Psychotropic-induced sexual dysfunction

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ABSTRACT

Psychotropic-induced sexual dysfunction is a common and bothersome side effect of psychotropic medications. The majority of information available on the subject primarily pertains to antidepressants, but antipsychotics can also cause significant sexual dysfunction. The mechanisms behind these adverse events are thought to be primarily due to antidepressants' effects on serotonin and to antipsychotics' anti-dopaminergic activity. Sexual dysfunction can have many causes, not just psychotropic medication, therefore this article aims to examine the etiology of sexual dysfunction, as well as discuss differential diagnoses. Treatment for psychotropic-induced sexual dysfunction will be discussed, with more data available for the treatment of antidepressant-induced sexual dysfunction. The paucity of data for antipsychotic-induced sexual dysfunction does make it more difficult to treat.

KEYWORDS

Psychotropics, sexual dysfunction, antidepressants, antipsychotics

INTRODUCTION

Psychotropic-induced sexual dysfunction is widely recognized as a potential side effect of the use of antidepressant and antipsychotic medications in the treatment of psychiatric disorders. Monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), typical and atypical antipsychotic medications, and novel antidepressant medications have all had reported cases of sexual dysfunction as a side effect of treatment. Despite increasing awareness of this problem, it is still difficult to quantify the incidence of these treatment complications since many psychiatric disorders themselves may have profound effects on relationships and consequently sexual function.[1-5] Treatment of sexual dysfunction in these patients may be further confounded if a patient's baseline sexual function is not assessed prior to medication therapy, its etiology is unclear, or their psychiatric disorder is otherwise being managed well by the psychotropic medication. This becomes a significant issue in patient care because psychotropic-induced sexual dysfunction is a common reason for poor treatment adherence.[6-10]

ETIOLOGY OF SEXUAL DYSFUNCTION

Sexual dysfunctions include a wide range of disorders that result in a clinically significant disturbance in either a person's ability to respond to sexual stimulus, or to experience sexual pleasure.[11] These dysfunctions may present as several different disorders and commonly involve a reduction in libido, diminished physical arousal, a decline in the frequency of intercourse, or a delay or inability to achieve orgasm, (Table 1). General medical illness, psychosocial factors, psychiatric disorders, and medications (psychotropic and non-psychotropic) can all contribute to sexual dysfunction and it is not uncommon for patients to present with multiple risk factors.[12,13] These dysfunctions can frequently result in altered interpersonal relationships, or partially be the result of a disturbed relationship. Therefore, a thorough work up is necessary, and subsequent treatment or therapy may be most successful if done in collaboration with a patient's partner, if possible and appropriate given a patient's circumstances.

Determining the incidence of sexual dysfunction and psychotropic-induced sexual dysfunction is difficult due to the variety of methods utilized to assess patients, the population of patients studied, the types of dysfunctions being assessed and the patients' perceptions of their sexual performance and their willingness to discuss these perceptions. Sexual dysfunction has been shown to be highly prevalent in men and women in the general population[3,4,14,15] and in patients receiving psychotropic medications.[8,9,16-19] In general, sexual dysfunction appears

Table 1. Common Causes of Sexual Dysfunction

Medical Causes		Psychotropic Medication Causes	Psychosocial Causes
Coronary artery disease		SSRIs	Relationship issues
Peripheral vascular disease		MAOIs	Stress, anger, frustration
Diabetes mellitus		TCAs	Abuse
Obesity		SNRIs	Depression, anxiety
Hormonal disorders		Antipsychotics	Lifestyle factors (e.g. career, children)
Neurologic conditions		Novel antidepressants	Sexual practices (e.g. habits, experience)
Arthritis			
Sexually transmitted diseases			
Medication			
Drug Abuse			
Men	**Women**		
Pelvic or prostate surgery	Urogenital atrophy		
Epididymitis	Dyspareunia		
Prostatitis	Vaginismus		
Trauma	Pelvic muscle disease		
	Menopause		
	Hysterectomy		
	Urinary incontinence		
	Pregnancy & post-partum period		
	Urinary tract infection		

to be more prevalent in women than men and is associated with other factors including age, poor health and lifestyle, low education attainment, social status, emotional problems or stress, and prior sexual trauma. It is also clearly apparent in the epidemiological data that patients will underreport sexual dysfunction if they are required to spontaneously report it to their clinician. Study participants have been shown to be 2 to 6 fold more likely to report sexual dysfunction if directly questioned compared to spontaneously reporting.[20,21] Therefore, the use of a validated direct assessment method should be utilized to evaluate sexual function before and during psychotropic medication use, especially when these medications are utilized for the treatment of psychiatric illnesses such as depression and anxiety that may increase a patient's risk of having or developing sexual dysfunction.

