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

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BEHAVIORAL SLEEP MEDICINE INTERVENTIONS FOR RESTLESS LEGS SYNDROME AND PERIODIC LIMB MOVEMENT DISORDER

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. Since these earliest accounts, diagnostic criteria for the condition have been established and refined. In the most recent version of the International Classification of Sleep Disorders, RLS is grouped with other movement disorders of sleep. 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, 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 age, the diagnosis is less clear because of the variability in symptoms. However, RLS can be distinguished from other movement disorders by the fact that it is worsened by inactivity and relieved by movement. RLS is often associated with PLMD, and the two conditions may be present together in some patients. The treatment of RLS is primarily pharmacologic, although behavioral interventions may also be helpful in some patients.

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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...
PERIODIC LIMB MOVEMENT DISORDER AND ITS PHARMACOLOGIC MANAGEMENT

This condition, initially referred to as nocturnal myoclonus, is characterized by nighttime limb movements during sleep. Sydmonds described the condition in 1953. Unlike RLS, no discomfort in the limbs is necessary for the diagnosis of PLMD. Patients might be completely unaware of the presence of these movements, were it not for a bed partner’s complaints. Of course, many patients who have limb discomfort (of any kind) may also have comorbid PLMD. These patients may or may not meet diagnostic criteria for RLS. Most patients who have RLS also have PLMD. PLMD is closely related to periodic limb movements of sleep, with one significant difference: patients who have PLMD have a sleep complaint, such as insomnia or daytime sleepiness.

PLMD is a relatively uncommon disorder. One study estimated that 3.9% of the adult population has PLMD, but these cases were identified by self-report and were not confirmed with polysomnography. PLMD can also occur in children. A 2004 case series suggested that 23% of prepubertal children presenting to a sleep disorders clinic had periodic limb movements on polysomnography. As with sleep-disordered breathing, the consequence of nighttime sleep disruption in a pediatric patient may not result in sleepiness, but rather in behavioral concerns. Specifically, symptoms of attention deficit hyperactivity disorder seem to be common in pediatric patients who have nocturnal sleep disruption from PLMD.

PLMD is diagnosed through a combination of history along with polysomnographic data. Again, it is most often a bed partner’s observation that a patient moves during the night. Particularly astute bed partners may notice that the movements are more likely to occur in the first half of the night. Non–rapid eye movement (NREM) sleep, when leg movements are far more common than in REM sleep, predominates in the first half of the night. There is variability in the timing of these movements, however, and many patients’ movements may continue throughout the entire sleep period.

On polysomnography, surface EMG activity from limb leads is recorded during the night. Using criteria recently established by the AASM, a limb movement can be scored if it has a duration of 0.5 to 10 seconds and has at least an 8 microvolt increase over the baseline resting EMG amplitude. If four of these movements occur within 5 to 90 seconds, the movements can be scored as a periodic leg movement series (PLMS). A PLMS index of greater than 15 movements per hour in adults and greater than 5 in children should arouse suspicion for PLMD. By strict criteria, movements that are precipitated by respiratory disturbances (such as apnea) should not be scored, and movements in this setting should not be considered periodic leg movement disorder. There is ongoing and considerable debate about whether disease severity, as assessed by PLMS index, has any correlation to patient complaints.

Correlative movements to this EMG activity can sometimes be witnessed using video monitoring. Classic clinical reports have characterized these movements as a partial or complete triple flexion response, with extension of the great toe, dorsiflexion of the ankle, and occasional flexion of the knee and hip. The movements, however, can often be more vigorous, causing significant disruption to a bed partner’s sleep.

Much has been written about clinical significance criteria for PLMD and how many if not most of these cases do not rise to this level and do not require treatment. Clinical judgment is often a guide in these cases. If these limb movements are uncovered on polysomnography that is otherwise devoid of other obvious causes for daytime sleepiness, then they should certainly be addressed. Many times, however, limb movements on PSG are simply incidental and do not require treatment.

Because it can be difficult to determine if the limb movements noted on polysomnography are incidental to sleep complaints, or if they are germane, treatment of PLMD can be more complicated than for RLS. If there is an identified cause of the PLMD (ie, arthritis, RLS), then treatment of the primary condition is recommended. The 2004 AASM guidelines consider treatment of RLS and
periodic limb movements of sleep to be one and the same.20 The recommendations discuss a host of treatments, but ropinirole and pramipexole have since become leading agents in treatment of PLMD. Occasionally, several agents might be tried before an effective one is identified. In the absence of limb discomfort, judging treatment efficacy can be somewhat challenging. Again, a bed partner’s reports are important to judge efficacy, as are patient reports of any improvements in sleep continuity or daytime sleepiness or fatigue.

BEHAVIORAL SLEEP MEDICINE INTERVENTIONS FOR RESTLESS LEGS SYNDROME AND PERIODIC LIMB MOVEMENT DISORDER

Behavioral sleep medicine (BSM) approaches to RLS and PLMD do exist, but the level of empiric support for their use is less complete than the body of evidence that exists for the use of BSM interventions in chronic insomnia, pediatric sleep disorders, and even continuous positive airways pressure adherence. Nonetheless, some BSM principles are already embedded in the existing treatment guidelines for RLS and PLMD. As conditions that tend to be chronic, RLS and PLMD are also appropriate targets for chronic disease management interventions with which practitioners in general behavioral medicine are familiar. There are also some data that support the direct and targeted treatment of RLS/PLMD with cognitive and behavioral interventions, some being specific to BSM and others coming from general behavioral medicine.

