

Raising More Than Moods: Escitalopram-Associated Priapism

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Selective serotonin reuptake inhibitors are a common first choice medication for anxiety and depression treatment, but health care providers should be aware of priapism as a possible adverse effect.

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CASE PRESENTATION

An 80-year-old white male was evaluated in a primary care clinic following a recent hospitalization for a suicide attempt. His past medical history included type 2 diabetes mellitus, chronic atrial fibrillation, essential hypertension and hyperlipidemia, and no prior psychiatric illness. Six weeks after his wife died of cancer, the patient attempted suicide by slitting his wrists, which resulted in significant blood loss and tendon damage.

After medical stabilization he was treated at an inpatient psychiatric facility for 10 days. There was no evidence of impaired memory nor psychosis during his hospitalization. He was prescribed doxazosin 1 mg twice daily and finasteride 5 mg daily for obstructive urinary symptoms, along with escitalopram 5 mg daily for depression and continuation of prior medications, including glipizide 10 mg twice daily, simvastatin 20 mg daily, metformin 500 mg twice daily, and lisinopril 20 mg daily. The patient's estimated glomerular filtration rate was 85 at the time of these events.

He was evaluated by the mental health staff at the time of his primary care outpatient visit and noted to have a Patient Health Questionnaire (PHQ-9) score of 5 (mild depression symptoms) and a Generalized Anxiety Disorder 7 Item Scale (GAD-7) score of 1 (minimum anxiety symptoms). Eleven days later during his counseling appointment, he mentioned to staff that he had experienced a painful erection the day before, which lasted 4 hours. The primary care pharmacist was consulted for review of potential medication triggers. It was noted that there

was a low frequency of priapism with both doxazosin and escitalopram, a selective serotonin reuptake inhibitor (SSRI). The provider team felt that the α blocker (doxazosin) was more likely than was the SSRI to cause the reported priapism event. Doxazosin was discontinued, and escitalopram 5 mg daily was maintained. His mood remained stable with no further suicidal ideation.

Eighteen days after discontinuation of doxazosin, the patient experienced a second priapism episode. He reported 2 days later that he experienced a prolonged, painful erection that lasted 4 hours and resolved without intervention. The patient's mood continued without further suicidal thoughts, his appetite was normal, he had good social support and played cards with friends regularly. At that time, the decision was made to discontinue the escitalopram. The SSRI was felt to be a possible cause of priapism due to the length of time off doxazosin in relation to the second event.

The patient continued to do well 15 months after discontinuation of these medications. Unfortunately, he did not seek medical care during either episode of priapism, but he was felt to be reliable in his report based on a normal mental status exam. He does not have any of the other known risk factors for priapism, suggesting a possible association with his α blocker and SSRI.

DISCUSSION

Priapism is a prolonged, painful erection lasting more than 4 hours and is considered a urologic emergency. It is divided into ischemic and nonischemic types. Ischemic priapism occurs with blood dyscrasias, such

as sickle cell disease, thalassemia, leukemia, neurologic conditions affecting the spinal cord, and malignancies of bladder/prostate. The lifetime probability of priapism in patients affected by sickle cell disease is estimated at 29% to 42%.¹ Medications associated with priapism include cocaine, ondansetron, antipsychotics, excessive use of erectile dysfunction drugs, and increasingly, antidepressants.²⁻⁸

Nonischemic priapism is usually associated with pelvic trauma. Cavernous blood gas obtained at the time of the event can help distinguish between the 2 types. The color of the aspirated blood sample is black in patients with ischemic priapism. Corporal blood gas analysis shows hypoxemia and acidemia. The color of blood is red in patients with nonischemic priapism and shows normal oxygen and pH. Priapism is a urologic emergency requiring aspiration of blood from the cavernous sinus to prevent ischemic tissue damage. At times surgical decompression may be required if aspiration is not successful.

Adrenergic α -blocking agents were developed for treatment of hypertension. They have become popular for management of lower urinary tract symptoms (LUTS) secondary to prostate enlargement. Doxazosin, prazosin, and terazosin are nonuroselective and have a higher risk of cardiac adverse effects (AEs), including dizziness and orthostatic hypotension. Lexicomp lists < 1% incidence of priapism associated with doxazosin.⁹ The drug is metabolized by CYP3A4 with secondary pathways, including CYP2D6 and 2C9 with a drug half-life of 22 hours. Newer agents (eg, tamsulosin, alfuzosin) are considered more uroselective, targeting the α -1b receptors. The older agents have more effect on the α -1a receptors, which are also present at higher level in the cardiovascular system.¹⁰ By blocking sympathetic stimuli responsible for penile detumescence, the nonselective α blockers have a higher propensity to cause priapism. There seems to be a direct correlation between higher doses and increased risk of priapism.¹¹ Our patient was at a relatively low dose (1 mg twice daily) of the nonselective agent doxazosin for treatment of his LUTS.

Primary care providers and psychiatrists treating depression are familiar with com-

mon sexual AEs of the SSRI class of medications. Decreased sexual desire and delayed orgasm and ejaculation are all issues that lead patients to discontinue treatment. Although SSRIs are considered first-line treatment for depression, reports indicate that up to 60% of patients with prior normal sexual function started on paroxetine may experience sexual AEs.¹² The exact frequency is difficult to estimate due to underreporting of these issues by patients.

A review of the literature for cases of priapism associated with SSRIs shows that often there is more than 1 possible drug trigger, and medications used in combination may be a risk factor. It is hypothesized that SSRI action on 5-HT₃ receptors may be responsible for priapism occurring in patients treated with SSRIs.¹³ One study cites a case of priapism in a veteran being treated with escitalopram, prazosin, and trazodone for posttraumatic stress disorder.¹⁴ Trazodone inhibits the neuronal uptake of serotonin and is used to treat depression in addition to off-label use in treatment of insomnia. Trazodone is implicated in cases of priapism via its α -blocking properties. In the aforementioned case, trazodone was initially thought to be the causative agent and was discontinued. The patient had recurrent symptoms at which time his prazosin was discontinued, and he had no further events.

Another case cites citalopram-induced priapism that occurred with an accidental overdose of citalopram 80 mg, when a patient confused his antidepressant with 81-mg aspirin tablets.¹⁵ He also had a prior history of priapism while taking trazodone. We found only 1 case listing escitalopram as the probable causative agent of priapism.¹⁶ Similar to our patient, that case had no risk factors prior to escitalopram administration. Lexicomp notes < 1% incidence of priapism reported in postmarketing studies.

Our patient had been off doxazosin for 18 days when his second event of priapism occurred. It is less likely given the half-life of doxazosin ($t_{1/2} = 22$ hours) that the α blocker was the causative agent, though a combination of the 2 agents cannot be excluded as a significant factor. The Naranjo Score is an algorithm for determining the likelihood of whether an adverse drug reaction is due to the drug or other factors.¹⁷

Scoring ranks the event as probable, possible, or doubtful. This case scored +3 (+2 = appeared after suspected drug given, +1 = improved when drug discontinued), indicating possible association of escitalopram and priapism.

CONCLUSION

In view of the frequent use of SSRIs in treatment of depression, it may be prudent to advise patients of this uncommon but serious medication AE. Recent use of α blockers may be a risk factor in combination with SSRI therapy. Patients should be counseled to seek emergency care in the event of prolonged erection when discussing potential AEs of SSRI therapy.

Author disclosures

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