• Sleep changes
• Psychomotor changes
• Fatigue or energy loss
• Guilt/worthlessness
• Diminished concentration
• Suicidality

Case Study

• 25-year-old female presents for evaluation because she thinks she needs an antidepressant. She finally has decent insurance and wants to get help. She says she has struggled with depression on and off every since she was a teenager. She was talking to a friend at work who told her that she herself was depressed and Zoloft change her life.
Case Study
(continued)

• So what do you do with a new patient?
  – Complete medical history
  – Complete surgical history
  – Complete medication history
  – Complete social history
    • Denies tobacco
    • Alcohol 1-2 x week
    • Experimented with some recreational drugs in her teens and college

Case Study
(continued)

• Complete ROS
  – She feels fatigued a lot – just doesn’t want to do anything
  – Sleep is inconsistent
  – Appetite is too good; eats constantly, has gained 19 lbs in the last 3 months
  – Chronically constipated
  – The remainder of ROS is negative

Case Study
(continued)

• HPI – pt reports that in the last two weeks (and probably for several months) she just hasn’t wanted to do anything. She does what she has to do; goes to work, pays bills, goes shopping, but she doesn’t look forward to anything. It’s not so much that she feels “sad” or “depressed…”
Case Study
(continued)
• …but that she isn’t interested in anything she is doing. She also admits to being chronically a poor sleeper. Sometimes she can’t sleep all night, other times she sleeps but wakes up a lot. Rarely does she wake up feeling well rested.

Case Study
(continued)
• She does admit to being irritable – she says people at work have commented that she is “snappy” a lot. In terms of appetite, as revealed in ROS she is eating a lot – has gained 19 lbs in the last 3 months. The patient denies any psychomotor changes.

Case Study
(continued)
• As noted in the ROS, she does feel tired most of the time – just no energy. Maybe it’s just disinterest. She’s really not sure. She denies a sense of guilt or worthlessness, but does find it hard to concentrate at work. Her mind does constantly wander, but probably because she isn’t interested in her work. She denies suicidality.
Analysis of HPI:

• Irritability +
• Decreased interest/pleasure +
• Weight change/appetite change +
• Sleep disturbances +
• Activity change –
• Fatigue/energy loss +
• Guilt/worthlessness –
• Concentration loss +
• Suicidality –

Case Study
(continued)

• Physical exam
  – Normal
  – Well groomed
  – Attends to hygiene
  – Good eye contact
  – Coherent thought
  – Normal flow of conversation
  – Voice well modulated

Case Study
(continued)

• What’s your diagnostic impression?
• How do you treat her?
  – SSRI
  – Pick a typical starting dose
  – Start daily with half a pill for 1-2 weeks then full pill
  – F/U in 4 weeks
  – Consider a therapist referral
Indications for SSRI

- SSRIs are the first line drug for major depressive episode/disorder in the primary care setting for the functionally depressed patient.
- Increasing serotonin concentration in the raphe nuclei has a clear impact on emotional depression -- often initially triggered by an external circumstance.

Indications for SSRI

- SSRI is not typically a first line choice for:
  - Non-functional patients
  - Patients with comorbid chronic pain
- Always caution patients regarding common adverse effects early in therapy:
  - GI effects
  - Frontal headache

Case Study
Follow-up Scenario 1

- Patient returns in 4 weeks as instructed.
- She reports absolutely no change – no side effects, but no effects; she feels no different.
- She is emphatic that she has been taking it every day just as you ordered.
How to Manage a Non-Responder at the 4-Week Follow-up

- Increase the dose for another 4 weeks
- Change to another first-line drug
  - SNRI
  - Bupropion SR or XL
  - Mirtazapine

Indications for SNRI

- SNRI adds the norepinephrine component to serotonergic effect
- More effective for patients with "cognitive" or endogenous depression
- Indicated for patients with
  - Non-functional depression at presentation
  - Comorbid chronic pain
  - Unresponsive to SSRI therapy

Indications for SDRI

- Bupropion (Wellbutrin) is commonly used SDRI
- Capitalizes on the third neurotransmitter implicit in mood disorders
- Particularly helpful in patients with anxiety component to depression or anxiety disorders
Indications for SDRI

