Bupropion XL Use in Comorbidity of Depression and Restless Leg Syndrome: A Case Report

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ABSTRACT:
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Restless leg syndrome (RLS) is a sensorimotor disorder with symptoms including uncomfortable subjective sensations in the legs and the urge to move them. This common disorder affects 10% of the population and may reduce quality of life. The pathophysiology of RLS is not well understood but dysfunction of dopaminergic pathways is the most prominent theory. Antidepressants, especially SSRIs, can aggravate the symptoms of RLS. Here we present a 42 year old woman diagnosed with major depressive disorder and comorbid RLS and who had been treated with paroxetine 20 mg/day for 2 months who benefited from switching to bupropion treatment. In this case the RLS symptoms had existed for approximately 3 years but were milder before paroxetine treatment. The patient met the diagnostic criteria for RLS. We used the International Restless Legs Scale (IRLS) and Montgomery-Asberg Depression Rating Scale (MADRS) to measure the patient’s symptom severity. The severity of her depressive symptoms was similar to baseline despite the two month paroxetine treatment. Due to symptoms of RLS and her ongoing depressive complaint, we decided to switch from paroxetine to bupropion. With 150 mg/day bupropion XL treatment, her RLS symptoms improved substantially at a one month follow-up while her depression severity was not changed significantly. Due to inadequate response for depression, bupropion XL was titrated to 300 mg/day. Her depressive symptoms improved significantly at a further one month follow-up. Comorbidity of RLS and depression was found to be as a frequent occurrence reported in the literature. We concluded that bupropion, as a selective noradrenergic-dopaminergic reuptake inhibitor can be a good alternative to the SSRIs for patients, who suffer from both depression and RLS.

Keywords: restless legs, depression, bupropion

Case Reports

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ÖZET:
Depresyon ve huzursuzacak sendromu birliktelğinde bupropion XL kullanımı: Bir olgu sunumu

Huzursuzacak sendromu (HBS) alt ekstremitelerde subjektif rahatsızlık hissi ve hareket etme ihtiyacı yaratan sensorimotor bir bozukluktur. Bu yaygın rahatsızlık toplumda %10 oranında görülmekte olup yaşam kalitesini bozabilmektedir. HBS’nin patofizyolojisi henüz tam olarak anlamadığımızda dopamin sistemleri ciddi teoridir. Bu olguda 2 aydır paroksetin 20 mg/gün kullanımı olan komorbid depresyon ve HBS tanısı alan ve bupropion tedavisine geçiş sonrası fayda gören 42 yaşında bir kadın hastayı sunuyoruz. Olgu HBS semptomlarının yaklaşık 3 yıldır mevcut olması karşın paroksetin tedavisinden önce daha hafif düzeyde olduğunu bildirmekteydi. Hastanın mevcut semptomlarını HBS kriterlerini karşılayordu. HBS semptom şiddetini ölçmek için Uluslararası Huzursuz Bacak Skalası (IRLS- International Restless Legs Scale) depresyon şiddetini için MADRS (Montgomery-Asperg Depression Rating Scale) skoru kullanıldı. Hastanın depresif semptomları paroksetin tedavisinde zayıflamıştı. HBS ve devam eden depresif semptomlar nedeniyle paroksetin 20 mg/gün tedavisinden bupropion XL 150 mg/gün tedavisine geçilmesine karar verildi. 1 aylik izlemde hastanın HBS semptomlarında belirgin düzelmeme karar verildi. Depresyon açısından yetersiz yan tedavisi bupropion 300 mg/gün dozuğunda verildi. HBS komorbiditesi literatürde çalışılmış ve sik olduğu bildirilmistir. Bupropionin seçici noradrenergik-dopaminergic geri alım inhibitörlü komorbid depresyon ve HBS olan hastalarda SSRi lar yerine iyi bir seçenek olabileceğini düşündüyuz.

