Psychotropic-Related Sexual Dysfunction: Clinical Insights

Letter to the Editor:
Psychopharmacotherapy remains the mainstay of treatment for severe psychopathology. Nonetheless, this approach is plagued with a panoply of somatic adverse effects including sexual dysfunction. The latter is commonly underreported and overlooked but is considered a major reason for medication nonadherence and consequently treatment failure (which can masquerade as pseudoresistance).[1] It behooves clinicians to be cognizant of psychotropic-related sexual dysfunction and avidly screen for it during routine follow-up clinic visits.

Psychotropic-related sexual dysfunction can be immediate or delayed. It tends to persist as long as the medication is being continued and occasionally even after phasing out treatment (eg, post–selective serotonin reuptake inhibitor [SSRI] sexual dysfunction).

Purported dynamic mechanisms involved in psychotropic-related sexual dysfunction include both direct/indirect and specific/nonspecific actions. Direct mechanisms involve dopamine inhibition by antipsychotics (D_2 blockade) in the mesolimbic area (related to hedonism) and medial preoptic area (related to consummatory responses) or facilitated serotonin neurotransmission by SSRI antidepressants (5-$HT_{2A/2c}$ agonism) in the lateral hypothalamus and nucleus paragigantocellularis. Genetic factors, eg, dopamine and 5-HT receptor polymorphism, might influence individual vulnerability to psychotropic-related sexual dysfunction. Hyperprolactinemia (eg, via antipsychotic dopaminergic blockade in the tuberoinfundibular pathway) is also linked to sexual dysfunction.[2] Psychotropic agents with anticholinergic actions are associated with reduced peripheral vasodilation and subsequent impairment in genital vascular response and erectile dysfunction. On the other hand, indirect mechanisms such as extrapyramidal syndromes/tardive dyskinesia and anticholinergic side effects (eg, dry mouth) might complicate intimate kissing for instance. Adrenolytic and antihistaminic actions can cause sedation and nonspecific listlessness, interfering with sexuality. Resultant metabolic syndrome[3] (class effect for most atypical antipsychotics) is a major vascular risk factor for erectile dysfunction, and on a psychological level, obesity-related poor self-image and self-esteem can negatively impact intimacy.

International, multicenter studies[4] have shown that 27%–65% of female and 26%–57% of male patients with depression undergoing treatment with 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 (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. Antidepressants with different mechanisms (eg, dopaminergic partial agonists, serotonergic partial antagonists, melatonergic agonists) are tied to fewer sexual side effects. Preferred agents are agomelatine, bupropion, mirtazapine, nefazodone/trazodone, selegiline, vilazodone, and vortioxetine.[5]

Moreover, it is estimated that sexual dysfunction affects 38%–86% of patients on antipsychotics. Preferred agents are prolactin-sparing antipsychotics including aripiprazole, quetiapine, lurasidone, and ziprasidone.[6] Preferred mood stabilizers are lamotrigine and lithium.[7]

Questionnaires (eg, Psychotropic-Related Sexual Dysfunction Questionnaire[8]) can be helpful assessment tools in clinical settings. It is advisable to maintain a broad differential when assessing psychiatric patients for sexual dysfunction. Sexual dysfunction can be part of psychopathology (eg, sexual anhedonia in major depressive disorder).[9,10] Furthermore, it could be part of the sociocultural burden of mental illness (eg, stigma and rejection, poor self-esteem). Substance use, vascular causes, other medications, relationship difficulties, and performance anxiety need to be ruled out/in prior to considering psychotropic-related sexual dysfunction.

Generally, management of psychotropic-related sexual dysfunction includes dose adjustment or drug holidays (which is not always feasible and can be complicated with relapse/withdrawal symptoms), switching to other agents with a better profile (which can compromise therapeutic response), and other medication adjuventia "antidotes" (eg, cyproheptadine,[11] yohimbine, bupropion, mirtazapine,[12] gingko biloba, PDE-5 inhibitors such as sildenafil, low-dose aripiprazole).

Marital therapy, "changing sexual scripts," sexual enhancement products, healthy diet, and physical exercise can improve sexual satisfaction.

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