• Dopamine is the neurotransmitter of emotional satiety
• Increasing dopamine in mood centers supports the neurological effect of anxiety-relieving behaviors, e.g., OCD, trichotillomania
• Also useful for smoking cessation
• Caution as it lowers seizure threshold

Case Study
Follow-up Scenario 1

• Patient returns in another 4 weeks as instructed
• She reports absolutely no change in symptoms
  – She may be having more headaches, a little nausea
• She is emphatic that she has been taking it every day just as you ordered
Case Study
Follow-up Scenario 2

• Patient returns in 4 weeks as instructed
• She cannot take this medication
• She is emphatic that she took it for the first 3 weeks as you ordered by had to stop
• It made her agitated, couldn’t sleep, and she actually seems worse; she is more impatient at work, people tell her she is “bitchy”

How to Manage Intolerable Adverse Effects at the 4-Week Follow-up

• Change to another first-line drug
  – SNRI
  – Bupropion SR or XL
  – Mirtazapine
• Encourage her to keep trying
• Refer to psychiatry

Why Don’t Depressed Patients Respond to Antidepressants?

• Inadequate dose
• Inadequate therapeutic trial
• Wrong diagnosis
Why Don’t Depressed Patients Respond to Antidepressants?

• With inadequate dose or inadequate trial, an inadequate response is likely
  – Partial responses are anticipated in that scenario
  – Patients may report “feeling a little better” but not where they hope to be

Why Don’t Depressed Patients Respond to Antidepressants?

– As you review the presenting symptoms, you may find some response to some symptoms, but not what you would call a remission
  – This is typically referred to as a partial response
  – Appropriate response is to max out drug one or add another first line agent

Why Don’t Depressed Patients Respond to Antidepressants?

• Wrong diagnosis more likely when:
  – Absolutely no response (no effect, no side effects)
  – Worsening of symptoms
  – Intolerable side effects with no improvement in presenting symptoms
Why Don’t Depressed Patients Respond to Antidepressants?

• When one of the indicators of “wrong diagnosis” occurs, we need to reconsider the diagnosis
• Most common misdiagnoses are:
  – Cyclothymia
  – Bipolar disorder

Levels of Mood

Levels of Mood -- Depression
Levels of Mood – Bipolar I

Mania
Hypomania
Euthymia
Dysthymia
Depression

Levels of Mood – Bipolar II

Mania
Hypomania
Euthymia
Dysthymia
Depression

Levels of Mood – Cyclothymia

Mania
Hypomania
Euthymia
Dysthymia
Depression
Differentiating Mood Disorders

• Depression (MDD) is not characterized by manic or hypomanic episodes
• Typically presents as the classic “5 of 9 domains”
• These patients respond best to antidepressants

Differentiating Mood Disorders

• Bipolar I characterized by classic cycling from depression to mania
• Bipolar II characterized by cycling from depression to hypomania
• Cyclothymia characterized by cycling from dysthymia to hypomania

Differentiating Mood Disorders

• Any patient who presents with depressive symptoms should be evaluated for a history of cycling
• Patients with BPI, BPII, or cyclothymia may have mania precipitated by an antidepressant
Differentiating Mood Disorders

• Before starting patients on antidepressants, history should include assessment for symptoms consistent with mania or hypomania

Differentiating Mood Disorders

• Symptoms of “up” mood
  – 2 or more sleepless nights
  – Hallucinations
  – Feelings of grandiosity or invincibility
  – Extreme/disproportionate anger
  – History of risk-taking behavior
  – Binge behavior – shopping, gambling, eating, sexuality

Differentiating Mood Disorders

• Patient history consistent with cyclic mood disorders
  – Family history of BPD
  – Younger age of onset
  – Periods of excess energy/sleeplessness
  – Hyperphagia
• Remember – patients often like their manic/hypomanic times and don’t report it
Our 25-year-old Patient

- She has struggled “on and off” with depression since adolescence
- She has “experimented with drugs in teens and college”
- Periods of sleeplessness
- She is hyperphagic and has gained 19 lbs
- People at work tell her she is “snappish”

To Refer or not to Refer?

