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CASE REPORT

Urinary hesitancy and retention during treatment with sertraline

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Abstract We report the cases of two women who began to experience urinary hesitancy and retention after starting treatment with sertraline for depression. Discontinuation of the drug resulted in complete symptom relief. Serotonergic neurons are involved at several levels in control of the lower urinary tract. Retention is apparently an uncommon complication of sertraline. Discontinuation should be considered for patients presenting with voiding difficulties.

Keywords Sertraline · Voiding dysfunction · Serotonin

Introduction

Sertraline is an antidepressant drug belonging to the selective serotonin reuptake inhibitor (SSRI) family. It is approved by the United States Food and Drug Administration for treatment of depression, obsessive–compulsive disorder (OCD), panic disorder, post-traumatic stress disorder, premenstrual dysphoric disorder, and social phobia. The recommended dosage ranges from 50 to 200 mg daily. We describe two cases of urinary retention and hesitancy symptoms after the usage of sertraline. These symptoms completely resolved in both cases after discontinuation of the drug. We also briefly review the role of serotonin in lower urinary tract function.

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Case reports

Case 1

A 57-year-old patient was referred to our clinic with hesitancy and dysuria symptoms lasting 2 years before her initial visit. She reported symptoms of difficulty with urination and a feeling of 'bladder spasms', especially when she drank fluids late in the evening and had to get up at night to urinate, which she did twice nightly. Her first nighttime void was typically associated with an inability to urinate with associated pain, which is relieved by eventually being able to void 2–15 min later. She also had dyspareunia and difficult defecation but no symptoms of incontinence, pelvic organ prolapse, or chronic pelvic pain. Her only medication included sertraline 25 mg daily for anxiety/depression. Past medical and surgical histories were unremarkable. On physical examination, there were no abnormal findings except for moderate tenderness of the pelvic floor tissues and an inability to voluntarily relax her tight pelvic floor muscles. Her postvoid residual urine volume was normal. She underwent a 4-month course of pelvic floor physical therapy with resolution of tenderness of the pelvic floor musculature, but no relief of her urinary hesitancy and pain. Biofeedback assistance of her pelvic floor rehabilitation was added, with little relief of her symptoms after a total treatment time of 9 months. At about that time, her prescribing physician recommended increasing her dose of sertraline to 50 mg daily, and the patient noted that her symptoms had become even more troublesome, with hesitancy of urination both day and night and an increased difficulty with defecation. We performed urodynamic testing with urethral electromyography (EMG) surveillance of the voiding phase to investigate her urinary hesitancy. The urethral EMG demonstrated normal baseline

activity, no complex repetitive discharges, normal activation, and recruitment during coughing and filling. With a full bladder, the patient was unable to void, and there was no quieting of the urethral EMG during attempts to void at a bladder volume of 300 ml. At this point, the patient realized that her urinary symptoms had first begun soon after she started sertraline and self-discontinued the medication. She had prompt and complete relief of both urinary and bowel symptoms. Eleven months later, she continues to be symptom-free.

Case 2

A 70-year-old patient was referred to our clinic for evaluation of new onset urinary retention. There were no symptoms of dysuria or constipation. Two days before seeing us for the first time, the patient had been seen in our emergency room (ER) for lower abdominal pain and difficulty with voiding. During that ER visit, her postvoid residual urine volume was 300 ml, and an indwelling catheter was placed. Her past medical history was significant for heart disease, valve replacement, hypertension, gastroesophageal reflux, and anxiety-depressive disorder. Her medications included digoxin, warfarin, metoprolol, and sertraline. According to the patient, her symptoms started a week after she began treatment with sertraline 25 mg daily for treatment of anxiety/depression. A physical examination revealed no abnormal findings. After a normal voiding trial in the clinic, the indwelling catheter was removed. Because the temporal sequence of events suggested that sertraline might be causing her retention, we recommended its discontinuation and began treatment with tamsulosin (Flomax, Yamanouchi Pharmaceutical) 0.4 mg daily for 1 month. Two days later, the patient was again seen in the ER with urinary retention and was catheterized for 450 ml. An indwelling catheter was maintained for 10 days and was again removed after a normal voiding trial. After this period, the patient's symptoms were markedly improved, and all postvoid residual urine volumes were normal. Currently, she is symptom-free 10 months after discontinuation.

Discussion

We present in this paper two case reports of urinary hesitancy or retention during treatment with sertraline. We could find just one similar case report, by Benazzi [2], in a 29-year-old woman who had been treated for OCD, panic, and erotomanic delusional disorders by haloperidol 2 mg daily and clonazepam 2.5 mg daily, with the addition of sertraline 50 mg daily to control her OCD symptoms. Five days after starting sertraline, the patient complained of severe constipation and urinary difficulties. A week after discontinuation of sertraline, her symptoms were relieved [2]. As the mean half-life of sertraline is approximately 26 h, it is likely that symptoms may take several days to resolve after its discontinuation.

In studies that established the efficacy and safety of sertraline [6, 7, 11], urinary retention is not mentioned as a side effect. However, Cohn et al. [4] did report a higher rate of micturition problems in patients treated with sertraline compared to those treated with amitriptyline (7.5 vs 3.8%, respectively) [4].

Serotonin has an important neurotransmitter role in control of the lower urinary tract [1], and as an SSRI, sertraline may affect voiding through its effect on the nervous control of the bladder. Serotonergic neurons are present in the Onuf nuclei, which innervate the external urethral sphincter, in the lumbosacral autonomic nuclei, which control the external urethral sphincter and detrusor muscle, and in the raphe nuclei of the medulla, which provide descending inhibition of the bladder [1, 5].

There are seven subtypes of serotonin receptors [10]. Therefore, when serotonin is given experimentally, it can result in inhibitory or facilitatory effects depending on the predominant receptor subtype at the site of action [1]. The excitatory effects on the bladder sphincter seem to be mediated by 5-HT_2 receptors, whereas the inhibitory effects on the bladder seem to be mediated by 5-HT_1 receptors [13]. Animal studies have shown that both serotonin (5-HT) [5] and noradrenaline in the sacral spinal cord facilitate the action of the external urethral sphincter activity to prevent urine leakage during the storage phase of the micturition cycle [12].

Duloxetine, a combined serotonin and norepinephrine (5-HT/NE) reuptake inhibitor (SNRI), has been proven an effective and safe drug in the treatment of stress urinary incontinence [8, 9]. Duloxetine has a significant effect on the excitability of pudendal motor neurons and on sphincter contractility in healthy women in vivo [3]. A meta-analysis done by Viktrup et al. [14], evaluating the side effects of duloxetine in the treatment of depression and stress urinary incontinence, found that urinary retention was more prevalent among women who received duloxetine for depression or stress incontinence compared to those receiving placebo (20 out of 2,097 vs 6 out of 1,732, respectively; $p<0.05$) but was uncommon overall [14].

Conclusion

We submit these case reports to alert clinicians to the possibility that sertraline can precipitate voiding difficulties. It is unclear whether voiding difficulty is truly a rare

complication of sertraline, or whether there is under-reporting of this side effect because the connection between voiding difficulty and the use of sertraline has not been described in the urologic literature. Our cases certainly support the rule that all medications should be checked when voiding difficulties arise.

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