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Pregabalin in the Treatment of Primary and Secondary Restless Legs Syndrome: Three Case Reports

Primer ve Sekonder Huzursuz Bacak Sendromunun Tedavisinde Pregabalin: Üç Olgu Sunumu

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Summary

Restless legs syndrome (RLS) is a sensorimotor disease characterized by a sense of discomfort in the legs and involuntary movements of the legs before falling asleep and while resting. Dopamine receptor agonists, L-dopa, dopamine agonists, opioids, benzodiazepines, and gabapentin are commonly used in the treatment of RLS. However, a treatment model that is most effective for RLS has not yet been defined. In the present case series, the successful results of administering pregabalin for neuropathic pain and fibromyalgia syndrome (FMS) are presented in three patients with RLS. The first two cases were considered secondary RLS, whereas the 3rd case was considered idiopathic RLS. Iron deficiency anemia and FMS accompanied RLS in the 1st case (42-year-old female). Both FMS and RLS symptoms were improved with pregabalin. The 2nd case (38-year-old female) had type 1 diabetes mellitus (DM) and diabetic neuropathy. Both the symptoms of diabetic neuropathy and RLS were relieved with pregabalin. The 3rd case (48-year-old female) was idiopathic, and RLS has been completely taken under control with pregabalin treatment. In conclusion, pregabalin may be a different treatment option for both idiopathic and secondary RLS. *Turk J Phys Med Rehab 2011;57:242-4.*
Key Words: Pregabalin, restless legs syndrome, treatment, neuropathic pain

Özet

Huzursuz bacak sendromu (HBS) dinlenme sırasında ya da uykuya dalmadan önce bacaklarda istemsiz hareketler ve rahatsızlık hissiyle karakterize, sensorimotor bir hastalıktır. HBS'nin tedavisinde dopamin reseptör agonistleri, L-dopa, dopamin agonistleri, opioidler, benzodiyazepinler ve gabapentin yaygın olarak kullanılmaktadır. Bununla beraber, HBS'de çok etkili bir tedavi yöntemi belirlenmemiştir. Buradaki vaka serisinde HBS'li üç hastada nöropatik ağrı ve fibromiyalji sendromu (FMS) için pregabalin verilmesinin başarılı sonuçları sunulmaktadır. İlk iki vaka sekonder HBS, 3. vaka ise idiyopatik HBS olarak belirlenmiştir. İlk vakada (42 yaşında kadın hasta) HBS, demir eksikliği anemisi ve FMS ile birliktedir. FMS ve HBS semptomlarının her ikisi de pregabalinle rahatlamıştır. İkinci vaka (38 yaşında kadın hasta) tip-1 DM ve diyabetik nöropatiye sahiptir. Diyabetik nöropati ve HBS semptomları pregabalinle azalmıştır. Üçüncü vaka (48 yaşında kadın hasta) idiyopatik olup HBS semptomları pregabalin tedavisiyle kontrol altına alınmıştır. Sonuç olarak, pregabalin hem idiyopatik hem de sekonder HBS için farklı bir tedavi seçeneği olabilir.*Türk Fiz Tıp Rehab Derg 2011;57:242-4.*
Anahtar Kelimeler: Pregabalin, huzursuz bacak sendromu, tedavi, nöropatik ağrı

Introduction

Restless legs syndrome (RLS) is a sensorimotor disease that is encountered two times more frequently among women of middle and advanced age compared to men (1). Patients complain about involuntary crawling- or creeping-like motions before sleep or while sleeping, as well as a sense of discomfort and pain in the lower extremities. These symptoms are relieved by active motions, such as standing up walking, or stretching (2). The quality of life is negatively affected because of difficulty in falling asleep, frequent awakening, difficulty in falling into deep sleep, and non-restful sleep.

Although the etiology of RLS has not yet been determined, it is thought to occur due to an imbalance in dopamine neurotransmission in the central nervous system and can be

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accompanied by peripheral neuropathy (3). Although it is generally idiopathic, RLS can be observed secondary to hepatic diseases, chronic renal failure, diabetes mellitus (DM), pregnancy and iron deficiency anemia (4).

Dopamine receptor agonists, such as ropinirole and pramipexole, and L-dopa are commonly used in the treatment of RLS (3). Although L-dopa initially causes a relief of symptoms, it has been suggested that the symptoms worsen within a few months (5,6). Alternative treatment options include dopamine agonists, opioids, benzodiazepines, and gabapentin (7). Nevertheless, an effective treatment model in RLS has not yet been defined. In the present case series, the effects of administering pregabalin for neuropathic pain and fibromyalgia syndrome (FMS) are presented in three patients with RLS.

Case 1

It was asserted that a 42-year-old female had undergone cesarean section under general anesthesia four years ago and suffered a serious hemorrhage during surgery. Six months after the delivery, she had complaints of pain and motion in her legs every few days, but which did not significantly impair the quality of her sleep. As these involuntary motions worsened over time, she was admitted to a psychiatry outpatient clinic and had been diagnosed with RLS. Short-term relief had been achieved with the administration of dopamine agonist drugs. However, the symptoms had reappeared after one month. Her complaints worsened due to an intense emotional stress she had experienced at that time. She had been referred to a physical medicine and rehabilitation outpatient clinic because of excessive fatigue and widespread body pain. Her laboratory findings were as follows: hemoglobin (Hb): 9.9 g/dL, hematocrit (Hct): 30.8%, and ferritin: 4.3 ng/mL, and iron deficiency anemia was diagnosed. Sensitivity at 12 FMS points was shown in the patient complaining of a sleep disorder and widespread body pain. 100 mg elemental iron supplementation and 25 mg of amitriptyline daily were prescribed to the patient for FMS RLS, and anemia. At her one month follow-up visit, she explained that she had not taken the amitriptyline because of its sedative effect, thus, 75 mg of pregabalin twice a day was substituted for amitriptyline. She attended the outpatient clinic after two days with complaints of vertigo and sedation. She was informed that such side effects would resolve in time and a follow-up visit was arranged 15 days later. At her follow-up visit, she stated that the side effects had resolved and the involuntary leg movements were reduced by >50%. The dose of pregabalin was increased to 150 mg twice a day. At her follow-up visit after one month, she declared that the pain and involuntary movements in her leg were relieved by >90%. Her relief remained unchanged at the three-month follow-up visit.

