Dopamine Agonists Aid Sleep in Restless Legs

BY HEIDI SPLETE
Senior Writer

MINNEAPOLIS — Two dopamine agonists—pramipexole and ropinirole—each improved symptoms and quality of life in adults with restless legs syndrome, based on data from studies presented at the annual meeting of the Associated Professional Sleep Societies. Both drugs are approved by the Food and Drug Administration for the treatment of restless legs syndrome.

Patients with restless legs syndrome (RLS) often report uncomfortable sensations deep in their legs accompanied by irresistible urges to move their legs. The symptoms worsen at night and tend to disrupt sleep, which has a negative impact on patients' quality of life.

Data from three randomized, double-blind, placebo-controlled studies of pramipexole showed that those who received the drug reported significant improvements in quality of life and in RLS symptoms, compared with placebo patients. The dosage used in the three studies ranged from 0.125 mg/day to 0.75 mg/day. The studies included a total of 784 adults (aged 18-79 years; average age 51 years); all patients met the diagnosis for RLS and had at least one postbaseline evaluation. All three studies were supported by Boehringer Ingelheim Pharmaceuticals Inc.

In the largest of the three studies, the 258 patients randomized to receive pramipexole for 12 weeks reported significant improvements in sleep quality, shorter time to fall asleep, and improved daytime symptoms, compared with 86 patients who received a placebo. Based on visual analog scale scores, daytime symptom severity improved by 49% in the pramipexole group, compared with 32% in the placebo group, and pramipexole patients reported an average of 57% improvement in sleep satisfaction, vs. 38% in the placebo group. The study was conducted by Dr. Robert D. Ballard of the University of Colorado Health Sciences Center in Denver.

Pramipexole did not increase daytime sleepiness, compared with placebo, across these three studies. In fact, the pramipexole patients who reported abnormal daytime sleepiness at baseline reported significant improvement in daytime sleepiness, compared with placebo patients, based on the Epworth Sleepiness Scale. No significant differences appeared in daytime sleepiness among patients in the two groups that reported normal levels of daytime sleepiness at baseline.

In a pair of similar studies of ropinirole, presented by Dr. Markus H. Schmidt of the Ohio Sleep Medicine Institute in Dublin, Ohio, the drug significantly improved the symptoms of restless legs syndrome and improved patients' quality of life in a randomized trial with an intent-to-treat population of 382 adults with RLS. The daily dose ranged from 0.5 to 6.0 mg, titrated as needed. Dr. Schmidt has received financial support from and has served as a speaker for GlaxoSmithKline, the company that supported the research.

After 12 weeks, the 187 patients who received ropinirole reported significantly greater improvements in symptoms, compared with the 195 placebo patients, in four areas of the Medical Outcomes Study Sleep Scale (reduction in sleep disturbance, reduction in daytime sleepiness, increased sleep adequacy, and increased sleep quantity). Adverse events were mild to moderate, and only 4% of the ropinirole patients and 3% of the placebo patients discontinued the medications because of adverse events. The most often reported adverse events in the ropinirole group vs. the placebo group were nausea (28% vs. 7%), headache (20% vs. 18%), and sleepiness (9% vs. 6%).

After treatment, nearly half (49%) of the ropinirole patients were classified as "not ill" or "borderline ill," compared with 31% of placebo patients, based on a clinician-rated scale. In addition, significantly more patients showed improvement in illness based on a patient-rated scale at 2 days, 3 days, and 4 days after starting treatment. On day 4, 42% of the ropinirole patients were classified as responders, compared with 24% of the placebo patients. ■

Vigilance Impaired in Drivers With Obstructive Sleep Apnea

BY AMY ROTHMAN SCHONFELD
Contributing Writer

BOSTON – People with obstructive sleep apnea syndrome showed poorer vigilance while driving than did normal controls, a result that could not be predicted by pretest measures of disease severity or subjective reports of sleepiness, according to a poster presented by Dr. Jon Tippin at the annual meeting of the American Academy of Neurology.

"[Obstructive sleep apnea syndrome] can now be added to the list of diseases, including dementing illnesses like Alzheimer's disease and Parkinson's disease, that cause vigilance problems [during driving]," said Dr. Tippin, a neurologist at the University of Iowa, Iowa City.

