Coenzyme Q10 Regulates Serotonin Levels and Depressive Symptoms in Fibromyalgia Patients: Results of a Small Clinical Trial.

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Coenzyme Q_{10} Regulates Serotonin Levels and Depressive Symptoms in Fibromyalgia Patients

Results of a Small Clinical Trial

To the Editors:

Despite discrepancies about the role of the serotonergic system in the pathophysiology of fibromyalgia (FM), the presence of disturbances of serotonin function in this disease is evident. Serotonin is an important modulator of pain perception, sleep, fatigue, cognition, and mood in normal subjects, supporting the conclusion that disturbances in these functions (hallmark symptoms of patients with FM) can be the result of abnormalities in serotonin content, metabolism, or transmission. Furthermore, serotonin function alterations have provided the basis for several therapeutic options in FM, being serotonin reuptake inhibitors widely used for its treatment.[1] Coenzyme Q (CoQ_{10}) deficiency is also another pathological alteration observed in patients with FM and it has been reported that CoQ_{10} supplementation significantly improves the clinical symptoms associated with the disease.[2–4]

CoQ_{10} possesses antidepressant properties and it has a major role in the pathophysiology of several diseases associated with depressive symptoms such as major depression, myalgic encephalomyelitis, and FM.[4,5] Following up our earlier work on the mechanisms of therapeutic effects of CoQ_{10} in FM in a clinical trial (ISRCTN 21164124),[2] here we show the effect of 40 days of CoQ_{10} versus placebo supplementation on serotonin levels in platelets from FM patients and depressive symptoms improvement.

The study protocol was reviewed and approved by the Ethical Committee of the University of Sevilla. All the participants of the study gave their written informed consent before initiating the study. This study was carried out in compliance with the Declaration of Helsinki, and all the International Conferences on Harmonisation and Good Clinical Practice Guidelines. Twenty patients diagnosed with FM were distributed in a clinical trial as described in Cordero et al.[2] The patients were diagnosed with FM by exclusion of other diseases and syndromes, and in accordance with the American College of Rheumatology criteria. Subjects were randomized in a double-blind fashion, according to a 1:1 ratio, to CoQ_{10} or placebo. Ten subjects received CoQ_{10} (Pharma Nord, Vejle, Denmark) in soft gel capsules for 40 days (300 mg/d CoQ_{10} divided into 3 daily doses), whereas another group of 10 subjects received a matching placebo.

Early-morning samples of blood were collected under fasting conditions and platelets were isolated. CoQ_{10} levels were determined by HPLC and serotonin levels by ELISA (GenWay, San Diego, CA). CoQ_{10} deficiency was induced in healthy platelets by 1 mM P-aminobenzoate (PABA; Sigma Chemical Co, St Louis, MO) treatment. Depression was evaluated by the Beck Depression Inventory (BDI) scale.

DISCUSSION

As expected, FM patients had markedly higher levels of depression [BDI, 22.3 (6.5)] compared with healthy controls [2.9 (1.1)] ($P < 0.001$). CoQ_{10} and serotonin levels in platelets isolated from FM patients were significantly reduced in respect to controls (Fig. 1A and B). Interestingly, CoQ_{10} and serotonin content in platelets from nontreated patients showed a strong positive correlation (Fig. 1C). Several studies have suggested that platelets are good models of neuronal serotonergic cells.[6] Both types of cells are major storage sites for serotonin, and interestingly serotonin levels in cerebrospinal fluid are strongly correlated with serotonin levels in platelets.[6] Therefore, our results may reflect the critical role of CoQ_{10} deficiency in the functional alterations of the serotoninergic system.

The evidence base for the clinical effectiveness of treatment with CoQ_{10} may be explained via its ability to ameliorate oxidative stress and protect mitochondria.[4] However, there is no information about the effect of CoQ_{10} treatment in serotonin levels. In our study, CoQ_{10} and serotonin levels in platelets from FM patients were restored in the COQ_{10}-treated group compared to placebo group (Fig. 1A and B). Interestingly, a notable improvement in depressive symptoms evaluated with the BDI scale was also observed in the CoQ_{10}-treated group compared to the placebo group [placebo group, 24.1 (3.5); CoQ_{10} group, 6.2 (1.9)] ($P < 0.001$).

To verify the role of CoQ_{10} in the serotonin alterations observed in FM patients, we induced CoQ_{10} deficiency in platelets from healthy controls by inhibiting the endogenous biosynthesis of CoQ_{10} with PABA treatment, a competitive inhibitor of polyprenyl-4-hydroxybenzoate transferase (Coq2p). Platelets were cultured for 24 hours in the presence of 1-mM PABA, or alternatively PABA + 10 μM CoQ_{10}, and PABA + 10 mM N-acetylcysteine (N-Acet) (Sigma Chemical Co). Serotonin levels in platelets were significantly reduced by PABA treatment (Fig. 1D). Reduced serotonin levels in platelets were restored in the presence of 2 antioxidants, CoQ_{10}, or N-Acet, being more significant in platelets treated with CoQ_{10}. Taken together, these results suggest that CoQ_{10} deficiency affects serotonin content in platelets and, presumably, in other cells such as neurons of the central nervous system. CoQ_{10} is an important component of the mitochondrial respiratory chain enabling the generation of adenosine triphosphate by oxidative phosphorylation. Because adenosine triphosphate levels have been observed to be reduced in platelets from FM patients and FM has been related with alterations of the hypothalamic-pituitary-adrenal (HPA) axis, and hormone and neurotransmitter secretion,[7] a possible explanation for our results is that CoQ_{10} may play an essential role in the regulation of bioenergetics status in platelets and in other cells such as neurons of the central nervous system and thus, it may affect serotonin content, transmission, and function. These results may also contribute to explain the antidepressant effect of CoQ_{10} treatment. Our findings also support the hypothesis that CoQ_{10} supplementation can be used as an alternative therapy for controlling depression. F1

Further analyses involving more patients in doubled-blind placebo-controlled clinical trials are required to confirm these observations. Indeed, our research group is currently working in this direction, based on the conclusions of the exploratory work discussed in this article.

