Available online: https://e-journal.unair.ac.id/jps

Case Report

Urinary Incontinence Associated with Sertraline use in a Young SSRI-Naïve Female Patient: a Case Report

Anna Elissa[1]

[1]Klinik Utama M³, Bogor, Indonesia

Submitted : May 11, 2023
Revised : July 19, 2023
Accepted : July 24 2023
Published : May 1, 2024

Correspondence Author:
Email: annaelissa.md@gmail.com

Abstract

Introductions: Urinary incontinence is a side effect of several antidepressants, especially those in the SSRI and SNRI groups. Sertraline, a popular SSRI effective against a wide range of mental disorders, is one such drug with a clear association with a new onset of UI. **Case:** A 20-year-old Indonesian Chinese woman, presenting with mixed anxiety and depressive symptoms, was initially treated with sertraline 50 mg. She experienced an acute onset of urinary urgency and a loss of bladder control. These symptoms resolved upon discontinuation of sertraline. She was then given 10 mg of fluoxetine, and she noted that the urinary problems did not return. The medication was gradually tapered up to 40 mg/day with no remarkable adverse events. **Discussions:** Sertraline tends to stimulate micturition through effects on M3 muscarinic receptors on the bladder's detrusor muscle and inhibition of the dopamine transporter in the central nervous system. On the other hand, fluoxetine acts antagonistically on 5-HT2C, inhibiting the voiding reflex and promoting urinary continence. Therefore, though both are SSRIs, sertraline and fluoxetine may exhibit different, clinically meaningful effects. **Conclusions:** Clinicians need to have a greater awareness of urinary incontinence as a side effect of sertraline, as it impacts patients' adherence and quality of life. When possible, switching to fluoxetine is recommended for patients with urinary problems in the event of sertraline use.

Keywords: Sertraline, Fluoxetine, Mental Health, Antidepressant, Urinary Incontinence

Cite this as: Elissa. A. "Urinary Incontinence Associated with Sertraline use in a Young SSRI-Naïve Female Patient: a Case Report". Jurnal Psikiatri Surabaya, vol. 13, no. 1, pp.94-99 2024. doi: 10.20473/jps.v13i1.45369

Introductions

Urinary incontinence (UI) is the involuntary leakage of urine [1]. While not life-threatening, it does impact general health and quality of life [2]. Some medications, including selective serotonin reuptake inhibitors (SSRI) and serotonin-norepinephrine reuptake inhibitors (SNRI), have been known to cause UI.

SSRIs remain the first-line treatment of choice for most depressive disorders [3], and anxiety disorders [4]. Sertraline is known to be effective against a wide range of disorders, such as major depressive disorder (MDD), obsessive-compulsive disorder (OCD), panic disorder (PD), posttraumatic stress disorder (PTSD), and premenstrual dysphoric disorder (PMDD) [5]. Up to 200 mg/day of sertraline has been very well tolerated. Adverse events are usually dose-related mild and transient in nature. They tend to decrease in frequency as treatment is continued, and rarely necessitate treatment withdrawal [6].

Most clinicians already have a good awareness of SSRI's more common side effects such as gastrointestinal disturbances, drowsiness, insomnia, headache, sexual dysfunction, and agitation [5]. However, urinary incontinence does not seem to be among those usually discussed with patients, perhaps due to its paucity in the literature. Here we describe a case of UI with first-time sertraline use and consider its possible biochemical pathways, in the hope of increasing clinicians' awareness and understanding of this side effect.

Case

A 20-year-old woman of Indonesian Chinese descent came to the clinic with mixed symptoms of depression and anxiety, including hypothymic mood, low motivation for work, inability to find pleasure in enjoyable activities, pronounced ideas of guilt, intrusive thoughts to comment on people's appearances, and ritualistic behaviors such as scrubbing her skin repeatedly when showering because she felt "dirty." Her appetite and sleep also decreased. Suicidal ideation was not present. The patient had never taken any psychiatric medications. She was then put on 50 mg of sertraline for 14 days.

