

Coenzyme Q₁₀ and Parkinson's Disease

On May 27, 2011, the National Institute for Neurological Disease and Stroke (NINDS), released a statement that their major study on the use of coenzyme Q₁₀ (CoQ₁₀) for Parkinson's disease (the QE3 Trial) was halted, because "interim analysis showed that it would be futile to complete the study because it would be very unlikely to demonstrate a statistically significant benefit of active treatment over placebo."¹ Needless to say, this announcement was very disappointing, both to Parkinson's sufferers and to the clinicians and nutritionists who treat them. A major hope was dashed.

In this letter, I am turning to the orthomolecular community for opinions and clinical experience regarding the use of CoQ₁₀ for Parkinson's disease (PD). Are we to accept the NINDS announcement as the final word on the subject? Is the case closed? Have you ceased recommending the use of this supplement for PD? Does the NINDS finding contradict your clinical experience? Is it ethical to continue to administer CoQ₁₀ to Parkinson's sufferers based on previous research and our anecdotal observations? Or, perhaps, it is unethical to discontinue? Basic medical ethics call on a doctor to give the best treatment he knows about. If he has treated even one person in a specific manner and has seen clear improvement, he hasn't proven anything, but he has certainly observed something. If he has seen this improvement in several individuals, then he should continue administering the treatment to others, especially if his observations were observed by other practitioners. Perhaps the most meaningful question of all is, if you were diagnosed with PD, would you take CoQ₁₀?

The QE3 Trial may be considered "best evidence" by staunch supporters of "evidence-based medicine" (EBM) and, therefore, the discussion should be closed. However, there is a growing awareness of the shortfalls inherent in EBM, as epitomized

in the book, *Tarnished Gold*, by Hickey and Roberts.² These authors suggest preferring "patient-based medicine." The conclusions of the QE3 study contradict a variety of various earlier findings.

Although PD is considered idiopathic, it is well established that mitochondrial dysfunction, cellular energy depletion and oxidative stress appear to play important roles in the pathogenesis of PD.³ This gives us treatment guidelines. We do know how to increase the concentrations of nutrients having the potential to improve mitochondrial function, including the electron transport chain, while providing antioxidants to protect the organelles and bioenergetic processes from oxidative stress. Administration of these nutrients is fundamental to orthomolecular theory and practice. A partial list of relevant substances includes all the B vitamins including the reduced form of nicotinamide adenine dinucleotide, L-carnitine, creatine, CoQ₁₀, and vitamins C and E, as well as glutathione and its precursors.

CoQ₁₀, sitting in a prominent position in the electron transport chain, was an obvious candidate for therapeutic administration. CoQ₁₀ is part of Complex I of the chain, the very section found to be dysfunctional in the substantia nigra of PD patients.^{4,5} Furthermore, "oral CoQ₁₀ was well absorbed in parkinsonian patients and caused a trend toward increased complex I activity."⁶ Biological plausibility is therefore established.

In early clinical research, CoQ₁₀ was found to be beneficial to PD patients. In the largest of several trials,⁷ where CoQ₁₀ was given at doses of 300, 600 or 1,200 mg, a linear trend was found between dose and slower disease progression. The difference between the 1,200 mg per day group and placebo was significant, but mildly so ($p= 0.04$). The trial authors cautioned that "the results need to be confirmed in a large study." Three of the researchers in this trial, Drs. Beal, Oakes and Shoulson, were later the principal investigators in the terminated QE3 trial.

Anyone who treats PD must decide whether to continue offering CoQ₁₀. My personal experience with clients has been posi-

tive, and I still recommend use of the supplement, since the substance is safe and the risk is only financial. However, I am searching for more information and opinions. I first wrote to the principle investigators, but received no reply. I then sent a short questionnaire by electronic mail or fax to over 100 physicians in 15 of the 68 centres that participated in the trial. After receiving only two replies, I ceased the mailings. Those two replies may be representative of the EBM approach, which is that the story of CoQ₁₀ and PD is signed, sealed and delivered, and there is nothing more to talk about.

The above-mentioned author, Dr. Steve Hickey, a PhD in Medical Biophysics, replied extensively to my inquiry. His abbreviated comments are as follows:

"Basically, the study is very poor and rather useless... The "interim analysis" would alter the nature of the QE3 trial. The probabilities used would change if an interim analysis were included... The "placebo" control was 1,200 IU of vitamin E a day. That is, the supposedly "inactive substance" or placebo was another fat soluble antioxidant!

Direct observation can trump a clinical trial... I have to reject the study as having little relevance to a patient with Parkinson's taking Q₁₀... When a trial goes against existing data it is less likely to be correct (Bayes' theorem). Do not be confused into thinking large trials are "better", they are just more difficult to replicate. It is as easy to screw up a large trial as a small trial. Sorry, I'll correct that. It is much easier to screw up a large trial, as the QE3 example shows... Given the known mechanisms and the data from small trials and case studies, I would take Q₁₀ if I had Parkinson's... Given the limited ability for medicine to help, not taking Q₁₀ would need justification. My personal choice would be to consume Q₁₀ and other antioxidants."

I, too, would take CoQ₁₀ if faced with a diagnosis of PD, and I continue to recommend it to my clients. However, I'm sure that others share my desire for more discussion on this, pro or con, in order to raise the confidence level supporting our recommendations, or lead us to a different conclusion.

Please send me your comments and answers, and I will condense and submit them for publication in a later edition of the *Journal of Orthomolecular Medicine*.

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References

1. National institute of neurological disorders and stroke. Statement on the Termination of QE3 Study. Retrieved from: [www.ninds.nih.gov/disorders/clinical_trials/CoQ10-Trial-Update.htm].
2. Hickey S, Roberts H: *Tarnished Gold: the Sickness if Evidence-Based Medicine*. Lexington, KY. CreateSpace. 2011.
3. Anderson DW, Bradbury KA, Schneider JS: Broad neuroprotective profile of nicotinamide in different mouse models of MPTP-induced parkinsonism. *Eur J Neurosci*, 2008; 28: 610-617.
4. Haas RH, Nasirian F, Nakano K, et al: Low platelet mitochondrial complex I and complex II/III activity in early untreated Parkinson's disease. *Ann Neurol*, 1995; 37: 714-722.
5. Navarro A, Boveris A: Brain mitochondrial dysfunction in aging, neurodegeneration, and Parkinson's disease. *Front Aging Neurosci*, 2010; 2: pii: 34.
6. Shults CW, Haas RH, Beal MF: A possible role of coenzyme Q₁₀ in the etiology and treatment of Parkinson's disease. *Biofactors*, 1999; 9: 267-272.
7. 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: 1541-1550.