AUTHOR DISCLOSURE INFORMATION

The authors declare no conflicts of interest.

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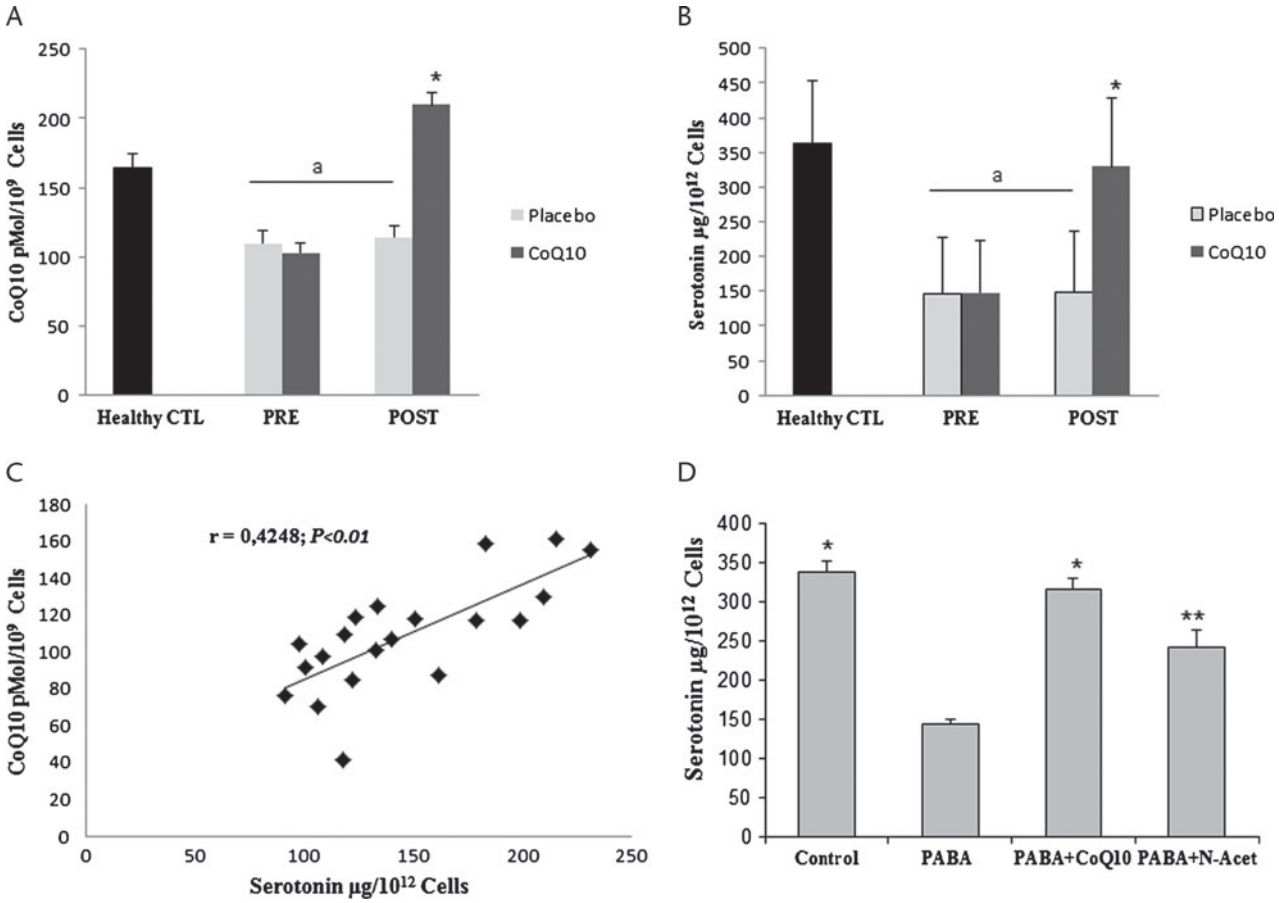

FIGURE 1. A, CoQ_{10} levels were reduced in platelets from FM patients. CoQ_{10} levels were restored after oral CoQ_{10} supplementation versus placebo. B, Serotonin levels were reduced in platelets from FM patients compared with platelets from healthy controls. After supplementation, CoQ_{10} induced a significant increase of serotonin levels. *$P < 0.01$ between before and after CoQ_{10} supplementation FM patients. [a]$P < 0.01$ between FM patients and healthy controls. C, Correlation between CoQ_{10} and serotonin levels in platelets. The strength of the association was established by calculating Pearson correlation coefficient (*r*). D, Induced CoQ_{10} deficiency in vitro leads to serotonin deficiency in platelets. Reduced levels of serotonin were restored by antioxidants but more significantly with CoQ_{10} treatment. Data represent the mean (SD) of 3 separate experiments. *$P < 0.001$ between control, PABA, and PABA with CoQ_{10}; **$P < 0.01$ between PABA and PABA with N-Acet.

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