

In Restless Legs Patients, Consider And Treat Symptoms of Depression

BY JANE SALODOF MACNEIL
Southwest Bureau

SANTA ANA PUEBLO, N.M. — People with restless legs syndrome were three times more likely to have a major depressive disorder in a study of 1,071 Baltimore residents reported by Dr. Hochang Benjamin Lee at the annual meeting of the Academy of Psychosomatic Medicine.

Investigators from Johns Hopkins University in Baltimore found major depressive disorder in 8 of 42 patients (19%) diagnosed with restless legs syndrome (RLS). Only 8.4% of those without RLS met the DSM-IV criteria for depression in diagnostic interviews.

"Depression and anxiety are common in RLS, and vice versa," said Dr. Lee of the Neuropsychiatry and Memory Group at Johns Hopkins. Previous population-based studies suggested a connection, but the new study is "probably the most definitive."

Dr. Lee described numerous overlaps between the two disorders, both of which are diagnosed on the basis of subjective reports from the patient. He said the two conditions have similar prevalence in the community, occur twice as often in women as in men, present with diurnal variation, and tend to run in families. Both also have a high placebo response rate in treatment trials.

Additionally, six of the nine symptoms that the DSM-IV lists for major depressive disorder are common in RLS patients, according to Dr. Lee, citing depressed mood, diminished interest, fatigue or loss of energy, diminished concentration, psychomotor retardation, and insomnia or excessive sleepiness.

Noting that no guidelines exist for managing depression in RLS patients, Dr. Lee recommended the following strategy:

- ▶ If an RLS patient presents with mild depression or dysthymia, treat the RLS first and see whether mood-related symptoms improve. If the patient continues to have depressive symptoms, treat these as well.
- ▶ If a severe major depressive disorder occurs along with mild RLS, treat the de-

pression first, preferably with agents that are *not* SSRIs or tricyclic antidepressants.

▶ If both RLS and depression are severe, however, consider treating the conditions simultaneously, but avoid using most dopamine agonists for RLS because of the possibility of the rare side effect of psychosis.

"Careful consideration is needed for treatment of major depressive disorder in patients with restless legs syndrome," Dr. Lee warned.

He ruled out many medications, saying that SSRIs and tricyclic antidepressants should be avoided whenever possible. Both can exacerbate periodic limb movements, which occur in 80%-90% of RLS patients, noted Dr. Lee.

Dr. Lee suggested nefazodone, trazodone, and bupropion as alternatives. These agents have not been reported to exacerbate periodic limb movements, he said, and they may produce improvement. Mirtazapine is sometimes recommended for depression in RLS patients, he added, but reports are conflicting.

Regarding adjunctive treatments for RLS, he said that antipsychotic medications generally exacerbate the syndrome.

While atypical antipsychotic agents are less likely to do so, he said there have been reports of risperidone, quetiapine, and olanzapine worsening RLS.

Aripiprazole might be worth

a trial in this movement disorder, given that it is a partial dopamine agonist.

Anticonvulsants do not usually worsen RLS symptoms, according to Dr. Lee. He described gabapentin and carbamazepine as "viable alternatives" for treating RLS. Valproic acid and lamotrigine also may be helpful, he said, but anecdotal reports suggest lithium can exacerbate RLS and periodic leg movements.

Benzodiazepines, particularly clonazepam, may be used as an adjunctive RLS treatment, Dr. Lee said. No data are available on cholinesterase inhibitors, however, and he warned that antihistamines such as Benadryl are poorly tolerated in this patient population.

Dopamine agonists are increasingly an option for treatment of RLS, but Dr. Lee said ergot-derived dopamine agonists should be avoided. He cited the possibility of heart valve abnormalities and other side effects. Instead, he suggested a trial of dopamine agonists that are not derived from ergot such as pramipexole and ropinirole.

Dr. Lee added, however, that high doses of dopamine agonists have been linked to hallucinations, compulsive gambling, and psychiatric side effects in Parkinson's disease patients. He expressed concern that widespread use will result in new issues for psychiatrists consulting on RLS patients. ■

MDs May Be at High Risk for Parkinson's

BY MARY ELLEN
SCHNEIDER
Senior Writer

Physicians and individuals with 9 or more years of education are at an increased risk of developing Parkinson's disease, according to a study by Dr. Roberta Frigerio of the Mayo Clinic in Rochester, Minn., and her colleagues.

Dr. Frigerio conducted the research at Mayo while on leave from the University of Milano-Bicocca, Monza, Italy.

Individuals such as construction and extractive workers, production workers, metal workers, and engineers who have more physically demanding jobs are at a reduced risk for the disease, the researchers found (*Neurology* 2005; 65:1575-83).

The researchers examined the education levels and occupations of 202 individuals in Olmsted County, Minn., who developed Parkinson's disease from 1976 through 1995.

Each case was matched by age and sex to a general population control who was free of Parkinson's disease and living in the same county. Of those individuals, they were able to obtain medical records for 196 cases and 196 controls. In ad-

dition, they obtained data from telephone interviews available for 149 cases and 129 controls.

But the findings should not be a cause for alarm among physicians or those with higher levels of education, said Dr. Demetrius Maraganore, a professor of neurology at the Mayo Clinic and one of the study authors, in an interview.

The number of physicians in the study was small and therefore the effect size is unstable.

"Parkinson's disease is a thousand-piece puzzle," Dr. Maraganore said.

More research is needed to figure out what these findings mean. For example, the findings could mean that being a physician is an indirect marker for other environmental factors.

Or it could be that being a physician or having more education are not risk factors at all, he said.

Instead, additional years of schooling and becoming a physician could be early manifestations of the disease, which affects personality and behavior.

A deficiency of dopamine could shape personality in a way that makes a person more inclined to sit at a desk and study, he said.

Hallucinations Foretell Parkinson's Progression

BY BETSY BATES
Los Angeles Bureau

SAN DIEGO — So-called benign hallucinations associated with dopaminergic treatment for Parkinson's disease rarely remain "benign," calling into question the accuracy of the term.

Researchers at Rush University in Chicago studied the clinical progression of 48 patients with Parkinson's disease who were diagnosed with hallucinations characterized by the patient's retention of the insight that the hallucinations are unreal.

These hallucinations have been called benign, and traditionally have been associated with a score on the Unified Parkinson Disease Rating Scale (UPDRS) of 2.

In 2 years, just 2 of the 48 patients at Rush continued to have benign hallucinations without requiring either a decrease in their dose of dopaminergic medications or an addition of neuroleptic agents to counteract the hallucinations or pro-

gressing to more serious hallucinations with loss of insight (UPDRS Thought Disorder score of 3) or to delusions (UPDRS Thought Disorder score of 4).

Most patients, 39 of 48, progressed to scores of 3 or 4.

Among nine patients who remained at a score of 2, seven required reduced dopaminergic medication doses in response to worsening hallucinations, and three required neuroleptics to control the hallucinations.

Although the median time to progression of hallucinations to the point where patients were frankly delusional was less than 2 years after the onset of the study, the total length of time that patients were suffering from hallucinations prior to enrollment in the study was not

certain, reported Dr. Christopher G. Goetz, director of the Rush movement disorders center, in a poster presentation at the annual meeting of the American Neurological Association.

However, the study made clear that even if hallucinations seem "benign . . . at the moment," they "portend serious consequences" and should not be given a label that suggests they are unimportant clinical developments, he said.

"Because hallucinations progress, the concept of benign hallucinations is prognostically misleading," Dr. Goetz and his associates said.

"The term benign hallucinations should be considered generally unsound and dropped from the operative vocabulary," Dr. Goetz and associates concluded. ■

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