Although pharmacologic management is the standard of care for both RLS and PLMD, treatment guidelines and algorithms and patient information pamphlets highlight several nonpharmacologic suggestions. These are most well developed for RLS, but most of the suggestions apply to PLMD also. The list of such approaches/suggestions can be extensive and detailed.21 They include eliminating medications that may cause or exacerbate RLS symptoms, especially dopamine-blocking agents (eg, neuroleptics), but also antiemetics and antihistamines (found in many over-the-counter allergy and sleep aids), and avoiding antidepressants that may cause or exacerbate periodic limb movements, especially the selective serotonin reuptake inhibitors. Other suggestions include maintaining a healthy weight and diet, getting moderate exercise, using support groups, and taking a hot bath, cold shower, or brief walk before bedtime. With the exception of exercise (see later discussion), none of these suggestions is based on anything other than anecdotal reports. The suggestions also usually mention some version of using good sleep hygiene.

Concerning sleep hygiene for RLS/PLMD, there are a two main points that bear highlighting. First, the avoidance of alcohol, caffeine, and nicotine should be underscored because of their potential contributions to RLS symptoms or PLMD. Second, other sleep hygiene practices may or may not have any usefulness for patients who have RLS/PLMD. Particularly when sleep hygiene is provided to patients as a handout or pamphlet, there is no indication that this helps promote sleep in any patient group. It is important for providers not familiar with delivering BSM interventions to know that sleep hygiene has little to no demonstrated efficacy as a monotherapy for insomnia. Moreover, even when it is delivered as part of a multipronged intervention, sleep hygiene as a psychoeducational therapy is an active process with patient–provider interaction, goal-setting, between-session homework assignments, and follow-up. In addition, it is equally important to note that some sleep hygiene or tips for good sleep include in them a suggestion that is not considered a sleep hygiene instruction, but a stimulus control instruction. In particular the suggestion to use the bedroom only for sleep and sex is a stimulus control instruction (without providing rationale for and complete instructions for stimulus control) and is in direct conflict with the suggestion to maintain a regular bed and wake time that is often an item on the same list. This suggestion is confusing to patients who may consistently go to bed at a regular time to abide by the latter instruction, regardless of whether they are sleepy, and get up at the same time each morning, despite waking much earlier than their rise time. In such cases, following good sleep hygiene may actually contribute to the development or maintenance of insomnia. A thorough BSM approach to sleep scheduling for patients who have RLS/PLMD is a much preferred approach than the standard sleep suggestions provide.

The treatment of comorbid insomnia or insomnia-like presentations in RLS/PLMD can be directly targeted with the cognitive-behavioral therapies for insomnia (CBT-I) that are the focus elsewhere in this issue.38 As with many medical and psychiatric conditions, RLS/PLMD may directly precipitate insomnia or directly exacerbate pre-existing insomnia. One manner by which this may occur is that when nocturnal RLS symptoms or periodic limb movements lead to repeated full awakenings, one or more such awakenings may lead to lengthy wake times and difficulty reinitiating sleep. As is the case with going to bed before being sleepy and remaining in bed for more than
15 to 20 minutes following final awakening in the morning, these can set the stage for excessive time in bed relative to total sleep time, and potentially to conditioned arousal as seen in psychophysiological insomnia. In one study, patients who had PLMD did not differ from primary insomnia patients in sleep hygiene factors (reading in bed), stimulus control behaviors (lying awake in bed), cognitive arousal, and physical arousal, whereas both groups differed significantly from normal sleepers on each of these domains. For patients who have PLMD there can thus be an insomnia-like presentation. In such cases, or when comorbid insomnia is diagnosed in RLS or PLMD, CBT-I should be considered.

To date, there has been only one controlled trial of CBT-I in RLS/PLMD. In this study by Edinger and colleagues, patients who had PLMD were randomly assigned to receive four weekly sessions of CBT-I or 4 weeks of clonazepam at 0.5 to 1.0 mg. Both groups had significant improvements in self-reported sleep variables with no between-group differences, except that the CBT-I group had significantly more reductions in daytime napping and the clonazepam group had significantly more reductions in periodic limb movement arousals. One consideration when delivering CBT-I is the possibility that sleep deprivation can worsen RLS. If this is a concern, then the sleep restriction component of CBT-I may be modified to limit this possibility by replacing it with sleep compression. On the other hand, in the seminal study of sleep restriction therapy for insomnia, two study participants who had both RLS and PLMD demonstrated significant improvements in sleep with no reports of increased RLS symptoms. Overall, CBT-I, with some potential modifications on a patient-specific basis, can be considered a potentially promising approach to both RLS and PLMD with further empiric work clearly needed.

