

Restless Legs Syndrome in an Elderly Patient Induced by Combined Use of Low Dose Quetiapine and Citalopram*

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ÖZET:

Yaşlı bir hastada düşük doz ketiapin ve sitalopram kombinasyonuna bağlı huzursuz bacaklar sendromu

Huzursuz bacaklar sendromu (HBS) nispeten sık görülen ancak sıklıkla tanınmayan ve etyolojisi bilinmeyen duyuşal-motor bozukluktur. HBS'nin temel klinik belirtisi hastaların bacaklarında ortaya çıkan, günlük yaşam ve uyku kalitesini etkileyebilen, "hareket ettirme dürtüsü" ve "hoş olmayan hisler"dir. HBS'nin tanısı klinik bulgulara dayanılarak konulur. Polisomniografi, rahatsızlığın uyku fizyolojisi üzerindeki etkilerini göstermede faydalı olabilir. Merkezi sinir sistemindeki (MSS) dopaminerjik bir disfonksiyonun veya bir demir hemostazında depresyona yol açacak bir değişikliğin, HBS'nin fizyopatolojisinde etkili olabileceği düşünülmektedir. Bu makalede, 20mg/gün dozunda sitalopram tedavisine 50 mg/gün dozunda ketiapin eklenmesinden sonra HBS semptomları geliştiren yaşlı bir erkek hastanın klinik tablosu tanımlanarak, genellikle gözden kaçırılan HBS'ye ve antipsikotiklerin normal endikasyonları dışında kullanımları esnasında ortaya çıkabilecek yan etkilere dikkat çekilmesi amaçlanmıştır.

Anahtar sözcükler: Huzursuz bacaklar sendromu, ketiapin, akatizi

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ABSTRACT:

Restless legs syndrome in an elderly patient induced by combined use of low dose quetiapine and citalopram

Restless legs syndrome (RLS) is a relatively common sensory-motor disorder. However, it is frequently unrecognized. The main clinical characteristics of RLS are "an urge to move" and "uncomfortable and unpleasant sensations" in the legs, which can affect quality of daily life and sleep. The diagnosis is based on clinical findings. Polysomnography can reveal its impact on sleep physiology. Dopaminergic dysfunction and a change in the regulation of iron homeostasis leading to iron depletion in the central nervous system (CNS) are thought to be involved in the pathophysiology of RLS. The aim of this paper is to point out the side effects with off-label use of antipsychotics and call attention to often overlooked RLS by describing an elderly patient who developed RLS symptoms after addition of 50 mg/d quetiapine to preexisting 20 mg/d citalopram treatment.

Key words: Restless legs syndrome, quetiapine, akathisia

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INTRODUCTION

Restless legs syndrome (RLS) is a sleep-related disorder characterized by abnormal sensations in the legs at rest in which the patients feel an urge to move the legs (1). Reported prevalances of RLS is between 2-15% (2). Unrecognized or misdiagnosed cases of RLS are not rare (3). The term describes the subjective and motor restlessness seen with the use of dopamine antagonist (antipsychotics or anti-emetics) (4). Symptoms occur with rest and resolve with movement (5). The symptoms get

worse at night, and the patients frequently develop difficulty falling asleep and awakening during sleep (6).

The pathophysiology of RLS is thought to involve the peripheral and central stimulus-processing mechanisms of the nervous system and some other elements of the motor system (7). There is substantial evidence for a role of the dopaminergic system and iron status in the pathophysiology of RLS (8). Similarity of clinical picture of RLS and dopamine antagonist-induced akathisia suggests a relative or absolute decrease in dopaminergic activity as a pathogenic mechanism (9). In 15 multiplex RLS families,

genetic research revealed novel susceptibility loci at 9p-24-22, with linkage to RLS (10) and the expressed mutation was Dopamine Receptor Specific Individual Sensitivity (DRSIS) (11). Resolution of symptoms upon treatment with dopamine agonists such as levodopa supports the role of dopamine system in RLS (12,13).

