Selective Serotonin Reuptake Inhibitor–Related Tardy Sexual Dysfunction

To the Editor: International, multicenter studies[1,2] have shown that 27%–65% of female and 26%–57% of male patients with depression undergoing treatment with selective serotonin reuptake inhibitors (SSRIs)/serotonin-norepinephrine reuptake inhibitors self-report either worsening of preexisting difficulties or emergence of new sexual difficulties in early weeks of treatment, especially anorgasmia (and hence the use of SSRIs for premature ejaculation). Substantial intragroup differences were shown (eg, in the SSRI group), and sexual dysfunction was much less common with fluvoxamine or escitalopram versus paroxetine.[1] Purported dynamic mechanisms involved in SSRI-related sexual dysfunction include a facilitated serotonin neurotransmission by SSRI antidepressants ([5-hydroxytryptamine [5-HT]$_{2A/2c}$ agonism]) in lateral hypothalamus and nucleus paragigantocellularis. Genetic factors (eg, 5-HT receptor polymorphism) might influence individual vulnerability to SSRI-related sexual dysfunction.[3]

SSRI-related sexual dysfunction tends to persist as long as the medication is being continued but occasionally even after phasing out of treatment. Although the latter remains underrecognized and poorly defined, 2 syndromes have been reported in the literature, namely, post-SSRI sexual dysfunction (akin to post-finasteride syndrome) and persistent genital arousal disorder, that merit a brief description.

Post-SSRI Sexual Dysfunction

Post-SSRI sexual dysfunction can manifest as genital anesthesia, pleasureless/weak orgasms, diminished sexual drive, erectile dysfunction, or premature ejaculation in males and decreased vaginal lubrication and nipple sensitivity in females. Postulated mechanisms might include epigenetic gene expression, persistent 5-HT$_{1A}$ downregulation, neurohormonal changes, serotonin toxicity, or altered ion channel transduction.[4] Although the evidence base remains flimsy, serotonergic antagonists, dopaminomimetics, and low-power laser irradiation (for penile anesthesia) have been trialed for this syndrome.

Persistent Genital Arousal Syndrome

Persistent genital arousal syndrome has been described chiefly in females. It is characterized by spontaneous and often unrelenting subjective sexual arousal in the absence of sexual desire/stimulation. This is in sharp contradistinction to compulsive sexual behavior, as these patients do not reveal heightened desire or failure to suppress sexual urges. Those afflicted tend to complain of genital throbbing, contractions, spontaneous vaginal/clitoral pain, and pain on penetration. Triggers can include physical stimulation, stress/anxiety, sitting, tight clothing, vibrating vehicles, and horse riding. Relieving factors include distraction, onanism, intercourse, and cold compresses. Although mood/anxiety, pudendal neuropathy, arteriovenous malformations, Tarlov cysts, and dietary habits (eg, soy products) were all incriminated, SSRI withdrawal has also been tied to persistent genital arousal syndrome.[5] Purported mechanisms include rebound anxiety, increased atrial natriuretic peptide, genital vasodilatation, or merely alleviated psychotropic-related sexual dysfunction. For SSRI-related syndrome, successful treatment with quetiapine and varenicline has been reported.

Conclusion

These syndromes remain ill-defined, with no current general consensus on epidemiology, diagnostic criteria, or treatment guidelines. However, it would be imperative for clinicians to be vigilant in including these syndromes in the working differential for psychotropic-related sexual dysfunction in psychiatric patients.

References

1. Rothmore J. Antidepressant-induced sexual dysfunction. *Med J Aust*. 2020;212(7):329–334.
2. Naguy A. Psychotropic-related sexual dysfunction: clinical insights. *Prim Care Companion CNS Disord*. 2023;25(6):23lr03609.
3. Jing E, Straw-Wilson K. Sexual dysfunction in selective serotonin reuptake inhibitors (SSRIs) and potential solutions: a narrative literature review. *Ment Health Clin*. 2016;6(4):191–196.
4. Peleg LC, Rabinovitch D, Lavie Y, et al. Post-SSRI sexual dysfunction (PSSD): biological plausibility, symptoms, diagnosis, and presumed risk factors. *Sex Med Rev*. 2022;10(1):91–98.
5. de Magalhães FJC, Kumar MT. Persistent genital arousal disorder following selective serotonin reuptake inhibitor cessation. *J Clin Psychopharmacol*. 2015;35(3):352–354.

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