On evaluation, she reported feeling better but also described a new onset of an uncontrollable urge to urinate with associated loss of bladder control. It had taken place acutely, only one day after starting sertraline, and lasted for as long as she was taking it. Because of its interference with her daily activities, she had decided on her own to discontinue the medication, and the urinary symptoms quickly resolved.

The patient had no previous history of urinary incontinence. She did not habitually consume caffeine and was not on any diuretic agents. She agreed to switch to fluoxetine 10 mg for one week, which was increased to 20 mg the second week. The patient noted that her urinary problems did not return, and although she felt the therapeutic effects of fluoxetine took more time to appear, she was more comfortable with it, so she continued with fluoxetine at 20 mg, gradually increasing to 40 mg. Treatment was then combined with psychotherapy to further process her excessive guilt.

Discussions

The lower urinary tract (LUT) is composed of two functional units: a reservoir (the bladder) and an outlet (the bladder neck, the urethra, and the urethral sphincter). Complex communication between the central, somatic, and autonomic peripheral nervous systems regulates it. The storage of urine requires the relaxation of the bladder wall, whereas voiding requires a coordinated contraction of the bladder and relaxation of the urethra. Unlike most other visceral functions, micturition is also under voluntary control and is therefore influenced by learned behavior [7]. This can be seen from the fact that micturition is involuntary in infants and toddlers, and after the age of 3 to 5 years old it becomes voluntary.

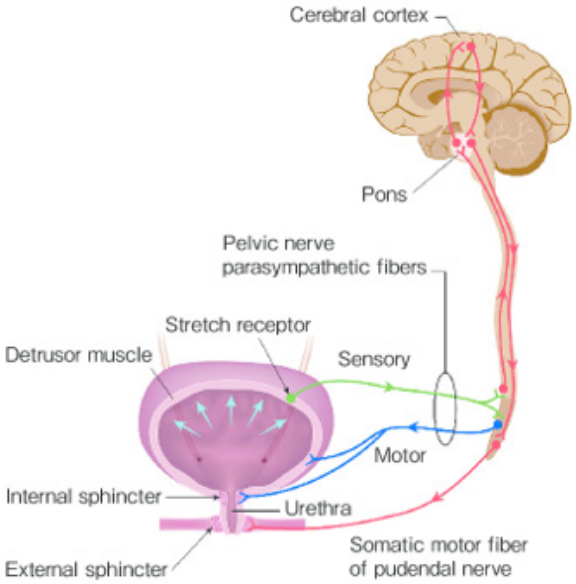

Figure 1. Neural control of micturition

The detrusor smooth muscle is the main muscular component of the bladder wall. This muscle relaxes during filling and contracts during emptying. Mechanoreceptors in the detrusor muscle respond to both passive distension as well as active contraction of the bladder. There are parasympathetic fibers in the pelvic nerve that send pressure signals to the lumbosacral plexus in the spinal cord (Figure 1). The signals then travel to the pontine micturition center and are processed in the cerebral cortex [8].

M3 muscarinic receptors are the principal receptors of the detrusor muscle [7]. The parasympathetic stimulation of M3 muscarinic receptors by acetylcholine (ACh) is involved in the voiding reflex [9], causing contraction of the detrusor muscle and increasing the emptying pressure. 5-HT receptors are found in the afferent terminal in the spinal cord [7], and recently they are also found in the urothelium [10]. However, the exact roles of serotonin seem to vary depending on the receptor subtype, receptor location, and the species of the subject [11]. Activation of the central serotonergic system is generally thought to suppress voiding by inhibiting the parasympathetic excitatory input to the bladder [11]. On the other hand, serotonergic inputs from the raphe nuclei in rats appear to evoke a small but significant contraction of the bladder, therefore promoting bladder emptying [10].

