SEXUAL MEDICINE REVIEWS

Sexual Consequences of Post-SSRI Syndrome

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ABSTRACT

Introduction: Sexual dysfunctions are well-known side effects of selective serotonin reuptake inhibitor (SSRI) use. Altered libido, erectile dysfunction, vaginal dryness, ejaculatory disorders, and orgasmic problems are frequently reported by patients treated with SSRIs. Moreover, these antidepressant-emergent sexual dysfunctions do not always resolve after discontinuation of the medication and can persist indefinitely. These complaints are termed post-SSRI sexual dysfunctions (PSSD).

Aim: To examine the existence of this clinical entity, possible theoretical mechanisms, possible risk factors, and possible treatment modalities.

Methods: Through literature research and clinical experience, the available information about PSSD is reviewed.

Main Outcome Measures: Summary of the current literature with insights into possible causes and management options.

Results: There are some indications that antidepressant-emergent sexual dysfunctions do not always resolve after discontinuation of the medication and can persist indefinitely in some individuals. Although some or all sexual side effects that start with the use of SSRIs might continue after stopping the medication, other sexual complaints can develop. Decreased capacity to experience sexual pleasure is the most frequent characteristic of this syndrome.

Conclusion: The research and understanding of PSSD remain limited and not well understood; however, the data support the existence of PSSD, which can have a substantial effect on the quality of life of these patients. More research is warranted to show the cause and possible mechanisms of PSSD that could lead to the correct diagnosis and treatment. **Reisman Y. Sexual Consequences of Post-SSRI Syndrome. Sex Med Rev 2017;X:XXX–XXX.**

Key Words: Selective Serotonin Reuptake Inhibitors; Sexual Dysfunctions; Depression; Post-SSRI Sexual Dysfunction

INTRODUCTION

The indications for the prescription of selective serotonin reuptake inhibitors (SSRIs) are depressive disorder, obsessive-compulsive disorder, panic disorder, anxiety disorder, and post-traumatic stress disorder.[1] SSRIs also are used as off-label treatment for premature ejaculation.[2] Reports have stated that up to 7% of the US population are using SSRIs, which is the third prescribed medication in the United States.[3] In some countries in Europe, estimations are that 3% of the population are using SSRIs.[4,5]

Sexual dysfunctions are well-known side effects of SSRI use.[6] Among these are altered libido, erectile dysfunction, vaginal dryness, ejaculatory disorders, and orgasmic problems such as delayed orgasm or anorgasmia and decreased pleasure during orgasm.[7–9] Some have reported the presence of genital anesthesia[6] and one report has suggested a persistent genital arousal syndrome.[10] An animal model of antidepressant-induced sexual dysfunction also has been described.[11] Initial SSRI registration studies found that such side effects were reported by fewer than 10% of patients. When doctors specifically asked about treatment-emergent sexual difficulties, some found that they were present in up to 70% of patients.[6–9,12,13] It should be mentioned that depression also can cause sexual dysfunctions. The prevalence of decreased desire and arousal has been reported in more than 50% of patients with depression.[14] The mechanism of action is most probably through direct and indirect effects on various neurotransmitters such as serotonin, dopamine, and norepinephrine.[14]

Sexual problems, sleeping problems, and weight gain are often cited as reasons for discontinuation of medication and some believe these effects are a major factor of failed treatment for depression.[15–17] These side effects can decrease or persist during

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the course of the treatment. They usually endure for as long as the medication is taken, but generally the presumption is that the side effects resolve after discontinuation of treatment.[14] However, the research literature does not include systematic follow-up in support of this presumption and there are no definite studies on whether and to what level sexual function recovers in patients who used SSRIs.

There are some indications that for some individuals the antidepressant-emergent sexual dysfunctions do not always resolve after discontinuation of the medication and can persist indefinitely.[18] Although some or all sexual side effects that start with the use of SSRIs might continue after stopping the medication, other sexual complaints can develop. Among these are decreased genital sensitivity, decreased intensity of orgasm, and a profoundly decreased physical capacity to experience sexual pleasure. These complaints are termed post-SSRI sexual dysfunctions (PSSD).[18–23]

In this article the available literature about PSSD is summarized with the aim of examining the existence of this clinical entity, possible theoretical mechanisms, possible risk factors, and possible treatment modalities.

