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Duloxetine and Venlafaxine Induced Akathisia: Two Case Reports

Filiz Izci[1], Selma Bozkurt Zincir[1], Guler Acar[1], Umit Basar Semiz[2]

ÖZET:

Duloksetin ve venlafaksin ile indüklenmiş akatizi: iki olgu sunumu

Akatizi, huzursuzluk ve rahatsızlık hissi veren hareketlerle karakterize istemsiz bir hareket bozukluğudur. İlaçların indüklediği akatizi daha sıklıkla antidopaminerjik antipsikotiklerle görülmekle birlikte, antipsikotik dışında olan bazı ilaçlarla da akatizi gözlenebilmektedir. Akatizinin akut, geç, kronik ve yoksunluk şeklinde alt tipleri vardır. Bu yazıda sırasıyla depresif bozukluk tanısı ile venlafaksin ve yaygın anksiyete bozukluğu tanısı ile duloksetin tedavisi alan iki olguda ortaya çıkan akut akatizi tablosu sunulmuştur.

Anahtar sözcükler: akatizi, venlafaksin, duloksetin

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ABSTRACT:

Duloxetine and venlafaxine induced akathisia: two case reports

Akathisia is a movement disorder characterized by involuntary movements resulting in discomfort and restlessness. Drug-induced akathisia is often seen with antidopaminergic antipsychotics but sometimes can be seen with other drugs. The four subtypes of akathisia are: acute, chronic, tardive and deprivation. In this paper, we discuss two discrete patients, who were given venlafaxine and duloxetine for treatment of depressive disorder and generalized anxiety disorder and thereafter developed acute akathisia.

Keywords: akathisia,venlafaxine, duloxetine

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[1]M.D., [2]Assoc. Prof., Erenkoy Neurological and Psychiatric Disorders Training and Research Hospital, Istanbul - Turkey

Address reprint requests to:
Dr. Barbaros Özdemir,
Gülhane Askeri Tıp Akademisi
Ruh sağlığı ve Hastalıkları Anabilim Dalı
Ankara, Türkiye

E-mail address:
filizizci@yahoo.com

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INTRODUCTION

Akathisia is a syndrome which results in subjective discomfort and movement symptoms (1). It is characterised by feeling of an inner tension and irresistible leg movements (2). The diagnosis of drug-induced akathisia is made clinically, by seeing subjective and objective symptoms after the use of a medication that is known to cause akathisia (3). Drug induced akathisia is usually seen with antidopaminergic antipsychotics but also can be seen after the use of antidepressants, antiepileptics, anticholinergics, sympathomimetics, calcium channel blockers, lithium and antiparkinson drugs (3-4).

In the literature, cases have been reported where SNRIs like venlafaxine induced akathisia, venlafaxine combined with methimazole induced akathisia and movement disorders, citalopram induced tardive akathisia and SSRIs induced akathisia (5-7). To explain the pathology of drug induced akathisia, it has been hypothesized that SSRIs cause akathisia by inhibiting the basal firing rates of dopaminergic neurons in the ventral tegmental area and decreasing mesolimbic dopaminergic activity (8) and in a similar way SNRIs cause mesolimbic dopaminergic pathway hypofunction (6,8). Drug dose, dose increases and drug potency are important factors in the emergence of akathisia (9).

In this paper, we report the cases of two discrete patients with diagnoses of depressive disorder and generalized anxiety disorder, who were given venlafaxine and duloxetine in increasing doses and developed acute akathisia.

CASE 1

K.F. was a 53 year old male patient who was married, retired from a factory and had graduated from primary school. He was admitted to our psychiatry clinic with complaints including; fear of death, worries about being disabled, being sick, and restlessness. He was accepted into our clinic for inpatient treatment. Except for a history of vasectomy twenty years ago, cholecystectomy three years ago, and venous varicose, there was not anything notable in his personal history. For about twenty years he had been diagnosed with anxiety disorder and depressive disorder and had used various antidepressant therapies from time to time. His physical examination, routine biochemistry, complete blood count and thyroid hormone profile were assessed as normal. In the mental status examination, he seemed to be his chronological age, his self-care was adequate, he appeared to be normal, his behavior and psychomotor activity were normal, he was cooperative during the interview, showed respect to the interviewer, his affect and mood were anxious and his speech amount and rate were normal. He had over valued ideas about somatic complaints and worries in his mind, and although his judgment was normal, his insight about his illness was partially impaired. There was not anything abnormal in terms of cognitive functions or memory and perception, but attention and concentration were slightly diminished. His Hamilton Anxiety Scale score was 22 and Hamilton Depression Rating Scale score was 10. The diagnosis of generalized anxiety disorder was based on the structured clinical interview for the DSM-IV (SCID-I) (10). Treatment with duloxetine 30 mg/day and alprazolam 0.5 mg/day had been started but during the clinical follow-up period no notable decline was seen in his complaints and HAM-A score, and therefore, the duloxetine dose was increased to 60 mg/day. A week after the duloxetine dose was increased to 60 mg/day, it was noted that the patient could not sit down and could not prevent himself from moving. The Barnes akathisia scale (BAS) was administered to the patient and a score of 9 was measured; thereafter, propranolol 40 mg/day was added to the treatment. With that treatment, the BAS score and the patient's complaints declined immediately. Since his complaints and HAM-A score declined with duloxetine 60 mg/day, alprazolom 0.5 mg/day and propranolol 40 mg/day, this treatment regimen was continued.

