

Study Suggests Coenzyme Q10 Slows Functional Decline in Parkinson's Disease

For release: Monday, October 14, 2002; National Institutes of Health, Bethesda, Maryland

Results of the first placebo-controlled, multicenter clinical trial of the compound coenzyme Q10 suggest that it can slow disease progression in patients with early-stage Parkinson's disease (PD). While the results must be confirmed in a larger study, they provide hope that this compound may ultimately provide a new way of treating PD.

The phase II study, led by Clifford Shults, M.D., of the University of California, San Diego (UCSD) School of Medicine, looked at a total of 80 PD patients at 10 centers across the country to determine if coenzyme Q10 is safe and if it can slow the rate of functional decline. The study was funded by the National Institute of Neurological Disorders and Stroke (NINDS) and appears in the October 15, 2002, issue of the *Archives of Neurology*.¹

"This trial suggested that coenzyme Q10 can slow the rate of deterioration in Parkinson's disease," says Dr. Shults. "However, before the compound is used widely, the results need to be confirmed in a larger group of patients."

PD is a chronic, progressive neurological disease that affects about 500,000 people in the United States. It results from the loss of brain cells that produce the neurotransmitter dopamine and causes tremor, stiffness of the limbs and trunk, impaired balance and coordination, and slowing of movements. Patients also sometimes develop other symptoms, including difficulty swallowing, disturbed sleep, and emotional problems. PD usually affects people over the age of 50, but it can affect younger people as well. While levodopa and other drugs can ease the symptoms of PD, none of the current treatments has been shown to slow the course of the disease.

The investigators believe coenzyme Q10 works by improving the function of mitochondria, the "powerhouses" that produce energy in cells. Coenzyme Q10 is an important link in the chain of chemical reactions that produces this energy. It also is a potent antioxidant - a chemical that "mops up" potentially harmful chemicals generated during normal metabolism. Previous studies carried out by Dr. Shults, Richard Haas, M.D., of UCSD and Flint Beal, M.D., of Cornell University have shown that coenzyme Q10 levels in mitochondria from PD patients are reduced and that mitochondrial function in these patients is impaired. Animal studies have shown that coenzyme Q10 can protect the area of the brain that is damaged in PD. Dr. Shults and colleagues also conducted a pilot study with PD patients which showed that consumption of up to 800 mg/day of coenzyme Q10 was well-tolerated and significantly increased the level of coenzyme Q10 in the blood.

All of the patients who took part in the new study had the three primary features of PD - tremor, stiffness, and slowed movements - and had been diagnosed with the disease within 5 years of the time they were enrolled. After an initial screening and baseline blood tests, the patients were randomly divided into four groups. Three of the groups received coenzyme Q10 at three different doses (300 mg/day, 600 mg/day, and 1,200 mg/day), along with vitamin E, while a fourth group received a matching placebo that contained vitamin E alone. Each participant received a clinical evaluation 1 month later and every 4 months for a total of 16 months or until the investigator determined that the patient needed treatment with levodopa. None of the

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participants or the study investigators knew which treatment each patient had received until the study ended.

The investigators found that most side effects of coenzyme Q10 were mild, and none of the patients required a reduction of their dose. The percentage of people receiving coenzyme Q10 who reported side effects was not significantly different from that of the placebo group. During the study period, the group that received the largest dose of coenzyme Q10 (1,200 mg/day) had 44 percent less decline in mental function, motor (movement) function, and ability to carry out activities of daily living, such as feeding or dressing themselves. The greatest effect was on activities of daily living. The groups that received 300 mg/day and 600 mg/day developed slightly less disability than the placebo group, but the effects were less than those in the group that received the highest dosage of coenzyme Q10.

The groups that received coenzyme Q10 also had significant increases in the level of coenzyme Q10 in their blood and a significant increase in energy-producing reactions within their mitochondria.

The results of this study suggest that doses of coenzyme Q10 as high as 1,200 mg/day are safe and may be more effective than lower doses, says Dr. Shults. The findings are consistent with those of a recently published study of patients with early Huntington's disease - another degenerative neurological disorder - that showed slightly less functional decline in groups that received 600 mg/day of coenzyme Q10.

The new study also used an efficient phase II clinical trial design - developed by biostatistician David Oakes, Ph.D., of the University of Rochester, and other study investigators - which should be useful for testing other drugs that might slow the progression of PD, says Dr. Shults. The design allowed the researchers to study the effects of three doses plus a placebo in less than 3 years, and to obtain useful data about the compound's effectiveness.

Dr. Shults and his colleagues strongly caution patients against taking coenzyme Q10 until a larger, definitive trial can be conducted. Because coenzyme Q10 is classified as a dietary supplement, it is not regulated by the U.S. Food and Drug Administration. The versions of the supplement sold in stores may differ, they may not contain potentially beneficial amounts of the compound, and taking coenzyme Q10 over a number of years may be costly, says Dr. Shults. In addition, the current study included only a small number of patients, and the findings may not extend to people in later stages of PD or to those who are at risk but have not been diagnosed with the disorder, he notes. Finally, if many people begin taking coenzyme Q10 because of these early results, it might make it impossible for investigators to find enough patients to carry out definitive studies of the compound's effectiveness and the proper dosages, since patients must not be taking any treatments in order to be considered for enrollment in a definitive trial.

The investigators are now planning a larger clinical trial that will examine the effects of 1,200 mg/day of coenzyme Q10, and possibly a higher dose as well, in a larger number of patients.