

Severe Venlafaxine Withdrawal Successfully Treated With a Short Course of Duloxetine

To the Editor: Venlafaxine is a serotonin- norepinephrine reuptake inhibitor (SNRI) with well-documented safety and efficacy in the treatment of major depressive disorder and anxiety disorders and is commonly used for treatment of hormonal hot flashes and chronic pain. Discontinuation of the medication may be required for a variety of reasons. Withdrawal symptoms are a well-known consequence of abrupt cessation from shorter-acting antidepressant medications, requiring gradual tapering in many cases to avoid them. While typically mild, withdrawal symptoms in some patients can be disabling and may make tapering and cessation extremely difficult. Venlafaxine is arguably the most common cause of severe withdrawal symptoms among modern antidepressants even when tapered.^{1,2} Whether patients suffer significant withdrawal from venlafaxine seems to be independent of dosage,³ indication for use, length of treatment,⁴ or taper duration.⁵ The most frequently reported adverse symptoms of tapering or stopping venlafaxine are nausea, vertigo, irritability, and lethargy,⁶⁻⁸ though more distressing symptoms have been reported, including visual disturbances,⁹ unpleasant physical sensations,^{10,11} motor and coordination problems,^{3,12} cataplexy,^{13,14} delirium,¹⁵ mania,¹⁶⁻¹⁸ and psychosis.¹⁹ Aside from causing significant distress, these symptoms may be mistaken for other illnesses, lead to unnecessary tests and treatment, and potentially force patients to continue a medication that could otherwise have been discontinued.

Duloxetine is a medication with similar pharmacodynamics to venlafaxine but lower selectivity for serotonin.²⁰ Data comparing patient tolerance of venlafaxine and duloxetine in terms of side effects during a full course of treatment are somewhat contradictory, but during withdrawal of the medication, significantly fewer duloxetine-treated patients report substantial adverse effects,^{21,22} most likely due to the lower serotonin activity.²⁰ Use of this similarly acting but more easily discontinued medication is a potential mechanism for treatment of venlafaxine withdrawal.

Case report. Ms A is a 43-year-old woman with chronic cervicgia and lumbago who was started on extended-release venlafaxine by her primary care manager in the summer of 2014 as an adjunct to pain medication. Venlafaxine was titrated upward to 75 mg daily and taken for a 2-month period. After 2 months, Ms A attempted to discontinue the medication on her own because of a low perceived benefit but was unable to continue more than 48 hours without taking it due to severe nausea, vertigo, and irritability. The symptoms consistently resolved upon restarting the medication and were attributed to venlafaxine withdrawal. Gradual attempts were made by the patient and her primary care manager to taper her off the medication over the next 4 months, but she was unable to reduce the dosage below 37.5 mg every 48 hours due to intolerable withdrawal symptoms. One attempt at stopping venlafaxine during this period led to chest pain, nausea, and diaphoresis that required hospital admission to rule out acute coronary syndrome; these symptoms resolved after restarting the medication. While cardiac side effects have been identified in connection with several antidepressant medications, this patient was found to have no cardiac abnormality, and her symptoms were attributed to withdrawal. It was then decided to switch from venlafaxine to duloxetine because it has a milder withdrawal profile. At 48 hours from her last dose of venlafaxine, Ms A began

taking duloxetine 30 mg daily and immediately reported a 50% decrease in her typical withdrawal symptoms of nausea, vertigo, and irritability. After 1 week of duloxetine 30 mg daily, the patient stopped duloxetine entirely, estimating her severity of withdrawal symptoms to be 25% of those from venlafaxine. Neither SNRI was restarted, and the symptoms attributed to withdrawal did not return.

Venlafaxine has shown significant benefit for the treatment of depression and anxiety and is increasingly used for other indications. Withdrawal from venlafaxine can be problematic, with symptom severity occasionally preventing cessation of the medication even when a prolonged taper is used. A potential option for treatment of venlafaxine withdrawal when further dosage tapering is not tolerated is to conclude treatment with a 1-week course of low-dose duloxetine. Given duloxetine is itself relatively short-acting, a reasonable alternative to this specific medication would be prescription for several days of a longer-acting selective serotonin reuptake inhibitor, which will provide a more gradual lowering of serotonin activity with no further titration.

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