CASE 2

I.K. was a 50 year old male patient who was married, retired, had three children and had graduated from primary school. He was admitted to our polyclinic with complaints including: feeling distress, lack of motivation, lack of appetite, forgetfulness and sleep disturbances. In his personal history, he had a nefrectomy twenty seven years ago and an operation for septal deviation more than two years ago. His first psychiatric complaints had started with feeling distress, sleep disturbances, nervousness and lack of motivation three years ago. After a short treatment period his complaints had completely disappeared. But 1.5 years ago, after similar symptoms had begun again, he had used various antidepressant drugs irregularly. After a psychosocial stressor exaggerated his symptoms one month ago, he was admitted our clinic for treatment as an inpatient. His physical examination, routine biochemistry, complete blood count and thyroid hormone profiles were assessed as normal.

In the mental status examination, he seemed to be his chronological age, his self-care was adequate, he appeared to be normal, his behavior and psychomotor activity were normal, he was cooperative with the interview, showed respect to the interviewer, his affect and mood were anxious and depressive, his speech amount was decreased and his speech rate was normal. He had over valued ideas and worries about his children in his mind. There was no perception of abnormal judgment. Memory, cognitive functions and insight were normal. Hamilton Anxiety Scale score was 21 and Hamilton Depression Rating Scale score was 21. Major depression was diagnosed by performing

the structured clinical interview for the DSM-IV (SCID-I)(10). A treatment with venlafaxine 75 mg/day, alprazolam 0.5 mg/day and mianserin 10 mg/day had been started but in psychiatric interviews performed daily, no notable decline was seen in his complaints and HAM-D score, and the venlafaxine dose was increased to 150 mg/day after a week. Two days after the venlafaxine dose was increased to 150 mg/day, it was noted that the patient could not sit down, was moving his legs nonstop and could not prevent himself from walking. The BAS was administered to the patient and the score was measured to be 10; thereafter, propranolol 40 mg/day was added to the treatment. Because there was no clear decline in his symptoms of akathisia, the venlafaxine dose was reduced to 75 mg/day. After that, his symptoms subsided and the BAS score declined. The HAM-D score decreased to 5, depressive sypmtoms reduced, anxiety and sleep disturbances regressed and he was discharged with the treatment of venlafaxine 75 mg/day, alprazolam 0.25 mg/day, and propranolol 40 mg/day.

DISCUSSION

Akathisia is a motor discomfort syndrome that emerges usually related with antipsychotic tratment. It is characterised by subjective symptoms like dysphoria and anxiety accompaniedby motions like swinging and wriggling of the legs, difficulty in sitting and standing immobile that may be observed objectively (11). It has been suggested that lesions seen bilaterally in the ventral tegmental area and post synaptic blockage in that dopaminergic pathway cause an akathisia-like syndrome. SSRI induced akathisia was suggested to be related to serotonergic reuptake leading to an inhibitory effect in the dopaminergic system (12). Drug-induced akathisia has been explained by the noradrenergic and serotonergic inhibitory effects in the mesocortical pathway, on the dopamineric transmission (13). In our cases, venlafaxine and duloxetine may have similar effects on serotonergic and noradrenergic systems and may have induced akathisia. In case 1, the akathisia symptoms began after a dosage increase. Propranolol given for akathisia treatment did not reduce the symptoms, which regressed only after decreasing the venlafaxine dose. Hence, it can be considered that, akathisia might have been dose-related. In our first case, akathisia was observed after a duloxetine dosage increase and when propranolol was started symptoms regressed. Since the current treatment dose had not been changed, we cannot say here that the occurrence of akathisia was dose-related.

Venlafaxine is associated with movement disorders, parkinsonism, tardive blepharospasm, malign neuroleptic syndrome that showed (6,13,14,15) with a combination of duloxetine and agomelatin induced akathisia, that had been associated with drug-drug interaction caused by neuroadrenergic overstimulation (16). There are not so many reports abot this topic except that a case with duloxetine therapy, in which tardive dyskinesia and tardive dystonia were observed after 18 months of duloxetine treatment. A schizophrenia patient with depression, beside clozapine duloxetine was started with the dose of 30 mg/day and 4 days later increased to effective dose of 60 mg/day, dyskinetic movements of the arms, trunk and lips were observed therefore doloxetine dose decreased to 30 mg/day. Because of no changes were seen in symptoms, duloxetine therapy was stopped (17). In our first case the dose of duloxetine had not been decreased because patient's complaints declined after propranolol treatment. On the other hand in second case; symptoms had regressed only after decreasing venlafaxine dose in accordance with that study in the literature.

It is clinically important that SNRIs may cause side effects like akathisia in a dose-related manner. It seems that case reports and wide ranging research are required to understand the pathophysiology of SNRI induced akathisia and whether there is a relationship with drug dose.

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