Let Frequency, Pain Guide Restless Legs Treatment

BY JOHN R. BELL
Associate Editor

BALTIMORE — In the decision of which drug to prescribe a patient with restless legs syndrome, the frequency and painfulness of symptoms are crucial to making the correct choice, Dr. Christopher J. Earley said at a neurology meeting sponsored by Johns Hopkins University.

"For [75%]-80%, depending on the population that you deal with, pain is not what they experience," said Dr. Earley, a neurologist at Johns Hopkins. A far greater portion instead describe their RLS as uncomfortable, he said. But for those with painful RLS, that pain must be treated. "So I tend to use the antiseizure medications [e.g., gabapentin, lamotrigine, pregabalin] or the opiates as my first line of treatment, as opposed to the dopamine [DA] agents, when I'm dealing with painful symptoms," he said. If it's partially responsive…then I will consider the dopamine agonists. If I really get desperate…I might consider sedation."

For painless nightly RLS, he advises a DA agonist as first-line therapy, opiates as a second-line choice, and sedatives as third-line treatment. Frequent painless RLS (2-3 nights per week) warrants a sedative first, followed by opiates and, if those fail, levodopa. For occasional RLS (less than twice per week), he advises either a half or whole tablet of carbidopa 25 mg/levodopa 100 mg (available as Sinemet and Parcopa brands) as needed for first-line therapy.

"This is going to be effective in 99.9% of patients, barring side effects like nausea," he said. He recommends a DA agonist and a sedative as second- and third-line treatment, respectively. Drugs that can aggravate RLS include neuroleptics and antiemetics, as well as SSRIs and tricyclic antidepressants (except for bupropion and trazodone) and antihistamines.

A disadvantage of the DA agonists is that they take 2 hours to reach peak dose effect (3 hours if taken with a meal or after symptom onset), compared with 30-60 minutes for opiates. Thus dopamine agonists are most useful for situations such as airplane flights, he said, but less practical for nighttime RLS. Dr. Earley favors levodopa for occasional nonpainful RLS. "If you have any doubts about whether this is RLS or not RLS, you can use the levodopa"-carbidopa combination (carbidopa 25 mg/levodopa 100 mg) of half to 1½ tablets for 3 days. "If they get no real benefits from that, this is not RLS—at least not the RLS that I know."

The DA agonists do have other disadvantages besides their delayed effect, Dr. Earley noted. They can cause compulsive behaviors—though this has been observed more in patients with Parkinson's disease than with RLS. They also can cause hypersomnia. "It's almost like narcolepsy," he said. Moreover, DA agonists risk the phenomenon of augmentation, whereby an increase in dosage leads to an increase in symptoms, so that a patient is treated effectively for a time period in which RLS occurs (e.g., bedtime), but then the RLS begins to occur either before or after the treated period. "Augmentation is the single biggest reason why you have to stop this drug," Dr. Earley warned. He consulted on the case of a woman whose RLS progressed over the course of 2 years from initially requiring one dose of Sinemet nightly "to taking Sinemet every hour on the hour, and she was only getting 2 or 3 hours of sleep."

He advised that when patients taking a DA agonist for sleep complain of RLS symptoms before or after bedtime, the physician should not prescribe additional drug. As long as the patient can sleep without RLS awakening them or interfering with their falling asleep, RLS symptoms at other times of the day are not worth medicating. They are free to walk around in the evenings and the primary lifestyle problem of RLS interference with sleep is still under control, he said.

Notably, opiates do not pose augmentation risk, he said. With opiates, "you're going to get about 85% of them up walking away relatively happy." Options in this drug category are codeine, propoxyphene, controlled-release oxycodone, methadone, and the fentanyl patch. Dr. Earley observed that methadone is by far the least expensive, at approximately $.05 per dose.

Iron deficiency has been implicated as a possible cause of RLS, he noted. "I check ferritins in everybody," he said. Deficiency is defined as less than 18 ng/mL or iron saturation less than 16%. He recommends ferrous sulfate 325 mg plus 200 mg vitamin C or orange juice, to be given on an empty stomach in the absence of calcium or milk. ■