Behavioral Sleep Medicine Interventions for Restless Legs Syndrome and Periodic Limb Movement Disorder

Wilfred R. Pigeon, PhD, CBSM[a,*], Michael Yurcheshen, MD[b]

KEYWORDS

- Restless legs syndrome
- Periodic limb movement disorder
- Behavioral • Cognitive-behavioral
- Behavioral medicine • Relaxation

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Restless legs syndrome (RLS) and periodic limb movement disorder (PLMD) are sleep disorders that are commonly seen in clinical practice, both by primary care providers and by sleep specialists. Unlike the vast majority of movement disorders, these conditions do not improve with sleep. The standard treatment recommendations for these disorders are pharmacologic, although behavioral interventions for these conditions are increasingly recognized, albeit underused.

RESTLESS LEGS SYNDROME AND ITS PHARMACOLOGIC MANAGEMENT

Although the first descriptions of RLS were recorded as early as 1672, Stephen Eckbolm is largely credited with the first modern report of the condition, identifying eight patients who had the condition in 1945.[1,2] Since these earliest accounts, diagnostic criteria for the condition have been established and refined.[3,4] In the most recent version of the *International Classification of Sleep Disorders*, RLS is grouped with other sleep-related movement disorders. Although this syndrome does not necessarily involve stereotyped movement, RLS is included among the movement disorders of sleep because of its close association with PLMD and periodic leg movements of wake. RLS has four features,[5] which include (1) a strong, ''nearly irresistible'' urge to move the legs; (2) sensations that are worsened with inactivity; (3) sensations that are improved or relieved with movement; and (4) symptoms that are exacerbated at night.

In clinical practice, not all of these features are necessary to make a diagnosis of RLS; there is also some variability in how frequently symptoms occur. In children younger than 12 years of

W.R.P. received funding support from NIH NR010408; Rochester Center for Mind-Body Research (NIH AG023956); VA Center of Excellence at Canandaigua, Canandaigua, NY; and Sanofi-Aventis.
The views and opinions expressed by the authors do not represent the views or opinions of the NIH or the VA.
[a] Department of Psychiatry, Sleep and Neurophysiology Research Laboratory, University of Rochester Medical Center, 300 Crittenden Boulevard, Box PSYCH, Rochester, NY 14642-8409, USA
[b] Department of Neurology and Strong Sleep Disorders Center, 919 Westfall Road, Building A, Suite 100, University of Rochester Medical Center, Rochester, NY 14618, USA
* Corresponding author.
E-mail address: wilfred_pigeon@urmc.rochester.edu (W.R. Pigeon).

Sleep Med Clin 4 (2009) 487–494
doi:10.1016/j.jsmc.2009.07.008
1556-407X/09/$ – see front matter

age, the condition can include probable or definite RLS, and diagnostic criteria are slightly different.[4,5]

This utilitarian description, however, in some ways minimizes the degree of sleep disruption that many of these patients experience. In some cases, the discomfort is so disruptive that afflicted patients wander nightly, sometimes for hours, until they finally collapse with exhaustion. The sensation has been described variably, and some descriptors of the sensation include ''tingling,'' ''stinging,'' or a ''creepy-crawly'' feeling. In up to 50% of cases, symptoms are severe enough to involve the upper extremities in addition to (or in rarer circumstances, instead of) the lower extremities.[6]

It is estimated that RLS has an incidence of about 5% to 15% in the general population, and most studies suggest it is up to twice as common in women.[7,8] RLS is commonly idiopathic, but many secondary causes of this condition have been identified. These secondary causes include, but are not limited to, neuropathy, diabetes, renal dysfunction, spinal stenosis, pregnancy, side effects from drugs/medications (such as antipsychotics or antiemetics), and iron or vitamin deficiency. A discussion of the secondary causes of RLS is beyond the scope of this article; however, a recent online review of RLS includes an extensive discussion.[9] Other less common causes of RLS have also been described. For instance, in a recent case series, five patients who had Chiari-I malformation were found to have RLS.[10] Some familial cases of RLS have also been identified, suggesting a genetic component. Indeed, a handful of genetic loci and polymorphisms of susceptible genes (including the BTBD9 gene) associated with RLS have been discovered.[11,12] Depending on the cause, symptoms may fluctuate. Pregnancy is a common example, with many women describing symptoms only during the term of pregnancy, but never before or after.

There has been some evidence that idiopathic RLS may actually be a harbinger of neurodegenerative conditions, such as Parkinson disease.[13] Confirmatory evidence of a definitive relationship between these conditions is lacking. A recent epidemiologic study also links RLS and vascular disease.[14] Causality and directionality in this association has not been firmly established.

The typical workup for RLS includes a diligent clinical encounter with close attention paid to sleep and past medical history. The physical examination should include a neurologic examination, particularly of the lower extremities. A comprehensive laboratory workup is of variable usefulness. Serum ferritin levels are often drawn, and some practitioners advocate for supplementing iron if the level is less than 50 ug/mL, although currently there are no clinical trials or even guidelines to support this practice. Although cerebrospinal fluid iron studies seem more sensitive for RLS, a lumbar puncture for such an evaluation is not recommended.[15] Neuroimaging of the lumbosacral spine and electromyography (EMG)/nerve conduction studies are not indicated in every patient. Polysomnography (PSG) is not routinely required in most cases of RLS, and an estimated 10% to 20% of patients who have RLS have a PSG free of any remarkable surface EMG finding.[16] Information from a nocturnal PSG can be useful in questionable cases of RLS or to identify the degree of sleep disruption from associated nighttime movements. The Suggested Immobilization Test (SIT) is a procedure wherein a patient rates their level of leg discomfort while surface EMG tracings of leg movements are recorded.[17] This test is used infrequently in clinical practice.

If a specific cause of RLS is identified, treating the underlying condition can be helpful in alleviating symptoms. Some examples include addressing any reversible causes of renal dysfunction, or delivery when pregnancy is the proximal cause.[18] The relationship between glucose control and RLS is just beginning to be explored.[19]

Treatment of the idiopathic form of RLS is most commonly pharmacologic. Standards of practice and algorithms for pharmacologic treatment have been developed, but the treatment landscape has changed since 2004 when these guidelines were published.[20,21] Specifically, dopamine D2 agonists have become first-line treatment of this condition.[22] According to the American Academy of Sleep Medicine (AASM) 2004 Practice Parameters, levodopa/carbidopa and pergolide are considered standards for treatment.[20] Since that time, pramipexole and ropinirole have been approved by the Food and Drug Administration for treating RLS, and many practitioners use these agents first. Evening administration at doses that are generally significantly less than what would be required for treatment of Parkinson Disease are usually effective. The most common side effects of these dopamine agonists include nausea and sleepiness. Dopamine dysregulation syndrome is uncommon, but should be considered when using dopamine agonists. Other agents that show significant efficacy include, but are not limited to, gabapentin and clonazepam.[23,24] Side effects to gabapentin include nonspecific drowsiness, nausea, and dizziness, among others. Clonazepam has a longer half-life than many benzodiazepines and therefore seems to carry a lower risk for abuse; however, clonazepam