Chapter 4
Discussion on the Use of Psychiatric Medications: Questions by W. Harley Sobin MD Answers by Thomas W. Heinrich MD

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1. Q: Most internists/gastroenterologists using antidepressants are using them to treat non-refractory depression, fibromyalgia, migraines, functional bowel disorders, etc. TCAs, in particular, are used much more to treat pain and functional symptoms, rather than depression by this group of non-psychiatrists. The doses used are generally much lower. Can you comment on the level of concern you would convey regarding the safety and risk of using TCAs in this clinical setting?

   A: Although there is a dose-response relationship to many of the adverse side effects of TCA, it still is worth

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respecting the potential for TCA to cause adverse events in susceptible patients (elderly patients, patients receiving polypharmacy, and with medical comorbidity). For example, given TCAs' classification as class 1A antiarrhythmics, they represent a risk for cardiac arrythmias in patients with a history of cardiac disease regardless of dose. Respect the medication.

2. Q: When choosing one of these drugs to treat depression and/or anxiety will you generally start with an SSRI if there is no pertinent personal history, family history, or painful syndrome?

   A: Yes. When I choose pharmacologic therapy to treat patients with uncomplicated major depression, I most often select an SSRI. They have proven efficacy across patient populations, are usually well tolerated and safe in overdose, relatively cheap, and once-a-day dosing can help improve adherence.

3. Q: In choosing an SSRI do you have any favorites, if you are dealing with a patient who has no pertinent exposure or family history. Who is basically a blank slate?

   A: My go-to SSRI is sertraline. It has minimal drug-drug interactions at lower doses and multiple therapeutic indications. It does not require dose adjustment in renal or hepatic dysfunction and has been demonstrated to be safe in patients with heart disease.

4. Q: If a patient doesn't respond to an SSRI, do you tend to go to a second SSRI or use a different class of drugs?

   A: It depends on the reason for the treatment failure. If it was due to intolerance that I can directly relate to the SSRI, I usually try to change class and avoid both SSRIs and SNRIs to avoid the risk of the patient experiencing the same adverse effects. If they had a partial response to the SSRI, I usually try to augment with a non-SSRI, trial another SSRI, or change to an SNRI.

5. Q: In choosing a drug to treat depression or anxiety, can you discuss which drugs other than SSRIs you tend to choose and in which setting?

   A: For patients experiencing chronic anxiety, pharmacotherapy starts with SSRIs. They are usually my first-line

pharmacotherapy for chronic anxiety as, when effective, they prevent future panic attacks or anxiety. For benzodiazepines to accomplish this, they have to be taken regularly on a scheduled basis, which raises the potential for the patient to develop tolerance, the need for escalating doses of medications, and the risk of withdrawal.

If a patient with depression or anxiety has comorbid pain, I may trial an SNRI as my first-line agent. Duloxetine is an excellent choice in this patient population as it has demonstrated efficacy for neuropathic and chronic musculoskeletal pain as well as fibromyalgia. If they have depression or anxiety comorbid with nausea or anorexia, I may elect to trial mirtazapine, although the evidence of mirtazapine and anxiety is less robust than for SSRIs and SNRIs.

6. Q: In choosing an SNRI, is there one you are more likely to use?

   A: When choosing an SNRI, it is important to recognize the fact that although they all inhibit the reuptake of both serotonin and norepinephrine, they do it to varying degrees. For example, at lower doses, venlafaxine is primarily a serotonin reuptake inhibitor. It is not until one achieves a dose of 150 mg/day or more that the norepinephrine reuptake inhibition becomes clinically meaningful. On the other hand, duloxetine exhibits uniform serotonin and norepinephrine reuptake across the dose range. In contrast, the newest SNRI, levomilnacipran, is a more robust inhibitor of norepinephrine reuptake than serotonin reuptake.

7. Q: Since sexual side effects are fairly common with SSRIs, do you tend to prescribe much sildenafil (or similar agents)?

   A: I have not utilized a phosphodiesterase type 5 inhibitor to treat antidepressant-induced sexual dysfunction. The data is quite poor. If a patient has had a good response to the SSRI or SNRI, but is experiencing sexual dysfunction, I will usually augment with bupropion. If that does not work, I would consider stopping the bupropion and replacing with amantadine, buspirone, or mirtazapine. If the SSRI

or SNRI was ineffective in treating the depression and causing sexual dysfunction, I would discontinue the offending medication and consider bupropion, mirtazapine, or one of the newer serotonin modular antidepressants.

8. Q: When you are using these drugs to treat patients who have underlying pain, do you tend to use TCAs more frequently or SNRIs?

   A: Given the propensity of patients with chronic pain to suffer from depression or anxiety, I tend to go straight for a medication that may address both of these conditions in the safest manner with the minimal risk of a large side effect burden. As a result, I tend to go with SNRIs in this patient population. Patients simply do not tolerate TCAs well at the doses it takes to achieve remission from depression or anxiety.

9. Q: Since most non-psychiatrists are not treating refractory depression, do you see MAO inhibitors being used by primary care doctors?

   A: No. They are really considered third-line agents.

10. Q: Primary care doctors are prescribing diabetic medications even though they are not endocrinologists and cardiac medications even though they are not cardiologists. Do you think it's equivalent to say the same for them prescribing psychiatric medications or do you think there is an inherent danger in that? In other words, do you think primary care doctors should be prescribing psychiatric medications without consulting with a psychiatrist? What are the biggest or most frequent mistakes made by primary care doctors in prescribing ADs?

    A: I may be biased as a family medicine physician and psychiatrist, but I think primary care clinicians are uniquely suited to address chronic conditions such as major depression and anxiety disorders. They often have the longitudinal relationship with the patient that allows them to identify a mental health condition. This could be through a population health approach, such as screening as recommended by the USPSTF, or through having a relationship with a patient and, thereby, knowing when

things are "off." This therapeutic relationship with the patient also improves adherence to treatment and likelihood of follow-up. In addition, it is not like we as primary care providers are not already seeing these patients as there simply are not enough psychiatrists nationally to address all the behavioral healthcare needs of the population.

11. Q: Are there any drugs that you encourage or discourage primary care doctors use in managing their patients with behavioral health problems?

    A: I usually recommend that primary care providers get comfortable with one or two medications from a given class of antidepressants. Of the SSRIs, I usually try and steer clear of paroxetine, as it has many drug-drug interactions and is quite anticholinergic. Fluoxetine also presents a risk of drug-drug interactions, so I tend to avoid it when polypharmacy is already an issue. Citalopram deserves a special mention given its FDA warning on risk of QT prolongation. As a result, I tend to avoid utilizing citalopram in patients with multiple risk factors for QT prolongation and/or torsades. If I am going to prescribe this medication to an at-risk patient, I will obtain a baseline and follow-up ECG to make sure the QTc interval is not prolonged.