The role of exercise remains a somewhat confusing topic with respect to RLS/PLMD. Moderate exercise is often suggested for RLS. This suggestion is based on several factors. First, RLS symptoms tend to increase with prolonged inactivity and to be alleviated with physical activity. On the other hand, some individuals report exacerbation of symptoms with exercise. Specific findings on the topic have been mixed with one study showing an increased risk for RLS associated with physical activity before bedtime and another showing an increased risk for RLS associated with lack of exercise. The discussion is aided by the existence of two randomized controlled trials of exercise therapy. The first such study was a crossover trial conducted in patients who had PLMD subsequent to spinal cord injury in which participants received 200 mg L-DOPA and 50 mg benserazide for 30 days or exercise on an ergometer three times a week for 45 days. Despite the limitations of this design and the small sample size, both treatments resulted in significant reductions in PLM index from 35.1 to 19.9 for L-DOPA and from 35.1 to 18.5 for the exercise program. Such studies bear replication in other RLS/PLMD populations.

The second exercise study was conducted in 23 patients who had RLS who were randomized to receive a 12-week trial of exercise therapy or a control condition. Both groups received basic instructions in lifestyle management that included cigarette and alcohol cessation, avoidance of excessive caffeine, and proper sleep hygiene, with no specific goals being set and no follow-up on these suggestions. The exercise intervention consisted of lower body resistance training exercises and 30 minutes of treadmill walking, which took place three times per week for 12 weeks at a local community center (participants were free to do more or less than instructed). Compared to the control group, the exercise group achieved significant reductions in RLS symptom severity at a 6-week assessment, which was maintained at the 12-week assessment. Notably, the control group had no improvements from baseline at either time point, an indirect test of the usefulness of lifestyle instructions for RLS. Although these are small trials, they begin to clear up some confusion with respect to exercise and suggest that an exercise program (as opposed to a suggestion to exercise), may be a promising approach to managing RLS/PLMD.

Although spontaneous, episodic, or treatment-specific remission of RLS/PLMD does occur, for many patients these are chronic conditions. Comprehensive nonpharmacologic approaches to other chronic diseases, either independent from or in concert with pharmacologic interventions, share some similarities with treatments for RLS/PLMD. For instance, one such approach, albeit untested in any controlled fashion, exists for RLS in the form of a patient guide that greatly expands the standard suggestions for RLS. In addition, Hornyak and colleagues have recently published results of an uncontrolled trial of CBT for RLS. In this preliminary study, 25 participants who had RLS (15 medicated and 10 unmedicated) took part in a weekly 90-minute group therapy sessions for 8 weeks. The intervention included modules on psychoeducation about RLS symptoms and treatments, mindfulness-based breathing relaxation, cognitive therapy for sleep disturbances, stress-reduction and coping...
strategies, cognitive therapy for depression, and identifying and managing individual triggers for RLS. Overall, participants reported significant improvements on subjective scales of RLS severity and quality of life (including satisfaction with sleep) at posttreatment and these gains were maintained at a 3-month follow-up assessment. Although further work is needed in this area, this study provides the first evidence that a comprehensive behavioral medicine approach can be implemented with positive outcomes for patients who have RLS.

SUMMARY

RLS and PLMD are most often treated pharmacologically as is suggested by standards of practice. Although treatment algorithms and patient materials do highlight the use of nonpharmacologic approaches, these are seldom delivered in any systematic or rigorous manner. Nonetheless, several behavioral sleep medicine approaches are available to assist in the management of RLS/PLMD. The first and perhaps most obvious use of a BSM approach in these conditions is in the case of diagnosed comorbid insomnia or the presence of several insomnia-like symptoms, wherein CBT-I would be indicated. Due caution is noted in using the all-too-pervasive lists of sleep hygiene and sleep tips as “hand-out” therapies. Except when such services are not available, there is little rationale for providing sleep hygiene instructions alone apart from multicomponent CBT-I. Second, the recent evidence supporting exercise therapy for PLMD and RLS and comprehensive CBT for RLS highlight their potential usefulness. Third, BSM and general behavioral medicine strategies can target lifestyle factors contributing to pathophysiology. Fourth, similar behavioral medicine approaches can be undertaken to help patients cope with their conditions using a model of chronic disease management. In addition, any or all BSM approaches may be useful for patients experiencing augmentation or tolerance to medications, and accordingly during a drug holiday.

The use of BSM approaches in RLS and PLMD represent not only an underused set of strategies that can be delivered to patients but also an area with several empiric questions to be addressed. Most, if not all, of the BSM interventions reviewed require additional support before being considered evidence-based treatments. Exercise therapy and comprehensive CBT, in particular, deserve some further assessment in randomized, controlled trial designs. There is also ample opportunity to assess various combinations of therapies, including modifying CBT-I to include exercise therapy or components of CBT for RLS. Similarly, research designs that could evaluate these BSM approaches as adjuvants to standard medication management would be informative.

In sum, it is incumbent on the sleep medicine field to more fully include BSM approaches in the management of RLS and PLMD. The emerging findings suggest that patients may benefit from a more multidisciplinary approach than is typically the norm, while underscoring the importance of conducting additional clinical research in this area.

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