Questions and Answers

Treating Sexual Dysfunction: Psychiatry's Role in the Age of Sildenafil

Question: Does the presence of depression affect treatment of erectile dysfunction? Or does treatment of erectile dysfunction affect depressive illness?

Dr. Seidman: The relationship between erectile dysfunction and depression is bidirectional and complex. It's often unclear which came first: depressive symptoms caused by erectile dysfunction or erectile dysfunction resulting from depression.

We know that sexual dysfunction is prevalent in about 30% to 40% of the population, with one of the most frequent problems being decreased sexual desire. We also know that decreased desire and erectile dysfunction can be symptoms of depressive illness. Other factors, such as aging, declining testosterone levels, comorbid medical conditions, and medications, affect sexual function and may contribute to the correlated depressive symptoms.

Question: We know that testosterone levels decrease with age. Do diminishing testosterone levels have psychiatric effects, and would testosterone replacement therapy alleviate the depressive symptoms?

Dr. Seidman: We suspect that there is a relationship between depressive illness and testosterone levels. The psychiatric effects of having low testosterone levels include reduced libido, erectile dysfunction, fatigue, irritability, depression, and anxiety, so you might conclude that there's a clear-cut relationship between depressive illness and testosterone levels, although we have not been able to find it yet. There have been reports that testosterone replacement therapy leads to improved mood, increased energy and libido, better sleep, and an improved sense of well-being. We have observed that administering exogenous testosterone appears to have a positive effect on sexual satisfaction and function. It is as effective as an antidepressant in some men *[Seidman SN, et al. Am J Geriatr Psychiatry 1999;7:18–33].* However, it is important to note that erectile dysfunction caused solely by low testosterone is rare.

Question: How does impairment of nocturnal penile tumescence correlate with depression? Is it simply organic or is it psychogenic?

Dr. Seidman: A number of studies have documented that impaired nocturnal penile tumescence (NPT) is a prime marker of depression. An age-related condition, impaired NPT is rarely found in men under the age of 50 and is characterized by reduced rapid eye movement latency, reduced cortisol latency, and blunted growth hormone secretion. The combined effects of advancing age and depressive disorders lead to expression of illness-related changes. Studies have found that depressed patients manifest abnormalities of underlying sexual neurophysiology and that depression can be associated with an NPT profile indistinguishable from that seen in organic impotence.

Question: Dr. Fava, I am a bit confused about the sexual side effects of SSRIs. As I understand it, a male who experiences sexual side effects after starting an SSRI will usually have problems with decreased libido and orgasm delay. There's not usually a problem with erection that is understandable in terms of pharmacologic effects. Would you comment?

Dr. Fava: It is a little more complicated than that, and SSRI-induced sexual side effects are not just an effect on libido. Often, patients will complain of numbing in the genital area and will report that sexual stimulation and intercourse are less pleasurable. They often complain of less firm erections. In fact, our study population had problems with decreased libido and erectile dysfunction, and we found that improvement in orgasm paralleled the improvement in erectile dysfunction after treatment with sildenafil *[Fava M, et al. Psychother Psychosom 1998;67: 328–331].*

Question: You said you were not impressed with priapism with sildenafil. But do you see an inverse relationship between the youth of the patient and priapism? Is a younger man more likely to experience this side effect?

Dr. Roose: Prolonged erections have been reported infrequently since market approval of sildenafil. The incidence of priapism is actually so low that it is not possible to say whether there is a relationship with age. In Phase II and III clinical trials, there were no incidents of priapism.

Question: I know you have discussed the issue of priapism, but I still have some concerns as to whether there's an increased risk of priapism in men taking sildenafil who have sickle-cell trait. Would you comment?

Dr. Fava: One needs to exercise caution in using sildenafil in patients taking medications or with medical conditions that are associated with priapism, such as trazodone. In our study, one patient was taking trazodone. I have used sildenafil in patients taking trazodone, and priapism was not a problem. Of course, I still warn the patient that there is a theoretical concern of increased chances of priapism.

Dr. Roose: That question is really not going to be answered other than by a placebo-controlled clinical trial that assesses the incidence of priapism in men with sickle-cell trait taking sildenafil compared with placebo. I would not want to withhold an effective treatment for erectile dysfunction from patients with sickle-cell trait, but I would assess each patient individually on the basis of his history.

