Just the Berries

Restless legs syndrome

John Hickey, MD

Restless legs syndrome (RLS) and periodic limb movement disorder (PLMD) are commonly seen in family practice. To review management of this problem, I searched MEDLINE back to 1996 and found 31 articles, using "restless legs syndrome" as the key word. Most of the studies had few patients. There were no meta-analyses, but there was a review article in *Sleep*[1] in which the authors had done a thorough search of the literature to April 1998. They had found that about half the studies used controlled methods, most commonly crossover methods with randomized subject allocation. Multicentre studies with large numbers of subjects and long-term controlled studies were not found. Bandolier (a National Health Service publication offering bullet points of evidence-based medicine) reviewed four well-conducted studies on use of pergolide for managing RLS.

Restless legs syndrome is an awake phenomenon characterized by an intense and irresistible urge to move the legs. It is often associated with paresthesias, motor restlessness, worsening symptoms at night, and relief with activity. It might be idiopathic or found in association with many other disorders, such as renal failure or Parkinson's disease. Although no definite etiology is known for RLS, supportive evidence shows that RLS is a central nervous system dysfunction involving the descending dopaminergic pathways. It can also occur with spinal disorders.

Periodic limb movement disorder is an asleep phenomenon characterized by periodic episodes of repetitive and highly stereotypic limb movements. Diagnosis is usually confirmed with polysomnography.[2]

Researchers estimate that RLS affects from 5% to 15% of the general population and occurs at a mean age of 27.2 years and before age 20 in 38.3% of patients.[3] It is often unrecognized and misdiagnosed. Diagnosis is clinical, and only rarely is polysomnography required. Symptoms often appear in one leg only, but involve upper limbs in about half of all cases. Most patients (94%) report sleep-onset insomnia. Of the 127 patients in the study, 80 (63%) reported that at least one of their first-degree relatives had RLS.

The condition is usually primary and treatable, but before medication is started, secondary causes should be sought, especially iron deficiency[4] (level 3 evidence) and peripheral neuropathy. When the source is an accompanying factor or condition, the syndrome might be curable.

The American Academy of Sleep Disorders has recently published standards of practice for managing RLS.[2] They emphasize that pharmacologic therapy should be used only for patients who meet the diagnostic criteria, especially those who

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Dr Hickey *is a family physician at St Martha's Regional Hospital in Antigonish, NS, and editor of "Just the Berries" for Family Physicians.*

experience insomnia or excessive sleepiness that is thought to occur secondary to RLS or PLMD. Because of the potential toxicity of some of the agents, it is important to monitor patients regularly.

No level 1 evidence supports use of any of the following agents for RLS. Most of the recommendations are based on level 2 to 5 evidence.

Levodopa is the agent most thoroughly studied. Dopaminergic treatment with L-dopa has proven the treatment of first choice for patients with RLS (level 2, 3, and 5 evidence). Unfortunately, augmentation of symptoms and end-of-dose rebound phenomena with L-dopa or decarboxylase-inhibitor treatment present severe problems for some patients.

Four recent studies on use of the dopamine agonist pergolide present level 2 evidence that it might be superior to L-dopa, giving good relief of symptoms with fewer side effects,[5-8] although it does have side effects, such as nausea, dizziness, and insomnia. Daytime augmentation occurred in 27% of patients, but it was mild and usually easily controlled with a supplementary afternoon dose of pergolide. Tolerance did not develop. Dosages for pergolide ranged from 0.05 to 0.65 mg/d.

Oxycodone and propoxyphene have been used for RLS and PLMD (level 2 and 5 evidence, respectively). Problems with side effects and risk of misuse must be considered with these agents. Carbamazepine has been used for RLS (level 2 evidence). Patients must be monitored for risk of bone marrow suppression. Clonazepam has been used for PLMD with some effect (level 2, 3, and 5 evidence), although mixed results have been reported with benzodiazepines. Gabapentin has been used for RLS, but there is limited level 5 evidence for this recommendation.[9] Iron is effective for patients who are iron deficient[4] (level 3, 4, and 5 evidence).

The Academy made no recommendations with respect to treatment of pregnant women or children with RLS.

It would appear that, although evidence is not conclusive for use of any of these agents, pergolide could be a reasonable alternative to L-dopa when side effects are encountered. There can be problems with long-term use of dopaminergic agents, so before committing patients to them, neurologic consultation might be considered. It is also important to rule out underlying disorders: treating them might reduce the symptoms of RLS.

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