

Sexual Side Effects of Milnacipran

To the Editor: Milnacipran is a serotonin-norepinephrine reuptake inhibitor (SNRI), with equal potency to block reuptake of serotonin and norepinephrine (NE).¹ The U.S. Food and Drug Administration has approved milnacipran for treatment of fibromyalgia. Double-blind clinical trials have proved its efficacy in major depression also.^{2,3} There have been case reports where milnacipran has reduced sexual side effects induced by other antidepressants,^{4,5} but not much is known about the sexual side effects of milnacipran itself.

Case Report

We report a case of 26-year-old Asian man who developed sexual side effects after treatment with milnacipran 100 mg/day for major depressive disorder. Shortly after starting treatment with milnacipran, the patient reported pain and swelling in the scrotum, with ejaculation failure. He also reported dull pain and a constant "heaviness" in the perineum. The patient reported mild swelling in the scrotum that was not associated with any localized redness. He also complained of a sensation of incomplete emptying of bladder, but no associated fever, burning micturition, urinary hesitancy, or dribbling of urine. The patient had been a healthy man, with no history of surgery, any medical problems, or similar complaints in the past. He was not taking any other medication. On examination, there was mild

enlargement of epididymis and scrotum bilaterally, with no overlying erythema. There was no evidence of any hernia or hydrocele. His CBC, blood chemistry, urinalysis, and ultrasound of the testes were within normal limits. The patient's physician discontinued milnacipran after the second dose. Scrotal swelling and pain in the perineum subsided within 24 hours of discontinuation of milnacipran, with resumption of normal ejaculatory function. Two days later, the patient restarted milnacipran without consulting his physician. He reported reemergence of swelling in the testis and heaviness in the perineum after just the first dose. This time, again, discontinuation of milnacipran resulted in immediate resolution of his symptoms.

Discussion

Milnacipran blocks the reuptake of NE along with serotonin and increases its concentration at the synapse.¹ NE, by its action on alpha receptors, contracts the bladder sphincter as well as the prostatic urethra. This not only blocks the flow of urine from the bladder but also leads to back-flow of seminal secretions because of constriction of prostatic urethra. Seminal secretions flow backward into the ejaculatory ducts, into the vas deferens and the epididymis. This leads to congestion at the epididymis and aseptic inflammation, which is responsible for pain and swelling in the scrotum and heaviness in the perineum. Constriction at prostatic urethra might be responsible for ejaculation failure in our patient. Milnacipran is considered to have a benign sexual

side-effect profile. Although the drug insert description includes sexual side effects like ejaculation disorder, erectile dysfunction, decreased libido, ejaculation failure, testicular pain, and swelling, but none of these sexual side effects have been reported. These side effects should be taken into consideration, and the patient should be educated about them while prescribing milnacipran for depression or fibromyalgia, as they can interrupt the continuity of treatment.

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