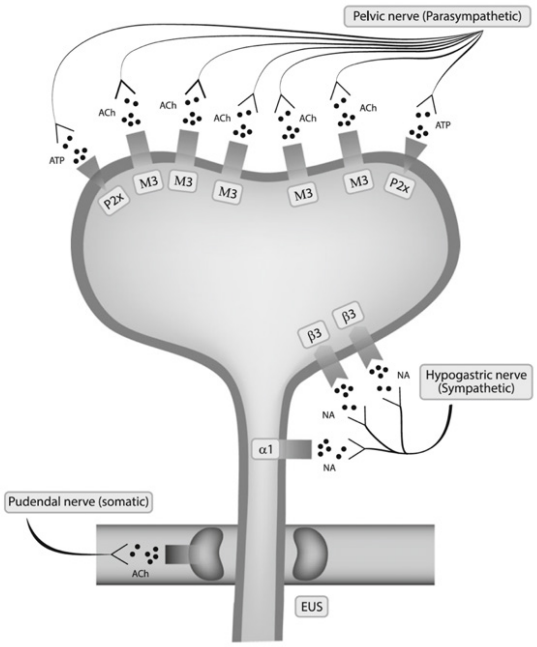

Figure 2. Neurotransmitter mechanisms regulating the urinary bladder and the external urethral sphincter (EUS) function

In addition to afferent sensors, the LUT also receives efferent innervation from the thoracic and lumbosacral plexus. Of interest, α-adrenergic receptors that receive norepinephrine (NE) signaling from the sympathetic hypogastric nerves are found concentrated in the bladder base and proximal urethra (Figure 2) [9, 12]. NE provides an excitatory input to the smooth muscle of the urethra and bladder and an inhibitory input to the smooth muscle in the bladder body [7]. These cause the overall promotion of urinary continence. However, some studies demonstrate that under pathological conditions, the norepinephrine-induced response in the bladder may increase to such an extent that its role in bladder relaxation is shifted to bladder contraction [13].

Sertraline has been reported to cause both sides of urinary problems: retention and

incontinence. At least three case reports have described urinary retention with sertraline [14–16]. Association between urinary incontinence and the use of SSRI, especially sertraline, paroxetine, and citalopram [17, 18], has been noted at a rate of 14 cases per 1000 patients per year [19], though this number is still lower than that of SNRI, especially of venlafaxine [19–22].

Various biological pathways have been proposed to explain incontinence problems with sertraline. Firstly, 5-HT4 receptor activation may potentiate M3 cholinergic neuromuscular transmission in the detrusor muscle [23], increasing the efficiency and frequency of bladder voiding. This excitatory effect is more pronounced at higher concentrations of serotonin [24]. Secondly, compared to other SSRIs, sertraline is a relatively strong inhibitor of the dopamine (DA) reuptake in the central nervous system (CNS) [25]. Therefore, sertraline may act as an indirect DA agonist, which further stimulates urine micturition.

The patient presented in our case experienced an improvement in her UI symptoms after switching to fluoxetine. Among the SSRIs, fluoxetine shows the least specific binding to serotonin transporters (SERT). It has direct 5-HT2C antagonism which functions to inhibit micturition [26]. This particular action also indirectly enhances NE release, contributing to the stimulation of the urethral sphincter tone, and thus improving urinary continence. 5-HT2C antagonism in fluoxetine seems to balance out the voiding reflex stimulation through the increased serotonergic actions on other 5-HT receptors, a unique property that sertraline does not have.

The problem with these explanations is that we do not yet know which actions are greater in a given situation and whether patient characteristics (e.g. age, gender, drug naïvete status, etc.) influence these actions, and if so, by how much. Furthermore, we do not know the pattern of use of sertraline to cause UI. A case series by Chaudhry and Alex [24], report three cases of UI occurring at a dose of 150 mg, 200 mg, and 200 mg respectively. Another report by Pease et al [27]. describes a case in which UI is induced at 300 mg of sertraline. All these patients experience UI a few days into taking the offending dosage and symptoms are relieved when the doses are gradually tapered down. However, the patient in our report already experience UI at a comparatively lower dose. Perhaps UI is an idiosyncratic effect and might be modified by other factors such as patients' ethnicities.

More studies need to be undertaken to complete our gap of knowledge. Meanwhile, clinicians should be cautious about a new onset of urinary problems in patients taking sertraline (or other SSRIs or SNRIs). Urinary complaints are more likely to predict nonadherence to antidepressants [28], so they need to be promptly addressed. Since this adverse event appears to be dose-dependent, lowering the dose or its total discontinuation followed by switching to another drug with better antienuretic effects, in this case fluoxetine, should lead to resolution of the problem.