Commonly used assessment tools in clinical practice (Table 2) in the United States and Europe include the Arizona Sexual Experience Scale (ASEX), the Changes in Sexual Functioning Questionaire (CSFQ), and the Sex Effects Scale (SexFX).[22-24] Also, the Derogatis Interview for Sexual Functioning (DISF, DISF-SR) and the Female Sexual Function Index (FSFI) are two sexual function scales used extensively in clinical trials.[25,26] The Psychotropic-Related Sexual Dysfunction Questionaire (PRSexDQ) has also been utilized in different samples of depressed and schizophrenic patients on psychotropic medication.[16,27] PRSexDQ addresses changes in sexual dysfunction since the beginning of drug treatment, the types of problems experienced, and the tolerability of those changes.

PHYSIOLOGY OF SEXUAL DYSFUNCTION

Several physiologic mechanisms and pathways have been implicated in sexual dysfunction. The predominant neurotransmitters include the serotonergic, dopaminergic, and cholinergic systems; the predominant hormones include estrogen, progesterone, oxytocin, and testosterone.[28-31] Other mechanisms, such as the production of nitric oxide, have also been implicated and offer other possible explanations for sexual dysfunction in patients.[32] Because many psychotropic medications involve these pathways, it is common for these medications to be implicated in patients diagnosed with sexual dysfunction.

Male libido is mediated by normal androgen concentrations, testosterone being the primary male androgen. It has been proposed that several psychotropic drugs (especially dopamine antagonists) can indirectly suppress libido secondary to increasing serum prolactin concentrations which may result in decreased testicular androgen production.[33] Despite testosterone having a known role in male libido, it cannot always offer a solution to impaired libido. For instance, giving elderly male patients excessive doses of testosterone to achieve supraphysiologic concentrations has not been shown to increase libido.[34]

Serotonin generally has an inhibitory effect on sexual function. It is hypothesized to modify dopamine levels in the brain and affect the nerves and smooth muscles of the vascular system of the sexual organs.[28] Therefore, serotonin chiefly impacts sexual arousal and orgasm, which explains why psychotropic medications which act primarily by increasing serotonin transmission are implicated in a variety of sexual dysfunctions involving decreased desire, decreased arousal (e.g. erectile dysfunction), and impaired ejaculation or orgasm.[28-30]

DIFFERENTIAL DIAGNOSIS

Since sexual function is a complex process that encompasses interpersonal relationships, attitudes,

Table 2. Commonly Used Sexual Functioning Scales

Rating Scale Name	Number of Items	Administration time/ modality	Domains measured	Comments
DISF/DISF-SR	25 (26 for self-report)	15-20 minutes each; interview and self-rated	Sexual cognition and fantasy arousal, sexual behavior and experience, orgasm, sexual drive and relationship	Gold standard for clinical trials; used in males and females
FSFI	19	10-15 minutes; self-rated	Desire, arousal, lubrication, orgasm, satisfaction, pain	Only for females; also a gold standard in clinical trials
ASFS	5	5 minutes; can be self-rated or clinician interview	Sex drive, arousal, vaginal lubrication/penile erection, ability to reach orgasm, and satisfaction from orgasm	Developed to assess sexual function in psychiatric patients; quick and simple to use
CSFQ	35 (36 for males)	15-20 minutes; clinician-rated	Sexual pleasure, desire/frequency, desire/interest, arousal, and orgasm	Designed to measure illness- and medication-related changes in sexual functioning; validated with DISF-SR
SexFX	13	5-10 minutes; clinician-rated	Sexual desire, arousal, orgasm, and frequency	Designed to assess treatment-emergent sexual dysfunction in depression
PRSexDQ	5	5 minutes; clinician-rated	Sexual desire, delay in orgasm, anorgasmia, vaginal lubrication/erection, impact of dysfunction in sexual relations	Shown valid psychometric properties in depression and schizophrenia; brief questionnaire

psychiatric wellness, health and functioning of neurologic, vascular, and endocrine systems, and may be altered with age, health status, personal experience and medication use – diagnosing and treating sexual dysfunction and drug induced sexual dysfunction can be a formidable task. The diagnosis requires the provider to obtain a detailed patient history to assist in defining the specific sexual dysfunction type (e.g. libido, arousal, orgasm), while also identifying other possible causative medical or psychosocial conditions. The onset, duration, and situational versus global symptoms for a patient's sexual dysfunction should also be determined. Questioning the patient about what they think may be causing the problem may also provide additional insight. The PLISSIT (Permission, Limited Information, Specific Suggestions, Intensive Therapy) and ALLOW (Ask, Legitimize, Limitations, Open Up, Work Together) are two strategies for facilitating discussion about sexual dysfunction and its management.[35,36] Identifying the presence of more than one dysfunction may also aid in determining possible treatments as certain patient factors may be dependent on one another (Table 1).[12,13,37]

Psychotropic-induced sexual dysfunction is common for patients to experience. It is important when addressing sexual dysfunction that may be associated with a psychotropic medication to assess symptoms since the beginning of treatment, the types of problems experienced and the tolerability of these changes. A patient's baseline sexual function should therefore be assessed prior to the initiation of antidepressant and antipsychotic medications both to determine the presence of sexual dysfunction prior to therapy initiation and to assess a patient's risk for the development of sexual dysfunction with psychotropic drug therapy.