Case 2

A 38-year-old female was being followed with the of type 1 DM and lumbar disc herniation (LDH). At the time of her admission to the outpatient clinic, she stated that the sense of discomfort and trembling in her legs had begun approximately three years ago and manifest when the blood glucose level could not be completely controlled. She asserted that the trembling in her legs and urge to move her legs, which begin prior to falling asleep and sometimes awakened her while sleeping, had become evident during stressful or premenstrual periods. The patient expressed that she had a sleep disorder and could not rest due to these complaints. The patient, who was administered insulin, had also complaints of a burning sensation and numbness in her feet. Her physical examination revealed a positive Lasegue test at an angle of 45 degrees on the right leg. Neurologic examination revealed normal findings. On magnetic resonance imaging (MRI), a protrusion at the L4-5 level that obliterated the right lateral recess and a central herniation at the L5-S1 level were detected. The patient was diagnosed with LDH, diabetic neuropathic pain, and RLS; non-steroidal anti-inflammatory drugs (NSAIDs) and myorelaxant treatments were administered for one week. Strengthening exercises for the muscles in the lumbar region were offered. Subsequently 75 mg of pregabalin twice a day was initiated. A week later, the patient was admitted with complaints of fatigue, a tendency to sleep, and vertigo. The medications were continued, informing the patient that the side effects would resolve in time. After 15 days, the patient stated that the burning sensation and numbness in her feet had resolved and the urge to move the legs was alleviated by 40%. The dose of the drug was adjusted to 150 mg twice a day. On her follow-up visit after one month, the symptoms of RLS had improved by 80%, whereas the complaints of numbness and burning sensation in the feet have completely resolved.

Case 3

A 48-year-old female was admitted to our outpatient clinic with complaints of fatigue, headache, sudden leg movements, and cramping in her legs towards morning. It was asserted that these complaints had begun a few years ago, and she had to get up and walk when these movements occurred. No abnormalities were indentified on her laboratory analyses. A trigger point was assessed on her right trapezius muscle, and a local anesthetic was injected. The patient was diagnosed with myofascial pain syndrome (MPS) and RLS, and 75 mg of pregabalin twice a day was initiated. She was warned about the potential side effects of the drug, such as vertigo, sleepiness and dizziness and it was recommended that she continue administering the drug and return for a follow-up visit after one week. At her follow-up visit, she expressed that there had been similar side effects during the first days, but were relieved within 4-5 days and the involuntary movements of her legs were slightly decreased. The dose of the drug was increased to 150 mg twice a day. At the follow-up visit after one month, she stated that her complaints were relieved by >70% and at the three-month follow-up visit she stated that they have been completely relieved.

Discussion

Although the etiology of RLS is not known, there are studies suggesting that RLS can be accompanied by peripheral neuropathy (3). Pregabalin is a compound administered in the treatment of FMS, epilepsy, anxiety, and neuropathic pain (8). Pregabalin cannot bind to δ-aminobutyric acid (GABA) receptors, even though it is a structural analogue of GABA (5). The anticonvulsant, analgesic and anxiolytic effects of pregabalin have been demonstrated in diabetic polyneuropathy and in neuropathic pain (9). Pregabalin acts by

decreasing the release of many excitatory neurotransmitters after binding to the alpha-2-delta sub-unit of voltage-sensitive calcium channels (10). Side effects, such as headache, vertigo, rash, dry mouth and a tendency to sleep may be observed, particularly with initial doses of pregabalin, but resolve with time (11).

Similar minor side effects were observed in the three cases in this case series, but were relieved within one week. The first two cases were considered secondary RLS whereas the 3rd case was considered idiopathic RLS. Iron deficiency anemia and FMS accompanied RLS in the 1st case. Both FMS and RLS symptoms were improved with pregabalin. However, this improvement may also be due to iron deficiency anemia treatment, because she concurrently used pregabalin and iron supplementation. The 2nd case had type 1 DM and diabetic neuropathy. Both the symptoms of diabetic neuropathy and RLS were relieved with pregabalin. The 3rd case was idiopathic and although not accompanied by neuropathy, RLS had been completely taken under control with pregabalin treatment. These results indicate that pregabalin is beneficial both in idiopathic and secondary RLS. Furthermore, pregabalin is also beneficial in neuropathies that accompany RLS. As far as we know, there is only a single report regarding the administration of pregabalin in RLS. Sommer et al. (5) reported attenuation of symptoms in 16 patients with secondary RLS treated with 300 mg of pregabalin daily. No information exists in the literature regarding the benefits of pregabalin in idiopathic RLS.

In conclusion, pregabalin may be a new treatment option for both idiopathic and secondary RLS. Placebo-controlled, double-blind, randomized trials that investigate the effect of this treatment on a large patient series are needed.

Conflict of Interest:

Authors reported no conflicts of interest.

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