- The “partial responder” may do well with an increased dose or add on drug – she is probably depressed; it’s appropriate to adjust her therapy in primary care
- The “no response” or “side-effects only” responder more likely has a mood disorder and will need a mood stabilizer; more appropriate to refer to psychiatry

Atypicals and Mood Stabilizers for Depression

- A wide variety of antidepressants are referred to as “atypicals”
- The still impact serotonin, norepinephrine and dopamine but they are not selective in the way that SSRI, SNRI, and SDRI are
- While mirtazapine is still recommended as a first line antidepressant, most atypical are tried when patients unresponsive to SSRI
Atypicals and Mood Stabilizers for Depression

- Atypicals include
  - Mirtazapine (Remeron)
  - Trazodone (Desyrel)
  - Nefazodone (Serzone)
  - Vilazodone (Viibryd)
  - Vortioxetine (Brintellix)

Atypicals and Mood Stabilizers for Depression

- Older atypical are used largely as sedatives now
- Newer atypicals capitalize on the serotonin aspect of depression management

Atypicals and Mood Stabilizers for Depression

- When mood stabilizers are successful in “depressed” patients it is often because the diagnosis is actually bipolar disorder
- Aripipazole (Abilify) is indicated for both biopolar and as and adjunct for MDD; particularly useful in patients with bipolar disorder and residual depression
What About Anxiety?

Diagnostic Criteria for Anxiety

• Excessive anxiety and worry (apprehensive expectation) occurring more days than not for at least 6 months about a number of activities or events such as work or school performance
• The worry is difficult to control
• The anxiety and worry are associated with at least three of the following:
  • Restlessness or feeling “keyed up” or “on edge”
  • Being easily fatigued
  • Difficulty concentrating or mind going blank
  • Irritability
  • Muscle tension
  • Sleep disturbance
Case Study

- A 42-year-old male presents requesting ADD medication. He has been seeing a therapist for bipolar disorder and anxiety for several months but he really thinks he has ADD; he was reading about it on-line. He says he has so much trouble staying focused at work and at home with his daughter; he shares custody and when he has her he really wants to be engaged.

Case Study

- He has been taking meds for bipolar disorder for years and he is actually doing well with that. He just can’t get much done at work, and that gives him anxiety and then he can’t sleep. He finds that he is not following through on things at work to the extent that he is less productive.

Case Study

- He knows he doesn’t pay attention to his daughter when he should; she often comments that he “isn’t listening.” He was never diagnosed with ADD before, but he has had bipolar and anxiety for decades.
Case Study (continued)

• So what do you do with a new patient?
  – Complete medical history
    • Bipolar
    • Anxiety
  – Complete surgical history
  – Complete medication history
    • Lamictal 100 mg b.i.d.

Case Study (continued)

• Complete ROS
  – Chronic anxiety about work
  – Sleep is generally not good; DFA, nocturnal awakenings
  – Occasional palpitations
  – The remainder of ROS is negative

Case Study (continued)

• HPI – The patient reports a persistent sense of difficulty attending to important things. He is a mortgage writer and often finds himself missing details that cost him work. He can’t stay focused. As a result he doesn’t get much done during the day…
Case Study  
(continued)  
• He co-parents his 10-year-old daughter and really wants to be involved, but he can never seem to pay attention. His girlfriend has the same complaints. The patient also admits to constantly worrying about income, relationships, and just generally worrying! Sometimes

Case Study  
(continued)  
• He doesn’t even know what he is worrying about. He denies panic attacks but sometimes will get so agitated that he just has to stop and forcibly relax. He was diagnosed with BPD as a teenager, has been on many drugs including lithium, but finally has settled in with

Case Study  
(continued)  
• Lamictal and feels that helps a lot. He denies mood swings – just a this daily difficulty focusing, and anxiety. He admits to being a “little obsessive” but not to the level of obsessive-compulsive disorder.” He is pretty obsessive about schedules, neatness, etc.
Diagnostic Criteria for Anxiety

