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Post-SSRI Sexual Dysfunction (PSSD) Ten Year Retrospective Review

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INTRODUCTION

- Use of SSRI/SNRI antidepressants for various conditions is very common.
- Sexual dysfunction due to an SSRI/SNRI, while on an SSRI/SNRI, is a common and well-known side effect (can be up to 70%). Generally, it was thought that this side effect resolves upon discontinuation of the SSRI/SNRI.
- Reports emerged in 2006 of sexual dysfunction that ***persisted*** upon discontinuation of SSRI/SNRI. This sexual dysfunction was termed Post-SSRI Sexual Dysfunction (PSSD). Prevalence of this is unknown.
- Persistent sexual dysfunction was referenced on the product label of the SSRI fluoxetine in 2011. Reference to sexual dysfunction persisting upon SSRI discontinuation was referred to in the DSM-5 (2013, page 449), the most well-known source of psychiatric diagnoses. Notable review articles include Reisman (2017) and Hellstrom et al. (2017). In 2019, the EMA (European Medicines Agency; European equivalent of FDA) recommended that SSRI/SNRI labels now include information about persistent sexual dysfunction upon discontinuation.
- Commonly have ED, hypoactive sexual desire disorder (HSDD), orgasmic dysfunction, and/or genital anesthesia.
- Precise etiopathogenesis unknown, but changes in serotonin regulation are suspected; epigenetic changes have been proposed to explain persistence.
- Notably, no known treatment currently exists for this condition.
- Many prior studies have consisted of online questionnaires, not in-office visits in a clinic.
- Aim: We wished to better understand PSSD, the frequency/severity of symptoms, and the results of diagnostic testing.

METHODS

- Retrospective chart review was performed; charts from 2009 to 2019 were reviewed
- History was reviewed for each patient's account of their symptoms
- International Index of Erectile Function (IIEF), a validated and frequently used questionnaire for sexual dysfunction, was completed by all patients
- Diagnostic testing included:

(a) Grayscale/Doppler Ultrasound during pharmacological erection (15.4 MHz probe; Aixplorer®Ultrasound) to look for cross-sectional inhomogeneity (hypo- and hyperechoic regions)

(b) Quantitative Sensory Testing (QST): measures vibration/cold/heat perception threshold values in the glans penis, R/L proximal, mid-shaft, distal aspects of the penile shaft, and R/L scrotum, using R pulp index finger threshold values as control

- Patients completed the Sexual Distress Scale-Revised (SDS-R), a validated questionnaire for distress from sexual dysfunction
- Inclusion criteria:

(a) Required to have had at least one in-person patient visit at San Diego Sexual Medicine (SDSM)

(b) Initial contact with SDSM prior to 12/31/19

(c) Male with age ≥ 18 years at time of initial contact

(d) History consistent with PSSD (had normal sexual function, took SSRI/SNRI, had sexual dysfunction after discontinuation of SSRI/SNRI)

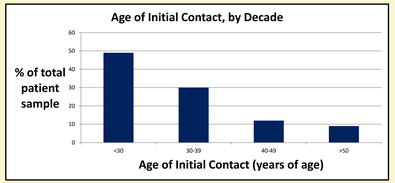
(f) Completed IIEF

- 43 patients qualified under these inclusion criteria

RESULTS

A) AGE OF INITIAL CONTACT: Age of Initial Contact as defined as age when patient first contacts SDSM (not age of initial sexual dysfunction)

Age of Initial Contact [n=43]	
Mean: 33yo	Standard Deviation: 10 years
Median: 30yo	Range (19yo-60yo)



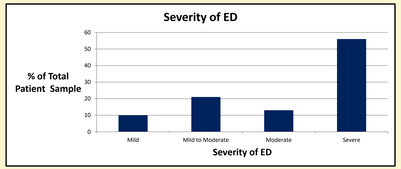
Note: 79% are under age of 40

B) INTERNATIONAL INDEX OF ERECTILE FUNCTION (IIEF):

IIEF Results (n=43)	
Erectile Function Domain	**IIEF Score (score 1 to 30)**
Mean	**12.6**
Median	**9**
Sexual Desire Domain	**IIEF Score (score 2 to 10)**
Mean	**4.3**
Median	4
Orgasmic Function Domain	**IIEF Domain Score (score 1 to 10)**
Mean	**6.3**
Median	6
Intercourse Satisfaction Domain	**IIEF Domain Score (score 0 to 15)**
Mean	**4.9**
Median	4
Overall Satisfaction Domain	**IIEF Domain Score (score 2 to 10)**
Mean	**3.1**
Median	2
IIEF Total Score	**IIEF Total Score (score 6 to 75)**
Mean	**31.2**
Median	30

IIEF EF Domain (Score 1 to 30) Analysis Using Severity Scale	
% of Patients (n=43) with ED (Score <26)	**91%** (39/43)
ED Severity in those with ED (n=39)	Percentages
Mild (Score 22-25)	*10% (4/39)*
Mild to Moderate (Score 17-21)	*21% (8/39)*
Moderate (Score 11-16)	*13% (5/39)*
Severe (Score <11)	***56% (22/39)***

Note: Severity rating used is from Rosen et al. (1999)



C) GENITAL ANESTHESIA: In review of patients' histories, many patients complained of genital anesthesia (often described as loss of erogenous sensation). See table.

