

Chronic Fatigue Syndrome Specialists Overburdened

BY MARY ELLEN SCHNEIDER
Senior Writer

WASHINGTON — The National Institutes of Health should increase its support for research into chronic fatigue syndrome in children to match the burden and impact of the illness, Peter Rowe, M.D., said at a meeting of the Health and Human Services Department's Chronic Fatigue Advisory Committee.

More philanthropic support is needed to advance the care of children and adults with chronic fatigue syndrome (CFS), said Dr. Rowe, a professor at Johns Hopkins Children's Center, Baltimore, and director of the center's chronic fatigue clinic.

Currently, few hospital- or university-affiliated clinical centers and no university research centers are treating children with CFS, and only \$1 million annually in NIH funds are targeted at children with CFS, he said.

"This isn't enough to create a critical level of interest in bringing good people into the field, and it does not make CFS seem like a viable option to the new pediatric researcher," Dr. Rowe said.

As a result, it's difficult for CFS patients to find physicians to care for them, Dr. Rowe said. CFS specialists are usually overburdened, and patients are so eager for a timely evaluation that they are willing to pay a premium, he said.

Dr. Rowe said he knows of one place where a patient can be evaluated fairly quickly—but at a price tag of \$5,800. "I think we have a responsibility to protect children and young families from this kind of economic risk," he said.

To be diagnosed with CFS, patients generally must have severe chronic fatigue for 6 months or longer with other known medical conditions excluded by clinical diagnosis, and they must concurrently have four or more of the following symptoms: substantial impairment in short-term memory or concentration; sore throat; tender lymph nodes; muscle pain; multijoint pain with-

out swelling or redness; headaches of a new type, pattern, or severity; unrefreshing sleep; and post-exertional malaise lasting more than 24 hours, according to the Centers for Disease Control and Prevention. The symptoms must have persisted or recurred during 6 or more consecutive months of illness and must not have predated the fatigue.

The heterogeneous nature of the illness itself also makes it difficult to recognize and treat the disease. For example, how CFS affects individual children depends on the child's developmental status, the duration of the illness, as well as the severity of the illness, Dr. Rowe said. And the patient's response to the illness is affected by the quality of support provided by family, friends, and the medical profession, he said.

The heterogeneity also impacts research and many of the current studies are underpowered and much

larger studies are needed to detect efficacy from other changes caused by comorbid conditions, he said. It's also difficult to control for just one variable in a randomized clinical trial on CFS because of the many overlapping and interacting pathophysiological dysfunctions associated with the condition, he said. Dr. Rowe proposes conducting randomized trials by withdrawing ostensibly effective therapies. For example, in an otherwise well-managed and clinically stable patient with CFS, the patient would be randomized to receive either a placebo or the active medication.

Another option would be to incorporate a "run-in period" for studies during which other influences to symptoms are brought under good clinical control before examining the efficacy of a single agent.

For example, Dr. Rowe said he had good results treating one patient with midodrine, but he might not have noticed its dramatic effect on the patient if he had started it before treating her pelvic congestion syndrome, since that condition appeared to have an independent effect on her orthostatic tolerance.

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Talk Therapy Reduces Teens' Chronic Fatigue

BY KATE JOHNSON
Montreal Bureau

Adolescents with chronic fatigue syndrome show significant improvement with cognitive-behavioral therapy, according to the first randomized controlled trial involving this age group.

"These results endorse the findings of previous studies on the efficacy of CBT for adults with chronic fatigue syndrome," reported Maja Stulemeijer and colleagues at University Medical Centre Nijmegen (the Netherlands).

Only one uncontrolled study in adolescents suggests that cognitive-behavioral therapy can reduce chronic fatigue, according to the researchers (BMJ 2005; 330:14).

"We believe that our results can be generalized to other adolescents who fulfill the diagnostic criteria for chronic fatigue syndrome," they noted.

The study followed 69 patients, aged 10-17 years, who met U.S. Centers for Disease Control and Prevention criteria for chronic fatigue syndrome.

Patients were randomized to either immediate therapy, or to remain on a waiting list for therapy. The intervention involved 10 individual sessions over 5 months, and therapy patients underwent one of two treatment protocols depending on whether they were considered active or passive patients.

Active patients were described as alternating between periods of activity and periods of rest;

passive patients were described as spending most of their time lying down and as going out infrequently.

For active patients, treatment started with teaching them to recognize and accept their fatigue and reduce their activity level accordingly. This was followed by a gradual increase in activity.

Passive patients started immediately with a systematic program of activity building. "In such patients it is thought to be counterproductive to reduce activity levels any further or to re-enforce the patient's need to respect limitations," according to the investigators.

Measures of fatigue and functional impairment decreased more significantly in the therapy group, compared with the untreated group. School attendance improved significantly more in the therapy group, with 58% of these patients returning to school full time, compared with 29% of patients on the waiting list for therapy.

Participants in the therapy group also reported significantly less muscle pain, headache, unrefreshing sleep, and impaired concentration. They were also less likely to feel ill after exercise, compared with patients on the waiting list.

There were no significant differences in outcomes between patients in the active or passive treatment protocols. However, the authors noted that patients in all arms of the study continued to report symptoms.

Fibromyalgia Pain Responds to Dopamine-3 Receptor Agonist

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.

"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, a rheumatologist in private practice in Renton, Wash.

Other drugs taken by the patients included 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 pramipexole group were taking daily narcotics for pain relief. 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 the Patients' Global Impression of Change questionnaire was reported by 63% of pramipexole-treated patients, compared with 38% of the placebo patients. Statistically significant improvements were seen on the Fibromyalgia 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, but there was no diagnosis and she returned to the study without incident.