CLINICAL EVIDENCE FROM THE LITERATURE

The issue of persistent sexual side effects after discontinuation of SSRIs was first introduced into the medical literature in 2006 by Bahrick[18] who used the acronym PSSD after people reported PSSD on the online support community, SSRIsex. In this publication, Bahrick highlighted the typical dysfunctions often captured as side effects but raised the concern about symptoms that differed from typical sexual dysfunctions, such as genital anesthesia and non-pleasurable orgasm. The study is based on data from non-scientific consumer groups and the indications for SSRI use were not clear, but it did explore information about the issue that was not available elsewhere at that time.

In the same year, two other publications of four case reports appeared. Bolton et al[19] described a man with genital anesthesia, loss of libido, and anorgasmia that persisted for 6 years after the use of sertraline. Csoka and Shipko[20] reported on three cases (two men and one woman) with loss of libido, genital anesthesia, and arousal disorder after the discontinuation of different SSRIs. In 2007, Kauffman and Murdock[21] described a 32-year-old woman with genital anesthesia and orgasmic dysfunction after the use of citalopram. A year later, Csoka et al[22] reported on three patients with the persistent sexual dysfunctions described earlier from three different SSRIs. Most of these patients used the medication because of depression, and one used it for anxiety disorder.

In 2012, the Dutch Pharmacovigilance Center published a report on 19 possible cases and emphasized the need for further investigation on this subject; indications for the use of the SSRI were not reported.[23] Stinson[24] preformed a psychological study of nine patients with PSSD, which showed a negative effect on quality of life. The indications for the prescription of SSRI were depression in four cases, post-traumatic stress syndrome in two, obsessive-compulsive disorder in one, and not reported in two. Stinson emphasized that patients often felt ignored, uncared for, and disregarded by health care professionals. Through internet portal data, Hogan et al[25] reported on 90 cases of PSSD from 22 countries. Their data showed comparable symptoms as those in previous reports. In their series, one patient had PSSD for 18 years after a brief use of fluoxetine.

In 2015, Waldinger et al[26] described a case study of a patient with PSSD consisting of orgasmic dysfunction, erectile dysfunction, and penile anesthesia after use of an SSRI for depression, which was treated, with partial success, with low-power laser irradiation. In the same year, Ben-Sheetrit et al[27] reported on 23 high probability cases selected from 532 subjects who completed an online survey with the aim of exploring possible explanations and exposure-response relations. All subjects were younger than 50 years, did not have confounding conditions, medications, or drug use, and had normal scores on anxiety and depression scales. The indications for the use of SSRIs were not reported. They found that genital anesthesia did not correlate with depression or anxiety but did correlate with the severity of sexual dysfunctions. Genital anesthesia and non-pleasurable orgasm were predictors of depression and the probability of PSDD. They concluded that their findings supported the existence of PSSD but were not explained by factors related to depression and anxiety. Surprisingly, no new publication concerning PSSD has appeared on PubMed since June 2015.

The SSRIs most often associated with PSSD were citalopram, fluoxetine, fluvoxamine, escitalopram, sertraline, paroxetine, and venlafaxine. The latencies ranged from days to years and the duration of treatment with SSRIs varied from a few weeks to a few years. Characteristics of the PSSD cases are presented in Table 1.

POSSIBLE EXPLANATIONS FOR PSSD

Sexual response is dependent on an interaction between the brain and the genitals; however, the exact mechanisms that explain how SSRI medications affect the brain and cause problems in the genitals are unknown. Moreover, it is not known what causes the sexual side effects of SSRI to persist so long after stopping the medication. Various hypotheses have been proposed, including biochemical and neurochemical changes and epigenetic gene expression alterations that probably do not normalize in some SSRI users.

Serotonin receptors are involved in the negative feedback regulation of the hypothalamic-pituitary-testicular axis. Serotonin is involved in different phases of the sexual response cycle mainly as an inhibitor and can be involved in some sexual dysfunctions, such as loss of desire, delayed ejaculation, anejaculation, or absent or delayed orgasm.[28] It is plausible that