Anahtar sözcükler: huzursuzacak, depresyon, bupropion

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Anahtar sözcükler: huzursuzacak, depresyon, bupropion

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INTRODUCTION

Restless leg syndrome (RLS) is a neurological disorder characterized by uncomfortable subjective sensations in the legs and the urge to move them. Although this sensori-motor syndrome is highly prevalent it is substantially underdiagnosed. It was first described by Karl A. Ekbom, a Swedish neurologist, in 1945. Sufferers describe the symptoms of this condition as tingling, crawling and itching in legs; and usually report poor sleep. The symptoms usually manifest at night or while resting and are relieved by moving the legs. The disturbing sensations cause the urge to move the legs voluntarily. Since these symptoms interfere with sleeping and resting, RLS is accompanied by low quality of life and comorbid psychiatric disorders such as depression and anxiety disorders and sleep problems. This syndrome is a common health problem that has a significant negative impact on quality of life, possibly more than other chronic diseases such as diabetes mellitus, depression and osteoarthritis. This common disorder approximately affects 10% of the population and is twice as prevalent in women as in men. Even though RLS is generally seen as a primary condition, there are some secondary conditions which result in RLS. The most common causes of secondary RLS are iron deficiency, chronic kidney disease, pregnancy, Parkinson’s disease, peripheral neuropathy and various medications including antidepressants. In these cases, RLS symptoms may be alleviated by treatment of the secondary conditions. Genetic factors also play an important role in development of RLS. A positive family history has been reported in 40 to 60% of RLS patients. There is sufficient data points to a relationship between RLS and antidepressant use. SSRIs and TCAs have been found to be aggravating factors of RLS symptoms. Case reports and studies have shown that particularly SSRIs exacerbated RLS symptoms while bupropion, a noradrenergic-dopaminergic reuptake inhibitor, improved or at least did not worsen RLS symptom severity. The pathophysiology of RLS is not well understood but dysfunction of dopaminergic pathways and iron deficiency in the brain are the most prominent theories. Bupropion is a relatively novel antidepressant with specific noradrenergic and dopaminergic mechanisms. Because it does not act on the seotonergic system, bupropion is distinguished from other antidepressants. Bupropion increases dopamine neurotransmission in the central nervous system by inhibiting the reuptake of dopamine. This dopaminergic activity may be meaningful in ameliorating RLS symptoms with respect to the hypo-dopaminergic hypothesis of RLS. In this case report, we present a woman who suffered from depression comorbid with RLS and benefited from replacing paroxetine with bupropion treatment.

CASE

Our case was a 42 year old woman diagnosed with major depressive disorder who had been treated with paroxetine 20 mg/day for 2 months. Her depressive symptoms had existed for two years. She had been suffering from anergia, anhedonia, avolition, pessimistic thoughts and sleep problems for two years but had no optimal treatment history until her last paroxetine treatment. She reported the use of citalopram and fluoxetine for short periods that probably were not long enough for an adequate response. At her follow up visit, she reported unpleasant sensations in both legs caused sleep disturbance. These sensations had existed for approximately 3 years but were milder before paroxetine treatment. She had not had medical treatment for these sensory complaints. She described the paresthesia in her legs as “pulling” and this complaint emerged particularly at night. She had trouble falling sleep and felt unrested in the morning. She had no neurological or chronic disease related with these sensory symptoms. Iron deficiency was checked with a blood test. The patient met the diagnosis of
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RLS based on the criteria described by the International Restless Legs Syndrome Study Group (IRLSSG). The International Restless Legs Scale (IRLS) was developed by the IRLSSG for measuring the severity of RLS symptoms. We used the IRLS to measure patient’s symptoms severity. Her baseline RLS rating scale score was 24 points when she described her RLS symptoms for the first time. Her depressive symptoms were similar in severity despite the two month paroxetine treatment. Due to symptoms of RLS and her ongoing depressive complaints we decided to switch from paroxetine to bupropion. Depression severity was measured with the Montgomery-Asberg Depression Rating Scale (MADRS) and her MADRS score was 30 at the beginning of bupropion treatment. Her first visit was planned to occur after two weeks but she made her first visit one month later. She reported no side effects from the bupropion. Her RLS symptoms had improved substantially at one month follow-up confirmed by an IRLS score of 7, while her depression severity had not changed significantly. Due to inadequate response for depression with 150 mg/day bupropion XL, we decided to titrate it to 300 mg/day. As the bupropion XL dosage was titrated to 300 mg/day, her depressive symptoms improved significantly as confirmed by a MADRS score of 12 (>50% reduction from baseline score) while her RLS symptoms remained improved as confirmed by an IRLS score of 6 points at one month follow-up.