Genital Anesthesia (n=43)
31 said yes, 1 said no, 11 did not refer to the issue of genital anesthesia
72% (31/43) of total sample have it
97% (31/32) of those who referred to the issue have it

D) DIAGNOSTIC TESTING

i) ULTRASOUND: Some ED patients had a grayscale/Doppler ultrasound (n=24). See table for inhomogeneity results.

Note: Mean Cavernosal Artery Peak Systolic Velocity values were left 33.1 cm/sec and right 31.2 cm/sec. Mean Cavernosal Artery Peak Diastolic Velocity values were left 1.2 cm/sec and right 1.0 cm/sec.

Grayscale/Doppler Ultrasound	
% with Inhomogeneity (of patients with ED who had an ultrasound)	**92% (22/24)**
Mild inhomogeneity (>0% but <25% cross-sectional area)	23% (5/22)
Moderate inhomogeneity (>25% but < 50% cross-sectional area)	68% (15/22)
Severe inhomogeneity (>50% cross-sectional area)	9% (2/22)

ii) QUANTITATIVE SENSORY TESTING (QST): Some patients with genital anesthesia underwent QST (n=24). See table.

Quantitative Sensory Testing (QST)	
% of Abnormal QST Results from Patients with Genital Anesthesia who Underwent QST	**88% (21/24)**

E) SEXUAL DISTRESS SCALE-REVISED (SDS-R): Scale measuring distress from sexual dysfunction (Score 0 to 52; higher the score, higher the distress). See table.

Sexual Distress Scale-Revised (SDS-R, score 0-52) [n=43]	
Mean(±SD) for PSSD Sample	**35.7±9**
Mean(±SD) of Generic Sexually Dysfunctional Male	26.2±11
Mean(±SD) of Generic Sexually Functional Male	13.9±11

Note: Data for generic sexually dysfunctional and generic sexually functional male from study by Santos-Iglesias (2018)

DISCUSSION

- This series of patients examined clinically (i.e. in-office visit as opposed to online questionnaire) is largest in known peer-reviewed literature for PSSD
- Consistent with previous studies, patients are young (mean: 33yo; 79% under age 40)
- Consistent with other reports on PSSD, patients have ED, hypoactive sexual desire disorder, orgasmic dysfunction, and genital anesthesia. Both IIEF and history supported this finding
- Orgasmic Function domain in IIEF might not capture true prevalence of orgasmic function (patients often talked about 'pleasureless orgasm' in the history, which is not specifically asked about in the IIEF)
- Genital anesthesia might be underestimated since it may not have always been explicitly asked about
- Combination and/or severity of symptoms leads to overall reduced intercourse satisfaction and reduced overall satisfaction, as evidenced by low IIEF scores for those domains
- This sexual dysfunction is very distressful for patients (as evidenced by SDS-R results). Potential adverse effects on a patient's relationships and qualify of life should be considered when treating these patients
- This study further shows that:

1) ED is most often severe (56% had severe ED)
2) Erectile tissue inhomogeneity is common, consistent with erectile tissue fibrosis/decreased erectile tissue expandability as an underlying vascular ED pathophysiology
3) QST is an example of a neurogenital test that can demonstrate how neurological dysfunction in PSSD relates to decreased genital sensation

- Future directions for PSSD research:

1) Develop a PSSD-specific questionnaire that precisely capture all symptoms of PSSD (orgasms that are pleasureless, reduced erogenous sensation in the genitalia, etc.)
2) Further examine use of diagnostic testing (ultrasound, neurogenital tests like QST) to help elucidate PSSD symptoms
3) Further study of the pathophysiology of PSSD (e.g. potential peripheral effects like penile fibrosis and central effects like neurotransmitter changes due to the SSRI/SNRI)
4) Analyze efficacy of potential treatments that could be symptomatic or disease-modifying (e.g. CNS agents) based on our understanding of the pathophysiology

CONCLUSIONS

1) Providers need to be aware that persistent sexual health consequences following SSRI/SNRI discontinuation exist and are significant
2) Providers should assess sexual function prior to, during, and after SSRI/SNRI use
3) **Most importantly, providers should inform patients of PSSD before they are prescribed an SSRI/SNRI**
4) Patients should be referred to sexual medicine specialists for management if they develop PSSD
5) PSSD is an iatrogenic condition that is multidimensional (i.e. more than just ED), is serious in severity, occurs in young people, and is distressing

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