Fibromyalgia Pain Responds to Pramipexole

BY NANCY WALSH New York Bureau

SAN ANTONIO — The dopamine-3 receptor agonist pramipexole significantly improved pain, function, and fatigue in patients with severe, longstanding fibromyalgia, Andrew J. Holman, M.D., said in a late-breaking abstract session at the annual meeting of the American College of Rheumatology.

In a double-blind, randomized, placebo-

controlled clinical trial that included 60 patients, pain as measured on a 10-point visual analog scale (VAS) improved by 36%, from a mean score of 7.0 at baseline to 4.5 after 14 weeks of treatment with pramipexole. By contrast, patients receiving placebo experienced only a 9% decrease in pain, from 7.54 to 6.82.

At baseline, all patients had fibromyalgia of at least 6 months' duration and a VAS pain score of at least 5.

Exclusion criteria included untreated

sleep apnea, cervical myopathy, uncontrolled psychosis, thyroid disease, and pregnancy. In addition, patients could not have had any prior exposure to dopamine agonists. "I wanted to make this as close to a real-world study as possible, so patients could continue other medications if they were clinically stable and maintained the same dose for 14 weeks," said Dr. Holman, who is a rheumatologist in private practice in Renton, Wash.

Other drugs taken by the patients in-

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cluded anticonvulsants, antidepressants, anxiolytics, and muscle relaxants. Mean disease duration was 8.6 years, and patients had taken an average of 10 different medications during that time.

On study entrance, 24% of the placebo group and 31% of the pramipexole group were clinically disabled. Moreover, 67% of the placebo group and 44% of the active treatment group were taking daily narcotics for pain relief. Only half were working. The pramipexole dose was titrated up to a target of 4.5 mg /day orally at bedtime.

"In terms of measuring efficacy for pain, we generally look at the number of patients who achieve a greater than 50% reduction in pain," he said. This outcome was achieved by 42% of patients in the pramipexole arm compared with 14% of those in the placebo arm.

Moderate or greater improvement on

Pramipexole, a dopamine-3 receptor agonist, is thought to inhibit excessive autonomic stimulation and arousal in the hippocampus' mesolimbic area. the Patients' Global Impression of Change questionnaire was reported by 63% of pramipexoletreated patients, compared with 38% of the placebo patients. Statistically significant improvements were seen on the Fibromyal-

gia Impact Questionnaire and the fatigue and function scores of the multidimensional Health Assessment Questionnaire.

Secondary end points that showed trends toward improvement with the active treatment include tender point scores, the Hamilton Rating Scale for Depression, and the Beck Anxiety Inventory.

"It was interesting to note that no outcomes favored placebo," he said.

Pramipexole, used for Parkinson's disease and restless legs syndrome, is thought to inhibit excessive autonomic stimulation and arousal in the mesolimbic area of the hippocampus. It is not a sedating medication. Rather, its effects on arousal may allow normal stage IV sleep. The result is that "we're not making them sleep; we're allowing them to sleep," Dr. Holman said.

The most pronounced side effect was weight loss, with 40% of the pramipexole group losing between 5 and 35 pounds.

Adverse events associated with pramipexole included increased anxiety, morning somnolence, diarrhea, and vomiting. The hallucinations commonly reported by Parkinson's patients did not occur in this study.

One patient experienced unexpected amnesia that lasted for about 4 hours. She was hospitalized and after 3 days of neural evaluation was discharged without a diagnosis. She wanted to continue in the study and did so without further incident.

One patient in the placebo arm died of causes not related to the study.

Further sleep studies will be needed to more fully elucidate pramipexole's mechanisms of action in the setting of fibromyalgia, he said.

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