The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided. The patient described in this column is a composite with characteristics of several real patients.

Management strategies for SSRI-induced sexual dysfunction

A 45-year old woman with major depressive disorder (MDD) and comorbid generalized anxiety disorder (GAD) reported a decrease in libido since her last depressive episode about 3 years ago. Despite being in remission for the last year and taking a 60 mg dose of paroxetine, she reported an overall decrease in sexual interest and activity.

Sexual dysfunction occurs through several brain pathways involving increases in serotonin (5-HT), decreases in dopamine (DA) and inhibition of nitric oxide synthase.[1] Increases in corticolimbic 5-HT result in decreased sexual desire, ejaculation and orgasm.[2] Consequently, it is not surprising that selective serotonin reuptake inhibitor (SSRI)-induced sexual dysfunction occurs in 30%–80% of patients[3,4] and is a main cause of treatment discontinuation.[5,6] Therefore, it is important to use strategies to alleviate treatment-emergent sexual dysfunction.

The key to addressing sexual impairment is to systematically assess the domains of sexual function. There are several validated sexual side effect scales available to clinicians.[7–9] The patient we describe received a score of 5 of 44 on the Sex Effects Scale[9] (SexFX; a high score is good), as paroxetine is known for its adverse effects on sexual function (Box 1). Pharmacologic methods to reduce sexual dysfunction involve dose reduction, augmentation, or switching medication. Since dose reduction is the least disruptive strategy it should be considered first, particularly in a responder. When our patient's dose was reduced to 40 mg, she remained in remission with reduced but persisting sexual dysfunction, particularly anorgasmia.

Box 1: Frequency of sexual dysfunction with antidepressant treatment*

< 10%	10%–30%	> 30%
Agomelatine	Citalopram	Fluoxetine
Bupropion	Duloxetine	Fluvoxamine
Mirtazapine	Escitalopram	Paroxetine
Moclobemide	Venlafaxine	Sertraline
Reboxetine	Milnacipran	

*Modified with permission.[10]

Altering 5-HT receptor antagonism and agonism can have favourable sexual effects, but may cause other adverse events. Mirtazapine antagonizes 5-HT2 and 5-HT3 receptors and it has been successfully used as an add-on therapy for antidepressant-induced sexual dysfunction, albeit with a relatively high rate of weight gain.[11,12] In addition, cyproheptidine, a 5-HT2A antagonist, has been found to relieve SSRI-induced anorgasmia,[13,14] but its use is limited by sedation. Buspirone, a 5-HT1A agonist, may also alleviate SSRI-induced sexual dysfunction.[15] Our patient was started on a 15 mg dose of mirtazapine, but it was discontinued owing to daytime sedation.

Sildenafil and tadalafil are phosphodiesterase inhibitors that increase nitric oxide, which in turn, helps to increase blood flow to genetalia. They have both demonstrated evidence for the reversal of SSRI-induced sexual side effects in men.[16–19] There is only preliminary evidence that these drugs improve sexual adverse events in women,[20,21] and neither was prescribed to our patient.

Evidence also suggests that DA release enhances sexual function.[1] The strongest evidence supports 150–300 mg of adjunctive bupropion XL for reversing SSRI-induced sexual dysfunction in men and women across the domains of desire, arousal and orgasm.[22,23] These benefits occur irrespective of the SSRI used or duration of sexual dysfunction.[24] There is also evidence to support drugs that have more pronounced effects on DA, including methylphenidate, dextroamphetamine, pramipexole or ropinerole.[25–27] However, caution should be exercised when using DA agonists, given reports of hypersexuality associated with pramipexole.[28] Our patient's regimen was augmented with 150 mg/day of bupropion XL, taken in the morning. She reported improved arousal and lubrication after 6 weeks, and her overall SexFX score improved to 13 (moderate impairment).

Several antidepressants, including bupropion, moclobemide, mirtazapine, agomelatine and vilazodone,[3,29] have little to no effect on sexual function compared with placebo when used as a monotherapy. Our patient's paroxetine was discontinued and the bupropion was increased to 150 mg twice daily. This switch resulted in a return to normal sexual function (SexFX 29) over the course of 4 weeks. At 3 months, she was still in remission.

For patients reluctant to add another medication to their regimen, nonpharmacotherapeutic options may be useful. Evidence suggests exercise can improve sexual function. A trial involving women treated with SSRIs found that exercise before viewing sexual stimuli significantly increased arousal.[30] Open-label trials have suggested yoga improves sexual function.[31,32] There is little support for neutraceuticals alleviating SSRI-induced sexual dysfunction.[33–35]

In summary, pharmacologic methods have the strongest support in alleviating SSRI-induced sexual dysfunction. Of the augmentation strategies, bupropion has the most support in terms of efficacy and tolerability. There are several possible treatment strategies: reduce antidepressant dose, augment with an antidote, or switch medication. However, it is better to take the importance of sexual side effects into consideration when prescribing an initial antidepressant. It is also important to query sexual adverse events specifically to ensure that

Psychopharmacology for the Clinician columns are usually based on a case report that illustrates a point of interest in clinical psychopharmacology. They are about 650 words long.

side effects are mitigated and to avoid treatment discontinuation.

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