Conclusions

Sertraline exhibits potent effects on M3 receptors on the detrusor muscle and indirectly acts as a DA agonist, resulting in greater efficiency and frequency of urine voiding. This may, at least partially, explains urinary incontinence with the consumption of sertraline. On the other hand, fluoxetine possesses a couple of antienuretic mechanisms through 5-HT2C antagonism that sertraline does not have. Switching to fluoxetine is a recommended step to reduce urinary side effects and improve patients' adherence and quality of life.

Acknowledgements

Not declared

Fundings

None

Conflict of Interest
The author declares no conflict of interest. There is no special funding for this article.

References

[1] P. Abrams et al., "The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society.," Urology, vol. 61, no. 1, pp. 37–49, Jan. 2003, doi: 10.1016/s0090-4295(02)02243-4.
[2] Tran LN Puckett Y, "Urinary Incontinence," in StatPearls, Treasure Island (FL): StatPearls Publishing, 2023.
[3] F. C. Gabriel, D. O. de Melo, R. Fráguas, N. C. Leite-Santos, R. A. Mantovani da Silva, and E. Ribeiro, "Pharmacological treatment of depression: A systematic review comparing clinical practice guideline recommendations.," PLoS One, vol. 15, no. 4, p. e0231700, 2020, doi: 10.1371/journal.pone.0231700.
[4] A. J. Melaragno, "Pharmacotherapy for Anxiety Disorders: From First-Line Options to Treatment Resistance.," Focus (Am. Psychiatr. Publ)., vol. 19, no. 2, pp. 145–160, Jun. 2021, doi: 10.1176/appi.focus.20200048.
[5] A. N. Edinoff et al., "Selective Serotonin Reuptake Inhibitors and Adverse Effects: A Narrative Review.," Neurol. Int., vol. 13, no. 3, pp. 387–401, Aug. 2021, doi: 10.3390/neurolint13030038.
[6] D. Murdoch, D, McTavish, "Sertraline," Drugs, vol. 44, pp. 604–624, 1992.
[7] W. C. de Groat, D. Griffiths, and N. Yoshimura, "Neural control of the lower urinary tract.," Compr. Physiol., vol. 5, no. 1, pp. 327–396, Jan. 2015, doi: 10.1002/cphy.c130056.
[8] H.-Y. Ko, "Autonomic Dysfunction in Spinal Cord Injuries: Anatomy and Clinical Assessment," 2023, pp. 395–414. doi: 10.1007/978-981-99-4542-9_21.
[9] G. Pelliccioni and P. Pelliccioni, "Neurophysiology and Neurophysiological Evaluation of the Pelvic Floor," 2015, pp. 43–60. doi: 10.1007/978-3-319-06947-0.
[10] N. Konthapakdee et al., "Serotonin exerts a direct modulatory role on bladder afferent firing in mice.," J. Physiol., vol. 597, no. 21, pp. 5247–5264, Nov. 2019, doi: 10.1113/JP278751.
[11] C. M. Morrison JF, Birder L, "Neural control," in Incontinence. 6th ed, W. A. Abrams P, Cardozo L, Wagg A, Ed. Bristol, UK: ICI-ICS International Continence Society, 2017, pp. 262–359.
[12] K.-E. Andersson and A. Arner, "Urinary bladder contraction and relaxation: physiology and pathophysiology.," Physiol. Rev., vol. 84, no. 3, pp. 935–986, Jul. 2004, doi: 10.1152/physrev.00038.2003.
[13] N. Yoshimura and M. B. Chancellor, "Neurophysiology of lower urinary tract function and dysfunction.," Rev. Urol., vol. 5 Suppl 8, no. Suppl 8, pp. S3–S10, 2003.
[14] L. Lowenstein, E. R. Mueller, S. Sharma, and M. P. FitzGerald, "Urinary hesitancy and retention during treatment with sertraline.," Int. Urogynecol. J. Pelvic Floor Dysfunct., vol. 18, no. 7, pp. 827–829, Jul. 2007, doi: 10.1007/s00192-006-0241-4.
[15] T. W, "Urinary retention, the sometimes-neglected medication side effect," J Pall Care, vol. 18, no. 8, pp. 187–188, 2013.
[16] N. A. Uvais and T. P. Mohammed, "Sertraline -Associated Acute Urinary Retention in a Patient with Benign Prostatic Hyperplasia," J. Integr. Nephrol. Androl., vol. 6, pp. 6–7, 2021, doi: 10.4103/jina.jina_16_18.
[17] M. Ibrahim Ramadan, A. Y. Khan, and W. E. Weston, "Response to SSRI-induced enuresis: a case report.," Journal of clinical psychopharmacology, vol. 26, no. 1. United States, pp. 98–99, Feb. 2006. doi: 10.1097/01.jcp.0000195912.51988.cf.
[18] F. Toros and K. Erdoğan, "Paroxetine-induced enuresis.," European psychiatry : the journal of the Association of European Psychiatrists, vol. 18, no. 1. England, pp. 43–44, Feb. 2003. doi: 10.1016/s0924-9338(02)00010-x.
[19] V. Solmaz et al., "Evaluation of Overactive Bladder in Male Antidepressant Users: A Prospective Study.," Int. Neurourol.

