

CARE-HD: Co-enzyme Q10 And Remacemide Evaluation in Huntington's Disease

No New Treatment, But A Useful Lead, From Huntington's Study

August 14, 2001...In the largest clinical study ever of a potential treatment for Huntington's disease, neither of two compounds tested had a statistically significant effect on slowing the progression of the disease. But the study leaves open the possibility that a popular nutritional supplement may help slow the decline of patients, though physicians say more evidence is needed before the treatment can be recommended.

The results of the experimental medication remacemide, under development by AstraZeneca, and coenzyme Q10 (CoQ10), a popular nutritional supplement, are in the August 14, 2001 issue of *Neurology*, the scientific journal of the American Academy of Neurology.

In the study of 347 patients at 23 sites in North America, some patients received remacemide, some received CoQ10, some received both, and some received neither; doctors then monitored their health closely for two and one-half years. Remacemide definitely had no effect on the progression of the disease in patients in the early stages. CoQ10 showed a trend toward slowing the disease an average of 15 percent, with patients able to handle daily responsibilities such as finances and domestic chores longer; patients also retained cognitive skills longer, were able to focus their attention better, and were less depressed and irritable than those not on CoQ10. A 15-percent slowing of decline would roughly translate into about one more year of independence for patients, notes principal investigator Karl Kieburtz, M.D., professor of neurology at the University of Rochester Medical Center.

But the Huntington Study Group that conducted the study, including Kieburtz and co-investigator Walter Koroshetz, M.D., of Massachusetts General Hospital, say there weren't enough patients in the study to say that the slowing of decline was definitive. There's a 15-percent probability that the slowed decline occurred simply by chance. To settle the question, they say a study involving at least 1,500 patients would be necessary.

Because of the odds that the slowed decline occurred simply by chance, the study investigators, along with the Huntington's Disease Society of America, the Huntington Society of Canada, and the Hereditary Disease Foundation, do not recommend that patients take CoQ10.

"This is an interesting lead, but we cannot recommend using CoQ10 without further research. It's premature to make a recommendation until we can define whether there really is a benefit," says Kieburtz.

"Huntington's is a lethal, progressively degenerative disease, and so far nothing has been shown to modify the course of the illness. This is the first real lead we've gotten from more than a dozen Huntington's disease patient trials. We can't ignore it. We've got something to chase," he adds.

Huntington's is an inherited disorder that affects about 30,000 people in the U.S. A genetic mutation results in the death of vital brain cells, resulting in involuntary movements of the limbs or facial muscles known as chorea, problems with coordination, cognitive difficulties, and depression and irritability. Symptoms usually begin in early to mid-adulthood, and patients generally live about 15 to 20 years after diagnosis.

Since there is currently no way to slow the progression of the disease, the findings raise some thorny issues, say the authors. Because the substance causes few side effects and appears to do no harm, there may be little obvious downside for patients to take the compound in the hopes that it slows the disease. But the price for a daily dose of 600 milligrams of CoQ10, which could run as high as \$150 a month at wholesale prices, is a steep one to pay for an effect that may or may not be real, the authors say.

Koroshetz and Kiebertz offer a number of other cautions as well. As a nutritional supplement, the substance is not regulated as closely as a drug, so the quality can vary a great deal from batch to batch. Second, participants in the study received specially formulated wafers, and their effects may differ from those of the standard 30-milligram tablets; a person would need to take 20 tablets each day to receive the same amount of the substance as the study participants. Finally, other compounds can affect how much of the substance is absorbed.

CoQ10 has been shown to help patients with another neurological disorder, familial ataxia, and the substance, though not regulated by the Food and Drug Administration, is used to treat ailments such as heart disease and gum disease. It's an anti-oxidant that helps soak up compounds known as free radicals that do damage to DNA and proteins in our body. The substance is found naturally in nearly all the cells in our body and plays an important role in keeping healthy the mitochondria, the cellular component that supplies cells with energy.

Remacemide is a compound that blocks the type of glutamate receptor that has been suspected of contributing to the death of brain cells in Huntington's patients. The results with remacemide were clear: Patients who received 200 milligrams of remacemide three times a day declined at the same rate as patients receiving no medication.

The study was the first multi-center clinical trial for Huntington's to be funded by the National Institute of Neurological Disorders and Stroke (NINDS). Funding also came from remacemide's developer, AstraZeneca, and by Vitaline Corp., which produces CoQ10.

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Huntington Study Group

The study was conducted by the Huntington Study Group (HSG), which is based at the University of Rochester Medical Center. The study was run through the Department of

Neurology's Clinical Trials Coordination Center and the Division of Experimental Therapeutics, where physicians design and conduct large multi-site studies of potential new treatments for diseases like Parkinson's disease, Huntington's disease, and neurological disorders related to HIV.

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