MSFM: DEPRESSION AND ANXIETY
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Disclosure of (No) Financial Relationships

James L. Levenson has no relationships with entities producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients.

Question 1

How should one treat the patient with depression who has not adequately responded to the selective serotonin reuptake inhibitor (SSRI) first prescribed? Switch to another medication in the same class? Switch classes? Or augment with another agent? What type of monitoring should be instituted, particularly with regard to suicidal ideation?

(Note to self: Isn't this **five** questions?)

Options if the first SSRI fails:

1. *Switch* to another SSRI
2. *Switch* to a different AD class

    --e.g. an SNRI, bupropion, mirtazapine, TCA

3. *Add* a 2nd AD from a different class
4. *Augment* with a nonantidepressant

    --e.g lithium, T_3, buspirone, antipsychotic

5. *Refer* for psychotherapy and/or psychiatric consultation

(How to tell if the psychiatrist is a good one)

Should we…

…switch?

…or, add another antidepressant?

…or augment the antidepressant?

Before doing anything, evaluate why the response is inadequate.

Evaluating Poor Response

- Adequate dose and duration?
- Is patient compliant? Cost?
- Is patient bipolar?
- Psychiatric comorbidity
  e.g. substance abuse, personality disorders
- Medical comorbidity
  e.g. sleep apnea, anemia, hypothyroid, chronic pain
- Drug effects
  e.g. caffeine, sedatives, interferon, corticosteroids
- Social comorbidity
  e.g. poverty, abuse, job loss

Should I switch drugs or add a second drug ?

SWITCHING

- Side effects
- Mild depression
- No response
- Polypharmacy
- Costs
- Compliance

ADDING

- Severe depression
- Partial response (but can’t raise dose)
- Maintain patient optimism about treatment (rather than sense of “failure”)

Switching Antidepressants

- Switching within class:
  - Possible efficacy if SSRI to SSRI, (up to 50% response), especially if switch due to side effects rather than poor clinical response
- Switching to new drug class is preferred by some experts.

Newest antidepressants

Vilazodone (Viibryd)

Vortioxetine (Brintellix)

Levomilnacipran (Fetzima)

- ***These are "me-too" drugs.***
- ***No evidence better than other much less expensive antidepressants.***
- ***Please do not accept and give out samples.***

Cheap and safe augmentation?

- Exercise: Modest effects as monotherapy, can't hurt as add-on to other Rx.

  Cochrane Database Syst Rev.2013 Sep 12;9:CD004366

- Vitamins
  - Vitamin D: Depressed patients have lower levels but doubtful supplementation is effective.

    J Clin Endocrinol Metab.2013 Dec 10:jc20133450

  - B vitamins: Low levels, esp. folate, have been associated with treatment-resistance, but supplementation not proven effective.
    - Deplin is l-methylfolate (very expensive folate).

- **My advice: Consider vitamin D if low, prenatal vitamin, and always encourage exercise (but not when very depressed).**

Summary of what to do after first antidepressant fails:

- Adequate dose and duration?
- Reassess diagnosis, compliance, and comorbidities.
- Switch if no response.
- Augment if partial response.
- Consider referral for psychotherapy.
- Or refer to a psychiatrist.

What type of monitoring should be instituted, particularly with regard to suicidal ideation?

- Ask the patient directly, and keep risk factors in mind: past attempts, SA, loss of job, loss of relationship, chronic pain, impulsivity, etc.
- Ask about firearms (ignore the NRA).
- Don’t start an antidepressant with next visit in 6 weeks.
- There is no measure with good PPV for identifying suicide attempts.
- Most patients with SI do not attempt, and most who attempt do not succeed.

Question 2

How should generalized anxiety disorder (GAD) be treated? When and how should benzodiazepines be used?

(OK, this one is only two questions…)

Generalized Anxiety Disorder (GAD)

- Chronic worrying, fatigue, muscle tension, restlessness, irritability, difficulty concentrating, insomnia.
- Often overlaps with depression.
- Treatment trials have been small and short-term.

First line treatments of GAD supported by randomized trials

- SSRIs, SNRIs (slowest onset, sexual SEs)
  - Clear choice if comorbid depression.
- Benzodiazepines (fastest onset, sedation, dependency)
- Buspirone (intermediate onset, less potent, dosed t.i.d.)
- Cognitive-behavioral therapy
  - Other psychotherapies: mindfulness, short-term psychodynamic therapy, etc.
- Exercise (more as add-on to other Rx)

When and how should benzodiazepines be used?

- Bzs are the most frequently prescribed medication for GAD.
- ***Contraindicated in patients with Hx of alcohol abuse.***
- The APA's Bz Task Force: "There are no data to suggest that long-term therapeutic use of Bzs by patients commonly leads to dose escalation or to recreational abuse."
  - But those at high risk are excluded from long-term trials.
- Not all patients develop tolerance.
- Immediate Sx relief not as important in GAD as in panic disorder.
- Intermediate half-life benzodiazepines (most often clonazepam) are preferred.

How should Generalized Anxiety Disorder be treated if first line therapies fail?

- Rx for treatment-resistant GAD supported by (small) RCTs:
  - SSRI+benzodiazepines
  - TCAs (as effective, but more SEs)
  - MAOIs
  - Pregabalin
  - Atypical antipsychotics

Summary of treatment for GAD

- First line options include SSRIs/SNRIs, benzodiazepines, buspirone, and CBT.
- Benzodiazepines can be used long-term in some patients without tolerance or abuse.
- Benzodiazepines are contraindicated in patients with alcohol abuse histories.

Question 3

What is the role of standardized depression screening tools in the primary care setting? Which have been validated and what is the data regarding sensitivity and specificity? When and how often do they need to be repeated?

(I thought I agreed to cover three questions, but there turned out to be **ten** in total!)

Screening instruments for depression?

“There is substantial evidence that routinely administered case finding/screening questionnaires for depression have minimal impact on the detection, management or outcome of depression by clinicians. Practice guidelines and recommendations to adopt this strategy, in isolation, in order to improve the quality of healthcare should be resisted. The longer term benefits and costs of routine screening/case finding for depression have not been evaluated.”

Screening and case finding instruments for depression. Cochrane Database Syst Rev. 2005;4:CD002792.

More recent data on screening

- Depression screening without substantial staff-assisted depression care is ineffective.

Screening for depression in adult patients in primary care settings: a systematic evidence review. Ann Intern Med. 2009;151:793-803

- The U.S. Preventive Services Task Force 2009 recommended screening only if such depression care is available.

More data…

Depression screening **with** such care programs has not been proven effective.

There are no randomized controlled trials that support the United States Preventive Services Task Force guideline on screening for depression in primary care: a systematic review. BMC Med. 2014;12:13

The Canadian Task Force on Preventive Health Care does not support routine depression screening in primary care.

Can J Psychiatry.2013;58:692-6

Summary for screening for depression

What is the role of standardized depression screening tools in the primary care setting?

- There is insufficient evidence to recommend routine screening. But absence of evidence is not evidence of absence. What has not worked in separate silo care may work in collaborative care models.

Am J Prev Med. 2012;42:550-2

Which have been validated and what is the data regarding sensitivity and specificity? When and how often do they need to be repeated?

Screen those patients you suspect as having depression.