Venlafaxine discontinuation syndrome: Prevention and management

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Most antidepressants lead to adverse discontinuation symptoms when they are abruptly stopped or rapidly tapered. Antidepressants with a short half-life, such as paroxetine and venlafaxine, can cause significantly more severe discontinuation symptoms compared with antidepressants with a longer half-life.

One culprit in particular

Among serotonin-norepinephrine reuptake inhibitors (SNRIs), venlafaxine is notorious for severe discontinuation symptoms. Venlafaxine has a half-life of 3 to 7 hours, and its active metabolite, desvenlafaxine, possesses a half-life of 9 to 13 hours. Higher frequency of discontinuation symptoms is associated with the use of higher dosages of venlafaxine and longer duration of treatment.

Venlafaxine is available in immediate release (IR) and extended release (XR) formulations. Venlafaxine XR has a slower release, extending the time to peak plasma concentration and, therefore, has once daily dosing and fewer side effects; however, it offers no substantial advantage over IR formulation in terms of diminished withdrawal effects. Desvenlafaxine also is marketed as an antidepressant and, although one can speculate that the drug would have a lower rate of discontinuation symptoms than venlafaxine, no evidence supports this hypothesis.

A range of venlafaxine discontinuation symptoms have been reported (***Table***).[1]

Preventing discontinuation symptoms

Patients for whom venlafaxine is prescribed should be informed about discontinuation symptoms, especially those who have a history of noncompliance. Monitor patients closely for discontinuation symptoms when venlafaxine is stopped—even if the patient is switched to another antidepressant. A gradual dosage reduction is recommended rather than abrupt termination or rapid dosage reduction. Immediately switching from venlafaxine to a selective serotonin reuptake inhibitor (SSRI) generally is not recommended, although it could alleviate some discontinuation symptoms[2]; cross-taper medication over 2 to 3 weeks.

Switching from venlafaxine to another SNRI, such as duloxetine, is less well studied. At venlafaxine dosages of <150 mg/d, an immediate switch to another SNRI of equivalent dosage generally is well-tolerated. For higher dosages, a gradual cross-taper is advised.[2]

Most patients tolerate a venlafaxine dosage reduction by 75 mg/d, at 1-week intervals. For patients who experience severe discontinuation symptoms with a minor dosage reduction, venlafaxine can be tapered over 10 months with approximately 1% dosage reduction every 3 days. Stahl[3] recommends dissolving the tablet in 100 mL of juice, discarding 1 mL, and

Table

Symptoms of venlafaxine discontinuation syndrome[a]

Psychological
Agitation
Anorexia
Anxiety
Confusion
Dysphoric mood
Hypomania
Insomnia
Nightmares
Neurologic
Dizziness and vertigo
Fasciculation
Fatigue, headache
Impaired coordination and balance
Paraesthesias and sensory disturbances
Somnolence
Tremor
Physical
Dry mouth
Flu-like symptoms
Nausea
Vomiting and diarrhea

[a]Not an exhaustive list
Source: Reference 1

drinking the rest. After 3 days, 2 mL can be discarded, etc.

Another strategy to prevent discontinuation syndrome is to initiate fluoxetine—an SSRI with a long half-life—before taper; maintain fluoxetine dosage while venlafaxine is tapered; and then taper fluoxetine.

Managing discontinuation symptoms

If your patient experiences significant discontinuation symptoms, resume the last prescribed venlafaxine dosage, with a plan for a more gradual taper. Acute discontinuation syndrome also can be treated by initiating fluoxetine, 10 to 20 mg/d; after symptoms resolve, fluoxetine can be tapered over 2 to 3 weeks.

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References

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