For those patients who did well on nefazodone, its withdrawal presents a treatment challenge, as its mechanism of action was quite novel. Nefazodone exerted its antidepressant action by blocking 5-HT2A, 5-HT2C and 5-HT3 postsynaptic receptors and through a modest inhibitory effect on reuptake of serotonin. Because of its unique postsynaptic blockade, it caused no significant sexual dysfunction and improved sleep architecture.

A relatively new antidepressant, mirtazapine, has postsynaptic activity overlapping that of nefazodone. Mirtazapine blocks 5-HT2 and 5-HT3 receptors; thus it improves sleep and does not cause sexual dysfunction. It is a logical alternative to nefazodone. The patient could be started on a dosage of 15 mg daily, which could be increased to 30 mg daily within a week and further increased to 60 mg daily, depending on response and watching for weight gain and excess sedation.

An alternative approach would be to replace nefazodone with a selective serotonin reuptake inhibitor (SSRI) or serotonin norepinephrine reuptake inhibitor (SNRI) (venlafaxine) and a low dosage of trazodone (25 to 100 mg) as a hypnotic. Trazodone blocks postsynaptic 5-HT2A and 5-HT2C receptors and mildly inhibits serotonin reuptake. It thus helps with sleep and may in some cases reverse SSRI-induced sexual dysfunction. Trazodone should not be used as a monotherapy for depression.

A further alternative would be to use an SSRI or SNRI and a low dosage (0.25 to 2.0 mg daily) of risperidone, which blocks postsynaptic 5-HT2A receptors and can improve slow wave sleep. Open trials also report a robust antidepressant effect when risperidone is added to SSRIs. (Controlled trials report a similar effect with olanzapine augmentation; however, concerns about weight gain with this patient would make olanzapine a second choice.)

If nefazodone was chosen because of SSRI-induced sexual dysfunction, it could be replaced with an SSRI combined with bupropion 100 to 300 mg daily. Bupropion is the best-studied agent for reversing SSRI-induced sexual dysfunction and improves sexual function for most patients. There is also randomized controlled trial evidence for the use of sildenafil in such patients. The advantage of using bupropion is that its noradrenergic function can also produce a robust antidepressant augmentation as well as a reversal of SSRI-induced sexual dysfunction.

The decision as to which of these options to pursue depends on the basis for choosing nefazodone and the patient’s key depressive symptoms. However, with attentive pharmacology, there is reasonable hope that this patient will maintain her recovery.

Suggested Reading


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