ANTIDEPRESSANTS

Due to serotonin's larger role in sexual dysfunction, drugs that increase serotonin activity may be more likely to cause sexual dysfunction. These include TCAs, MAOIs, and SSRIs. In contrast, drugs like bupropion and mirtazapine appear to have a lower incidence of sexual dysfunction.[38,39] The prevalence of antidepressant-induced sexual dysfunction varies widely depending on several factors, such as, the type of sexual dysfunction being reported (e.g. decreased libido, anorgasmia, erectile dysfunction, etc.), the method of collecting information from the patient (self-report vs questionnaire vs direct questioning), and the patient population being studied. Prevalence ranges from as low as 2% to as high as 71% with SSRIs.[40] It is not clear if one particular SSRI has lower rates of sexual dysfunction than another.

There are several strategies which can be employed to treat antidepressant-induced sexual dysfunction. One option is to wait for the development of tolerance to this side effect. An exact incidence of tolerance has not been established, but there is evidence to suggest that it may be related to a response in psychiatric symptoms.[28,41] The

patient's sexual dysfunction may improve as his or her depression or anxiety improves.

Drug holidays have been recommended in the past, but without much data to support their use.[42] Drug holidays involve brief interruptions in drug treatment, perhaps during the weekends. This practice could potentially put the patient at risk for withdrawal symptoms during the holiday period, as well as a relapse of their psychiatric condition.

In men, evidence supports the use of the phosphodiesterase-5 inhibitors (PDE-5I) sildenafil and tadalafil. Results showed patients with antidepressant-induced erectile dysfunction had a similar response to patients suffering from erectile dysfunction from other etiologies.[43,44] Doses used in these studies ranged from 25-100 mg for sildenafil and 10-20 mg for tadalafil.

There is some evidence to support to the use of either bupropion or mirtazapine as augmenting agents to SSRI treatment.[45-47] However, these results have either not been consistently replicated or the studies are of a weak methodology. This practice of augmenting agents, may also put the patient at higher risk of side effects.[47] Treatment should be tailored to fit patients' needs. Augmentation may be an option in patients whose psychiatric symptoms are well-controlled on a SSRI, but are experiencing significant sexual side effects.

Data for the treatment of antidepressant-induced sexual dysfunction in women are lacking. Considering that the prevalence may actually be higher in women, more studies are definitely needed.[40] There are a few case reports showing positive evidence for the PDE5-I, however evidence is limited.[48] Augmentation strategies with bupropion and mirtazapine have also been studied in women and have shown some improvement in sexual dysfunction, but again the data are limited.[45-47,49]

Overall, due to the limited amount of data for the treatment of antidepressant-induced sexual dysfunction, a definitive recommendation cannot be made. Patient education about sexual side effects is important since this will give the patient some control over their treatment. The PDE-5I may provide some symptomatic relief of erectile dysfunction, however patients will continue to experience sexual dysfunction from their medication, and it may not be ideal for them to take a PDE-5I consistently. It may be reasonable to switch to a different antidepressant, even within same class, to alleviate sexual dysfunction. However, the patient's psychiatric condition should be evaluated before making a change to their antidepressant. The use of bupropion or mirtazapine as monotherapy is also an option, as they have a lower incidence of sexual dysfunction.[38,39]

ANTIPSYCHOTICS

Sexual dysfunction is a problem that is not often mentioned when discussing antipsychotics. However, given their mechanism of action of dopamine blockade and increasing prolactin, sexual dysfunction is a common problem. One survey found that 43% of 202 patients reported sexual dysfunction from their antipsychotic medication.[50] Hyperprolactinemia can result in loss of sexual desire in both men and women, as well as erectile dysfunction. It is unclear if one antipsychotic may cause more sexual dysfunction than another, but some data suggest that drugs that cause more hyperprolactinemia are more likely to cause sexual dysfunction.[31]

There is, unfortunately, insufficient evidence to recommend any drug treatment for antipsychotic-induced sexual dysfunction. If the side effect is of significant bother to the patient, it may be prudent to decrease the dose or try an alternative medication.

CONCLUSION

Psychotropic-induced sexual dysfunction is a common side effect. Patients should be assessed for severity of symptoms before and after initiation of psychotropic medications. Unfortunately, evidence is lacking on how to best treat this side effect. The PDE-5Is have the best available evidence to treat men suffering from antidepressant-induced erectile dysfunction, however, there is limited evidence for their use in women. Switching to a different antidepressant or decreasing the dose of an antipsychotic may alleviate this side effect.

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