J., vol. 21, no. 1, pp. 62–67, Mar. 2017, doi: 10.5213/inj.1732652.326.
[20] G. Polimeni et al., "Venlafaxine-induced urinary incontinence resolved after switching to sertraline.," Clin. Neuropharmacol., vol. 28, no. 5, pp. 247–248, 2005, doi: 10.1097/01.wnf.0000188205.25750.2d.
[21] L. K. Hansen, "Venlafaxine-induced increase in urinary frequency in 3 women.," The Journal of clinical psychiatry, vol. 65, no. 6. United States, pp. 877–878, Jun. 2004. doi: 10.4088/jcp.v65n0622a.
[22] N. A. Votolato, S. Stern, and R. M. Caputo, "Serotonergic antidepressants and urinary incontinence.," Int. Urogynecol. J. Pelvic Floor Dysfunct., vol. 11, no. 6, pp. 386–388, Dec. 2000, doi: 10.1007/s001920070009.
[23] K. L. L. Movig, H. G. M. Leufkens, S. V Belitser, A. W. Lenderink, and A. C. G. Egberts, "Selective serotonin reuptake inhibitor-induced urinary incontinence.," Pharmacoepidemiol. Drug Saf., vol. 11, no. 4, pp. 271–279, Jun. 2002, doi: 10.1002/pds.705.
[24] S. Chaudhry and N. Alex, "Case series suggesting an association between sertraline and urinary side effects in a Sheffield child and adolescent mental health services (CAMHS) population," BJPsych Open, vol. 7, pp. S242–S242, 2021, doi: 10.1192/bjo.2021.646.
[25] C. Damsa et al., "'Dopamine-dependent' side effects of selective serotonin reuptake inhibitors: a clinical review.," J. Clin. Psychiatry, vol. 65, no. 8, pp. 1064–1068, Aug. 2004, doi: 10.4088/jcp.v65n0806.
[26] Y. Mbaki, J. Gardiner, G. McMurray, and A. G. Ramage, "5-HT 2A receptor activation of the external urethral sphincter and 5-HT 2C receptor inhibition of micturition: a study based on pharmacokinetics in the anaesthetized female rat.," Eur. J. Pharmacol., vol. 682, no. 1–3, pp. 142–152, May 2012, doi: 10.1016/j.ejphar.2012.02.010.
[27] E. Pease, B. Singh, M. Ziegelmann, and H. Betcher, "Dose-Dependent Urinary Incontinence with Sertraline Use in Obsessive-Compulsive Disorder.," Psychopharmacol. Bull., vol. 51, no. 4, pp. 117–121, Nov. 2021.
[28] R. Uher et al., "Adverse reactions to antidepressants," Br. J. Psychiatry, vol. 195, pp. 202–210, 2009, doi: 10.1192/bjp.bp.108.061960.