

Venlafaxine-Induced Restless Legs Syndrome

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ABSTRACT

Venlafaxine-induced restless legs syndrome

Restless legs syndrome is a movement disorder characterized by complaints of a strong urge to move the legs predominantly during the periods of rest or inactivity. It is observed as a side effect related to the administration of antidepressants in 9% of patients.

A case reporting restless legs syndrome symptoms associated with venlafaxine 75 mg/day is described. The patient was a 44-year-old woman affected by chronic migraine headaches with depressive symptoms. Her symptoms had began during a course of venlafaxine and resolved with its discontinuation.

Based on this report, venlafaxine should be added to the list of agents that can induce restless legs syndrome.

Key words: Antidepressants, restless legs syndrome, venlafaxine, serotonin-norepinephrine reuptake inhibitors

ÖZET

Venlafaksinin neden olduğu huzursuz bacak sendromu

Huzursuz bacak sendromu; dinlenme veya hareketsizlik dönemlerinde daha belirgin olarak ortaya çıkan, bacakları hareket ettirme yönünde güçlü bir ihtiyaç ile karakterize hareket bozukluğudur. Huzursuz bacak sendromu, antidepresan kullanan hastaların %9'unda ilaç kullanımıyla ilişkili bir yan etki olarak kaydedilmiştir.

Depresif semptomları da olan 44 yaşındaki kronik migrenli bir kadın hastada, 75 mg/gün venlafaksin kullanımı ile ortaya çıkan bir huzursuz bacak sendromu tablosu sunulmaktadır.

Semptomlar venlafaksin ile başlamış ve ilacın kesilmesi ile düzelmiştir. Bu vaka temelinde, venlafaksinin huzursuz bacak sendromuna neden olabilecek ilaçlar listesine eklenmesi gerektiği düşünülmektedir.

Anahtar kelimeler: Antidepresanlar, huzursuz bacak sendromu, venlafaksin, serotonin-norepinefrin geri alım inhibitörleri

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Date of receipt:
January 4, 2011

Date of acceptance:
January 27, 2012

INTRODUCTION

Restless legs syndrome (RLS) is a sensorimotor phenomenon characterized by distressing sensations deep inside the limbs and motor restlessness, typically occurring during the periods of rest or inactivity and at bed time. Symptoms lead to an irresistible urge to move the limbs which provide temporary relief (1).

The etiology varies from an idiopathic form, genetic or unknown origin to other symptomatic forms associated with many causes.

Several medications may induce or exacerbate RLS such as antiemetics, antipsychotics, antihistamines, some antiepileptics or certain antidepressant drugs including tricyclic antidepressants (TCAs), the selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) (2).

A RLS case whose symptoms were induced by venlafaxine is reported.

CASE REPORT

A 44-year-old woman affected by chronic migraine headaches with depressive symptoms started to take venlafaxine as a prophylactic treatment. It was started at a dosage of 37.5 mg/day, which was titrated up to 75 mg/day. Within three days of starting 75 mg/day dose, she began to complain of unpleasant sensations in her legs during the night or bedtime which was relieved by movement, at the expense of sleep and quality of life. She denied occurrence of any similar symptoms in the past and had no family history of RLS.

General and neurological examinations were normal. International Restless Leg Syndrome Study Group (IRLSSG) rating scale score was 32 and these symptoms were considered as severe RLS.

All clinical evaluations for secondary causes of RLS including blood count, measurement of iron, iron stores, BUN, creatinine, thyroid and liver functions, glucose, magnesium were unremarkable. Ferritin level

was normal (76 ng/ml). She had no history of excessive alcohol, caffeine or tobacco use. Also peripheral neurography excluded neuropathy.

According to the Naranjo adverse drug reaction probability scale which assesses the probability of drug-induced adverse event, her score was 9. It indicated definite or highly probable adverse drug reaction. Consequently, we decided that one of the SNRIs, venlafaxine had a potential role on provoking of RLS symptoms in this case.

Reducing the dose to 37.5 mg/day resulted in slight improvement of RLS symptoms but not completely. Within four days of warranting the discontinuation of venlafaxine therapy, her RLS symptoms entirely improved. Two weeks later, she could sleep better and did not feel unpleasant sensations in her legs any more.

DISCUSSION

Although the central dopaminergic system seems to be implicated in the development of the symptoms of RLS, its pathophysiology is still unknown (3).

Sleep medicine textbooks and review articles on RLS regularly cite antidepressants such as TCAs, SSRIs and SNRIs as known causes of the emergence or worsening of RLS symptoms but the evidence consists only of some case reports (4).

Although serotonergically mediated dopaminergic inhibition has been demonstrated, the exact mechanism of venlafaxine-induced RLS is not fully enlightened.

Venlafaxine is a structurally novel phenylethylamine antidepressant with a dual mechanism of action which acts as both a serotonin and a norepinephrine reuptake

inhibitor. It probably acts as an SSRI at low doses (5). In the present case, venlafaxine was used at a dose of 75 mg/day which makes it possible to act as an SSRI.

In the study of Rottach et al. (6), RLS was a common side effect during the usage of mirtazapine (28%). Both in the group of pure SSRIs (citalopram, escitalopram, sertraline, paroxetine and fluoxetine) and in the group of SNRIs (duloxetine and venlafaxine), the average frequency of drug-induced RLS was just below 5%. By contrast, no case occurred during the use of reboxetine which is a norepinephrine reuptake inhibitor. Another result of this study is that drug-induced RLS usually occurs within the first days of treatment as it was in our case.

In the present case, we could not manage to relieve RLS symptoms by reducing the dose so it was discontinued. If RLS discomfort is intolerable in case of drug discontinuance, other possible approaches that demonstrated efficacy in treating RLS may be suitable like a dopaminergic treatment such as levodopa or benzodiazepines, opiates, gabapentin and possibly bupropion (7).

In conclusion, this case describes a rare but important side effect associated with venlafaxine. Based on this report and additional data published with other antidepressants, we would like to emphasize that clinicians should be aware of the potential for venlafaxine for RLS symptoms. Moreover, this finding needs to be confirmed by well-designed epidemiologic or randomized prospective studies in future.

Acknowledgements

No supporting grants and conflicting interests exist.

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