

Coenzyme Q₁₀ in Early Parkinson's Disease

Shults CW, Oakes D, Kieburtz K, et al. Effects of coenzyme Q₁₀ in early Parkinson disease: evidence of slowing of the functional decline. *Arch Neurol* 2002;59:1541–50.

Study Overview

Objective. To determine the safety and tolerability of coenzyme Q₁₀ over a range of dosages and its effect on functional decline in Parkinson's disease (PD).

Design. Randomized, parallel-group, placebo-controlled, double-blinded trial with an intention-to-treat analysis.

Setting and participants. Multicenter trial involving 10 study enrollment sites within the United States. Participants were eligible for the trial if they had the following 3 features of PD: resting tremor, rigidity, and bradykinesia. Patients were 30 years of age or older and had received the diagnosis of PD within the previous 5 years. Exclusion criteria included (not all listed) use of any PD medications for 60 days prior to the baseline visit, drug-induced parkinsonism, use of any antioxidants 60 days prior to trial initiation, an unstable dosage of drugs with central nervous system effects during the 60 days prior to the baseline visit, diagnosis of a disease with features of PD, history of epilepsy, diagnosis of severe depression, history of a stroke, diagnosis of dementia, presence of any serious illness, history of brain surgery, structural brain disease, or electroconvulsive therapy.

Intervention. Patients were randomly assigned to receive either placebo or coenzyme Q₁₀ at a dosage of 300, 600, or 1200 mg/day. The medication was divided into 4 doses each day.

Main outcome measures. Participants were evaluated at 1, 4, 8, 12, and 16 months after the baseline visit. The primary outcome measured was the change in the total score on the Unified Parkinson's Disease Rating Scale (UPDRS) from baseline to the last visit. For this study, the last visit was defined as the visit in which the investigator judged that the participant's disability progressed to requiring levodopa therapy; the last visit before a premature termination; or the 16-month visit. Assessment of disability requiring drug therapy was standardized based on clinical interview. Other outcomes included adverse events and abnormal laboratory values, plasma levels of coenzyme Q₁₀, mitochondrial assays which included complex I, complex I/III, and citrate synthetase activities.

Main results. 89 patients underwent initial screening for the study. Of these patients, 6 were ineligible, 1 declined, and 2 were screened after enrollment was closed, resulting in 80 patients randomized. 16 patients received placebo, 21 received 300 mg/day, 20 received 600 mg/day, and 23 received 1200 mg/day. 3 patients (2 from the placebo group and 1 from the 1200 mg/day group) prematurely terminated or were lost to follow-up. All groups had similar baseline characteristics, UPDRS scores, and disability scores.

The adjusted mean changes (a positive value indicates worsening) in the total UPDRS score from baseline to the final visits were +11.99 for the placebo, +8.81 for the 300 mg/day group, +10.82 for the 600 mg/day group, and +6.69 for the 1200 mg/day group. The *P* value for the analysis of trend was 0.09, which was considered a positive test based on the authors predefined statistical criteria. The difference in the change of score between the placebo group and the 1200 mg/day group was 5.30 (95% confidence interval, 0.21–10.39)

When comparing specific treatment groups with placebo, there was a statistically significant (*P* = 0.04) difference in the 1200 mg/day group. No statistically significant differences were seen in the other dosage groups. There were no statistically significant differences in reported adverse events between the intervention groups and the placebo group. Groups receiving coenzyme Q₁₀ had highly significant increases in mean plasma coenzyme Q₁₀ levels from baseline to the last visit (*P* < 0.001).

Conclusion. Coenzyme Q₁₀ was safe and well tolerated at all dosages. Patients receiving coenzyme Q₁₀ at any dose seemed to develop less disability than placebo, with the highest dose receiving the greatest benefit.

Commentary

Parkinson's disease affects 1% of Americans older than 65 years and is a progressive degenerative neurological disease with no cure [1]. New insights into the mechanism of the disease have suggested that impaired mitochondrial function could have a role in the destruction of dopaminergic neurons in the substantia nigra [2]. Studies in mice have shown that oral supplementation of coenzyme Q₁₀ (an antioxidant that functions as an electron acceptor in the mitochondrial electron

transport chain) can reduce the loss of dopaminergic neurons in drug-induced parkinsonism [3]. This well-designed study by Shults et al investigates the use of coenzyme Q₁₀ on functional status in patients with early Parkinson's disease.

While the findings are promising and reveal a novel target for potential PD therapies, the study overall was small and underpowered to detect a true difference. The authors designed the study to test for a dosing trend, which would be statistically significant based on a 73% power to detect a difference of 6 points in total UPDRS score. While this reduced power was no doubt required due to the sample size, it does reduce our overall confidence in the results. Furthermore, on the secondary analysis, the difference between the placebo and the 1200 mg/day dose was significant at 0.04 but was not adjusted for multiple comparisons. Regardless, these finding should be the impetus to a larger trial that could confirm these results.

Applications for Clinical Practice

The progressive functional decline seen in PD might be delayed by coenzyme Q₁₀; however, larger studies are needed to confirm these results. Coenzyme Q₁₀ appears to be well tolerated by patients.

—Review by Harvey J. Murff, MD, MPH

References

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