DISCUSSION

RLS is a common sensorimotor disorder that has a remarkable impact on quality of life. Since awareness of the disease has increased, some pharmacological and non-pharmacological methods have been used for the treatment of this disorder. Comorbidity of RLS and depression has been reported frequently in the literature. One study found that RLS was more frequent in depressive subjects compared to the general population. Although this comorbidity was reported as frequent, this result can be due to an overlap between RLS and depression-related symptoms. Although the causality or validity of this comorbidity is a debatable issue, it is well known that insomnia is frequent among RLS sufferers whereas it is an inducing factor or predictor for depression. However, antidepressants, particularly SSRIs, are the preferred drugs in depression, although they aggravate the symptoms of RLS. RLS has been noted as a possible side effect of the use of several SSRIs and SNRIs. Mirtazapine has been found to be cause RLS symptoms more than some other SSRIs. In a case report, another psychotropic agent, quetiapine, which is often used for sleep problems in clinical practice, was found to be related to RLS symptoms even at low doses. The etiology of RLS remains unknown but dysfunction in central dopaminergic pathways is the most accepted theory. Some studies revealed altered dopaminergic profiles in some regions of the brain such as the substantia nigra and putamen in individuals with RLS. Dopaminergic medications such as levodopa, pramipexole, ropinirole and rotigotine are the mainstay of treatment in RLS. In addition to dopaminergic drugs, low dose opiates (oxycodone, tramadol), benzodiazepines (clonazepam) and antiepileptic drugs (gabapentin, pregabalin) are other medical options. Due to increased dopaminergic activity or sleep quality, dopaminergic agonists may also relieve some depressive symptoms. Dopamine dysfunction is implicated in the pathophysiology of depression as well as in RLS. Medications that have direct dopaminergic action have been demonstrated to be effective in some cases of depression. These findings suggest that subtypes of depression may stem from dopaminergic pathways. Moreover, inadequate response to most preferred antidepressant medications such as SSRIs or SNRIs in some depression cases supports this theory. Bupropion is a selective noradrenergic-dopaminergic reuptake inhibitor used to treat depression. Bupropion differs from other antidepressants due to its inhibitory effect on noradrenergic and dopaminergic transporters and re-uptake pumps. Due to this unique pharmacological profile, bupropion increases
dopamine neurotransmission in both the nucleus accumbens and prefrontal cortex, which are very important regions in the neurochemical pathways of depression. Bupropion causes no serotonergic activity in contrast to most of other antidepressants. RLS symptoms are not seen in patients, who use bupropion because of its specific noradrenergic and dopaminergic mechanism. In management of depression comorbid with RLS, drug selection can be a complex issue due to adverse effects of antidepressants. It is well known that SSRIs, such as paroxetine, may potentially aggravate the symptoms of RLS. As confirmation, our case reported that the RLS symptoms she experienced had existed but were milder before paroxetine treatment. By switching to bupropion, she reported that the symptoms of RLS improved better than she had before with paroxetine treatment. Paroxetine, a widely used SSRI, did not work in this patient’s depression whereas bupropion improved her depressive symptoms and RLS symptoms. This finding may be a sign of dysfunction in dopaminergic pathways in this case. Increased dopaminergic activity due to bupropion treatment may be helpful in relieving symptoms of RLS since some reports about its efficacy in RLS exist in the literature.

**CONCLUSION**

We concluded that bupropion XL could be a good alternative to SSRIs for patients, who suffer from both depression and RLS.

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