Vigilance was assessed using the Simulator for Interdisciplinary Research in Ergonomics and Neuroscience (SIREN), an interactive driving simulator adapted from a car fitted with projection screens in front of and behind the driver. Drivers were asked to respond by clicking the high-beam control as soon as they detected light targets flashed at unpredictable temporal intervals (average one per minute) at seven locations across the forward horizon. Hit rates (HR) and reaction times (RT) were the outcome measures. The hour-long test was administered in the late afternoon.

The overall hit rate was lower in drivers with obstructive sleep apnea syndrome (OSAS) (n = 25) than in normal controls (n = 41) ($P = .018$).

The data also suggested that peripheral targets were more likely to be missed by people with OSAS than were those located in the central field of vision ($P = .0862$). "These people do not have visual field impairments but rather they show inattention to things in the peripheral field. As [drivers] becomes more inattentive, they focus more on the things right in front of them," said Dr. Tippin.

Although slower reaction times predicted poorer driving performance in all drivers (P is less than.03), there was no difference in mean reaction times between the groups.

People with OSAS were not sleepier than controls before the test, as indicated by the predrive Stanford Sleepiness Scale test. OSAS drivers were sleepier than controls at the end of the drive ($P = .027$), but only in OSAS drivers did the increased sleepiness correlate with poorer vigilance (as measured by lower hit rates, $P = .0135$). Objective tests of sleepiness, such as polysomnography and the Multiple Sleep Latency Test done on the evening of and day after the drive, respectively, also did not correlate with vigilance or driving performance.

"For patients with OSAS, the problem is less one of falling asleep than maintaining attention," said Dr. Tippin.

Factors such as age, obesity, and a sedentary lifestyle raise the risk for OSAS.

For truck drivers, many of whom have several of these risk factors, the likelihood of OSAS may be elevated to four times that of the general population, said Dr. Tippin. Sleep deprivation and fragmentation may compound the problem in this population.

Stakeholders such as the Federal Motor Carrier Safety Administration (FMCSA), the trucking industry, and insurance carriers are working to develop guidelines regarding illness and driving.

Dr. Tippin suggested that OSA should be added to the list of conditions that compromise driving capability. ■

Screen Arnold-Chiari Patients for Sleep-Related Breathing Problems

BY HEIDI SPLETE
Senior Writer

MINNEAPOLIS — Adults with Arnold-Chiari type I malformations are at greater risk for sleep-disordered breathing, compared with healthy controls, based on data presented at the annual meeting of the Associated Professional Sleep Societies.

In light of this finding, "We should be screening all Arnold-Chiari I patients for sleep-disordered breathing," said Dr. Nate Watson, a neurologist at the University of Washington, Seattle.

Snoring, sleepiness, and obesity/hypertension were significantly more common among AC-1 patients than controls, according to questionnaire results.

The displaced brain structures that characterize Arnold-Chiari I (AC-1), a benign developmental brain anomaly, can compress the brainstem, impeding breathing, he said.

To better assess the risk of sleep-disordered breathing in AC-1 patients, Dr. Watson and his colleagues compared 18 women with AC-1 (mean age 36 years) with 35 age- and sex-matched controls.

The researchers used several subjective questionnaires, including the Epworth Sleepiness Scale, to assess sleep-disordered breathing and sleepiness. Based on these results, the AC-1 patients were at significantly greater risk for sleep-disordered breathing, compared with controls (69% vs. 20%). Specifically, the results from the questionnaires showed that three factors—snoring, sleepiness, and obesity/hypertension—were significantly more common among AC-1 patients vs. controls, and occurred in 44% vs. 6%, 78% vs. 46%, and 64% vs. 34%, respectively.

The AC-1 patients were significantly more likely to report other symptoms associated with sleep-disordered breathing, including nighttime choking or gasping and nighttime shortness of breath, compared with controls. And when they woke up, the AC-1 patients also reported sore throats, heartburn, and headaches significantly more often than did controls.

In addition, the AC-1 patients reported sleeping significantly fewer hours (6.3 hours vs. 7.6 hours) and taking significantly longer to fall asleep (61.4 minutes vs. 18.6 minutes), compared with controls

Consider decompressive surgery for patients if respiration is their main complaint, but remember that they need to be followed, said Dr. Watson during the discussion after his presentation. Previous studies indicate that decompression surgery makes a difference. Data from 16 consecutive patients with AC-1 malformations showed a significant improvement in the central apnea index from 14.9 to 1.3 based on full-night polysomnography conducted approximately 200 days after decompression surgery (Neurology 2006;66:136-8).

Future studies of AC-1 patients need to continue to focus on objective measures and comparison of patients before and after decompressive surgery, Dr. Watson said. ■