Question: Is there any evidence that sildenafil might increase sexual appetite other than through psychological mechanisms?

Dr. Roose: The data from the initial studies are clear. Over 3000 men were studied. The effect on libido was looked at carefully, and there was no change. The effect of sildenafil on sexual desire is peripheral.

Question: Dr. Fava, did I understand correctly that you used nefazodone and mirtazapine to counteract the sexual side effects of the SSRIs? Are they needed on a daily basis?

Dr. Fava: Yes, that is correct. I have used nefazodone, which is a serotonin-2 ($5\text{-}HT_2$) antagonist, and mirtazapine because it blocks $5\text{-}HT_2$ and $5\text{-}HT_3$ and is an α_2 antagonist. Both nefazodone and mirtazapine have to be used on a daily basis.

Dr. Roose: One of the "take-home" messages is that a wide variety of pharmacologic interventions have been tried ranging from serotonergic and α_2-adrenergic receptor antagonists to *Ginkgo biloba*, and many physicians report their anecdotal successes. The only double-blind, placebo-controlled study that was done showed no difference between the study drugs, amantadine and buspirone, and placebo *[Michelson D, et al. Presented at the 37th annual meeting of the American College of Neuropsychopharmacology; Dec 14–18, 1998; Las Croabas, Puerto Rico]*. We are at the stage where physicians have their opinions and experience as to what is effective, but there are few data to substantiate a common practice.

Question: Dr. Fava, sildenafil comes in 25-, 50-, and 100-mg doses. What dose do you start with for the treatment of SSRI-induced erectile dysfunction?

Dr. Fava: We typically start with 50 mg. None of our patients dropped out owing to side effects, so that dose is well-tolerated. I know that in other clinics, the starting dose is 25 mg, and it is titrated upward if there is no response. We have advanced to the 100-mg dose only in a couple of patients.

Question: Dr. Leiblum, you have said that erectile dysfunction is a couple's problem. Would you define what effect erectile dysfunction has on the man and his partner and how that combination of reactions affects their relationship?

Dr. Leiblum: There is, indeed, a range of responses to the initial or repeated experience of erectile dysfunction. For many men, it challenges their sense of manhood and masculinity. They view it as a signal that they're getting old, that this is the first sign of an inevitable decline of youth and attractiveness. They fear that they may be stuck in a joyless bachelorhood or an unsatisfying relationship. Typically, the first response is concern and worry. Men may attempt a sexual encounter the next morning, even though they're not in the mood. Attempts to try harder are accompanied by tremendous performance anxiety and are likely to fail. Repeated failed attempts lead to greater feelings of embarrassment, anxiety, and depression. Men may begin to avoid affectionate touching of their partner, believing that it's better not to start something they can't finish. Displays of affection begin to decline along with sexual intimacy. However, men rarely rush to a sex therapist or family physician to announce that they're having a problem. In my experience, the couples I see as a sex therapist tend to be men who were brought there by their wives.

Question: How does the partner respond to her mate's erectile dysfunction?

Dr. Leiblum: Initially, she tends to be very supportive, very reassuring. "Don't worry, it will get better tomorrow. You're stressed, you're worried about your job, you've eaten too much." But it doesn't get better, and she begins to wonder: "Is it something about me?" Or she may become suspicious: "Is he doing it with someone else?" Ultimately she may begin to feel sad: "Is sex over between us? Is this the end of our intimate relationship?"

Question: What is the impact of erectile dysfunction on the relationship?

Dr. Leiblum: For many couples, the relationship begins to feel increasingly empty. As affectionate touching and intimate time together decrease,

relationship tension and irritability increase. For some, it can lead to fantasizing about other possible sex partners. Or they may use pornography or retreat to their computer for a diet of stimulation without the risk of being humiliated by failure. These reactions result in greater distance between partners, coupled with a sense of alienation.

Question: Does the ability to have an erection mean that the relationship is restored?

Dr. Leiblum: Good sex doesn't start with the ingestion of the pill. You must address relationship issues, and you must be able to anticipate and develop strategies for dealing with unsuccessful intercourse.