- Excessive anxiety and worry (apprehensive expectation) occurring more days than not for at least 6 months about a number of activities or events such as work or school performance
- The worry is difficult to control
- The anxiety and worry are associated with at least three of the following:
  - Restlessness or feeling “keyed up” or “on edge”
  - Being easily fatigued
  - Difficulty concentrating or mind going blank
  - Irritability
  - Muscle tension
  - Sleep disturbance

Diagnostic Criteria for ADD

- Six or more of the following
  - Often fails to give close attention to details or makes careless mistakes in work or other activities
  - Often has difficulty sustaining attention in tasks
  - Often does not seem to listen when spoken to directly
Diagnostic Criteria for ADD

– Often does not follow through on instructions and fails to finish schoolwork, chores or duties in the workplace
– Often has difficulty organizing tasks and activities
– Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort

Diagnostic Criteria for ADD

– Often loses things necessary for tasks or activities
– Is often easily distracted by extraneous stimuli
– Is often forgetful in daily activities

Analysis of HPI

• He’s got criteria for both anxiety and ADD
• Anxiety
  – Excessive worry/anxiety which is difficult to control
  – Irritability
  – Concentrating difficulty
  – Sleep problems
Analysis of HPI

- ADD
  - Fails to give close attention
  - Difficulty sustaining attention
  - Doesn’t listen
  - Doesn’t follow through
  - Avoids tasks that require sustained mental effort
  - Easily distracted

Case Study (continued)

- Physical exam
  - Normal
  - Well groomed
  - Attends to hygiene
  - Good eye contact
  - Voice well modulated
  - Conversation is mildly distracted

Case Study (continued)

- What’s your diagnostic impression?
- Inattentiveness is a common symptom of anxiety
- Anxiety is less likely a symptom of ADD
- Typically adults with ADD have a childhood history of ADD although it’s not required
- A stimulant will exacerbate anxiety
- Maybe it’s suboptimally controlled BPD
Diagnosis and Management

- He was diagnosed with anxiety and started on escitalopram (Lexapro)
- His Lamictal was continued
- Advised to continue working with a therapist
- Follow-up in 4 weeks

Follow-up

- Lexapro didn’t help at all
- He was started on Adderall 10 mg q.a.m.
- In follow-up he noticed a marked improvement, but asked if he could take it twice a day
- He was increased to a.m. and 1:00 p.m.
- He has had a 100% improvement in all symptoms on this regimen

Management of Acute Anxiety

- While SSRI, SNRI, and SDRI are all commonly used for chronic anxiety management, many patients need treatment for acute episodes
- Benzodiazepines are extremely effective and therefore highly subject to abuse
When to Use Benzodiazepines?

- Benzodiazepines are meant for *acute* episodes
  - Patients acutely fearful, e.g., have to get on an airplane
- Patients who have panic attacks
  - Impending doom
  - Tachycardia/palpitations
  - Diaphoresis
  - SOB

Benzodiazepines

- Mechanism of action potentiation of GABA receptors
- Functionally this class of medication is similar to liquid ETOH
- They are a challenge because they are very effective while simultaneously not indicated for long term use

Alternatives to Benzodiazepines

- Several medications that suppress the sympathetic nervous system are used as alternatives
  - First generation antihistamines (e.g., hydroxyzine)
  - Antiadrenergic agonists (clonidine)
  - Beta adrenergic antagonists (propranolol)
- Not as acutely effective as benzodiazepines, but preferred in those at risk for addictive behavior
Pharmacogenetic Testing

- May be useful in evaluating patients with atypical responses to commonly used medications
- Helps to identify patients with abnormal metabolism patterns
  - Ultra metabolizers
  - Intermediate metabolizers
  - Poor metabolizer

- Not routinely indicated for all patients
- Expensive and often not necessary
- Consider and discuss when the therapeutic response to typical regimens is poor

Take Home Messages

- Anxiety, hypomania, and ADD can all be intermingled and it’s confusing!
- True anxiety is characterized primarily by pervasive anxiety and worry, usually about something ill-defined
  - Medication regimens almost identical to MDD
- Listen to the patient’s primary concerns; that will often identify the right diagnosis
Take Home Messages

• Patients who don’t respond to depression therapy may not be depressed!
• Pharmacogenetic testing should be considered when the diagnosis is well established and the patient is not responding as expected.

References