

VENLAFAXINE INDUCED DELIRIUM IN A WITHDRAWAL SYNDROME

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Abstract: *Venlafaxine is a dual antidepressant very popular in the treatment of major depression and anxiety disorders. There are many side effects of venlafaxine data but very little about the effect of abrupt discontinuation of treatment.*

We present a case of 34 years male patient diagnosed Major Depression Disorder who developed delirium after abrupt stopping treatment with venlafaxine XR. The patient was treated with venlafaxine XR 150mg/day over 3 months for depressive symptoms that were added delusions of death and marked anxiety. 12 hours after abrupt discontinuation of venlafaxine XR he began to be agitated, disorientated, with visual hallucinations, tachycardia and sweating. After 72 hours of treatment the patient's condition has improved significantly with remission of symptoms of delirium. The venlafaxine withdrawal syndrome diagnosis was established after evaluation of all parameters, including brain CT and laboratory blood tests.

Despite its therapeutic effects, venlafaxine should be prescribed with care when lower dose is needed or treatment has to be stopped due to any reasons in order to prevent withdrawal syndrome.

Key words: *venlafaxine, withdrawal, major depression.*

1. Introduction

The treatment of mood disorders has been an active field of research for over 50 years. Many compounds with the promise to alleviate depression have been discovered and handfuls have been tested. Venlafaxine XR is a wide used dual-action serotonin-norepinephrine reuptake inhibitor antidepressant from and may be associated with a discontinuation syndrome. There are many side effects of venlafaxine XR data but very little about

the effect of abrupt discontinuation of treatment. It acts as a serotonin reuptake inhibitor at doses below 150 mg and as a dual-action antidepressant from 150 to 300 mg, while at higher doses it acts on the dopamine and neurotransmitter systems.

Efficacy, safety, and tolerability of venlafaxine XR has been established for depression (Smith et al 2002), generalized anxiety disorder (Gelenberg et al 2000), and social anxiety disorder (Allgulander et al 2001).

In the vast majority of controlled trials the side-effects reported were: insomnia,

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constipation, dry mouth, anorexia, sweating, ejaculation or orgasm problems, somnolence, palpitations, vasodilatation, hypertension, nausea, (Khandker et al 2005, Bradwejn et al 2002, Katz et al 2002).

As with TCAs, MAOIs, and SSRIs, discontinuation symptoms have been reported with venlafaxine XR (Pinzani et al 2000, Reeves et al 2003). Venlafaxine XR discontinuation symptoms have been clinically reported as soon as 6 hours and as long as 9 days after discontinuation of the drug, but typically emerge in 1–4 days.

Due to short half-life of venlafaxine and its active metabolite, O-desmethylvenlafaxine, (5 ± 2 and 11 ± 2 hours) treatment raise a significant risk of developing a severe withdrawal syndrome. Despite the controversies regarding the withdrawal syndrome development the mechanism may include the effects on 5-HT receptors which is potential similar with the mechanism involved in withdrawal syndrome associated with SSRIs.

Venlafaxine withdrawal symptoms may include somatic symptoms such as elevated blood pressure, headache, nausea, sweating and restlessness. Psychiatric symptoms were usually represented by agitation, visual and auditory hallucinations, delirium, impaired concentration, recurrence of depression. There are a few articles regarding the withdrawal syndrome after discontinuation of venlafaxine and most recommendations are based on personal experience of experts (Haddad 2001, Schatzberg et al 2006).

2. Case Report

We present a case of a male patient of 34 years, diagnosed with major depressive disorder for over 10 years and hospitalized for relapse who developed delirium after abrupt discontinuation of venlafaxine XR.

The first psychiatric hospitalization of the patient was in 2000 for symptoms of major depression (depressive mood, tension, nervousness, insomnia, anhedonia, loss of appetite). He complained of apathy, loss of energy and initiative and the treatment with several antidepressants did not have the expected effects (sertraline, paroxetine, mirtazapine, escitalopram, imipramine). Antidepressants were combined with anxiolytics (alprazolam, lorazepam), hypnotics (zolpidem, zopiclone) and mood stabilizers (sodium valproate). The augmentation with low doses of antipsychotic (amisulpride, quetiapine) remained without major effects.

In the last 3 months the patient was treated with venlafaxine 150 mg/day for depressive symptoms without improving but with worsening of clinical condition.

The day before hospitalization the patient stopped treatment with venlafaxine XR. After 12 hours he developed symptoms of delirium with psychomotor agitation, confusion, visual hallucinations, tachycardia, sweating. The treatment consisted of administration of lorazepam 3 mg/day, zopiclone 7.5 mg/day, sodium valproate 1000 mg/day, 5% glucose infusion 1000 ml/day, monitoring of vital signs in intensive care department. After 72 hours the patient's condition improved significantly with remission of symptoms of delirium.

The venlafaxine withdrawal syndrome diagnosis was established after evaluation of all parameters, including brain CT and laboratory blood tests that were normal. Only the blood pressure and pulse values were out of range. Symptoms appeared within 12 hours upon drug cessation, which was probably caused by the short half-life of venlafaxine. Symptoms of withdrawal were severe enough and the patient needed treatment in intensive care unit. The status of patient was improved 72

hours after abrupt discontinuation of venlafaxine. The patient continued treatment in hospital with another antidepressant combined with a second generation antipsychotics (quetiapine). He was discharged improved after 21 days of hospitalization.

3. Discussion

Venlafaxine has been linked to delirium in few cases in context of serotonin syndrome or hyponatraemia after initiation of treatment or after rising doses. Extremely rare was reported regarding delirium through withdrawal. Withdrawal syndrome may occur after stopping or rapid tapering of venlafaxine treatment even it is intentional or accidental.

It is not possible to determine which patients are likely to develop the most severe symptoms of the discontinuation syndrome before cessation or dose reduction is attempted. This risk requires that all patients be monitored during any increase of dose when the patient present the risk of developing serotonin toxicity and dose should be increased with precaution.

Patients who restart venlafaxine or a higher dosage following a failed attempt to discontinue the drug are in great risk of developing serotonin toxicity (Dunkley et al 2003).

Our case is one of the few reported worldwide. The withdrawal symptoms after abrupt discontinuation of venlafaxine XR at a daily dose of 150 mg at his own discretion 12 hours before hospitalization and he developed symptoms of delirium.

This case has shown that it is important to know that withdrawal syndrome symptoms can develop after rapid discontinuation of venlafaxine.

Symptoms may range from mild to severe. This experience will help to avoid

similar events or to recognize the symptoms of venlafaxine withdrawal.

4. Conclusion

Despite its therapeutic effects, venlafaxine should be prescribed with care when lower dose is needed or treatment has to be stopped due to any reasons in order to prevent withdrawal syndrome. Patients and physicians should be informed of this potential side effects occurrence because popularity of venlafaxine and the wide spread availability in treatment of anxiety or depression are increasing. The symptoms that can result from venlafaxine reduction or discontinuation should be prevented by strict dosage discipline and adequate warnings.

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