A study by Akpınar suggests a role for EEG alpha activity dysfunction in the pathogenesis of primary RLS (14). The forced EEG shifts from alpha activity to delta or high alpha during changes in vigilance, may alter the state and function of dopaminergic receptors and cause RLS symptomatology. RLS and neuroleptic induced akathisia (NIA) may be accepted as the clinical affectation models of the diencephalospinal dopamine system (DSDS). DRSIS of the dopamine receptors at the DSDS neurons may occur either due to antipsychotic medications as in NIA or due to loss of alpha activity gate control in case of RLS. In both instances the result is a deficiency in dopamine transmission at the DSDS (15).

The clinical similarity between RLS and akathisia renders RLS diagnosis difficult. Clinicians must remember that antipsychotic drugs, even those with a relatively low dopamine D2 receptor affinity, may induce RLS. The following case presentation of RLS, induced by combined use of quetiapine and citalopram, illustrates this fact.

CASE REPORT

A 75-year-old male patient with a past history of alcohol dependency presented with recent complaints of difficulty falling asleep. His sleep problems started 6 years ago, after the cessation of alcohol consumption. His past medical history was noncontributory and his psychiatric history revealed neither any previous sleep-related disorder nor any comorbid axis I disorder. No cognitive impairment was observed during his initial psychiatric examination. He was started on mirtazapine 15 mg/d with a diagnosis of insomnia. One month later at the follow-up visit, mirtazapine treatment was discontinued due to lack of any improvement and zopiclone 7.5 mg/d was started. Eight weeks after the start of zopiclone therapy, an implicit obsessive-compulsive personality disorder was also diagnosed which led to the addition of citalopram 20 mg/d to the therapy regimen. Partial improvement in the patient's overall situation was observed after another eight weeks of zopiclone and citalopram combination therapy. Over the

following three weeks, the daily zopiclone dose was gradually lowered and completely stopped. Soon after the cessation of zopiclone, the patient's complaints regarding insomnia began to resurface. He was having difficulty falling asleep and was sleeping 2 hours per night, but was not taking naps during the day. Due to his past history of alcohol dependency and possible risk of zopiclone abuse, zopiclone was not chosen for a second time; instead quetiapine 50 mg/d was started as a sedative agent. Four days after the start of quetiapine therapy, the patient reported a tingling sensation in both of his legs, he and his wife complained about the involuntary movements of his legs when he was in bed. This sensation and involuntary movements disappeared upon standing up and walking. These symptoms gradually faded away over one week after stopping quetiapine and reappeared in 4 days after 50 mg/d quetiapine was restarted. He had no prior history or family history of leg movement disorders. He had no comorbid physical illness. Neurologic examination did not show any abnormalities. The laboratory data did not reveal any evidence of renal failure or anemia. His iron and ferritin levels were within normal limits.

DISCUSSION

This report discusses RLS in an elderly patient caused by combined use of low dose quetiapine and citalopram. In clinical practice, psychotropic medications are extensively used for various off-label indications such as sleep, eating or personality disorders. Quetiapine is commonly prescribed for treatment of insomnia in clinical practice (16). In a study of normal healthy volunteers given quetiapine 25 mg or 100 mg 1 hour before bedtime, it was found that quetiapine increased total sleep time, sleep efficiency, percentage of stage 2 sleep, and subjective sleep quality (17). Data regarding treatment of primary insomnia with quetiapine are scarce (18,19). It has been suggested that some psychotropic drugs, for example antipsychotics, are the cause of symptomatic RLS (20). It is known that dopamine antagonists can aggravate RLS (9). Quetiapine, however, has a relatively low affinity for D2 receptors compared to most second generation antipsychotic drugs, which accounts for its near-plateau rate of extrapyramidal adverse events (21).

In our patient, we thought that the etiology of RLS was dopaminergic receptor blockade by quetiapine with a

possible contribution of citalopram via an indirect dopaminergic antagonism.

Since the necessary equipment for a polysomniographic evaluation was not present in our hospital, the patient was referred to an outpatient clinic with a polysomniography laboratory. Due to objection of patient, polysomniography could not be done, but the described case fulfills the RLS diagnostic criteria established by the International Restless Leg Syndrome Study Group (22).

There are clinical similarities between RLS and dopamine antagonist-induced akathisia. As for differential diagnosis, the cardinal feature of RLS is the circadian pattern of symptoms predominating at night (5). In akathisia, the symptoms do not improve when the patient moves his/her legs (23). Antipsychotic-induced RLS has been reported rarely, yet it is important to distinguish RLS from akathisia.

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