Short communication

Coenzyme Q_{10}: A novel therapeutic approach for Fibromyalgia? Case series with 5 patients

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Abstract

Coenzyme Q\textsubscript{10} (CoQ\textsubscript{10}) is an essential electron carrier in the mitochondrial respiratory chain and a strong antioxidant. Low CoQ\textsubscript{10} levels have been detected in patients with Fibromyalgia (FM). The purpose of the present work was to assess the effect of CoQ\textsubscript{10} on symptoms of five patients with FM. Patients were evaluated clinically with Visual Analogical Scale of pain (VAS), and Fibromyalgia Impact Questionnaire (FIQ). Patients with CoQ\textsubscript{10} deficiency showed a statistically significant reduction on symptoms after CoQ\textsubscript{10} treatment during 9 months (300 mg/day). Determination of deficiency and consequent supplementation in FM may result in clinical improvement. Further analysis involving more scientifically rigorous methodology will be required to confirm this observation.

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1. Introduction

Coenzyme Q\textsubscript{10} (CoQ\textsubscript{10}) is present in every membrane of all cells in the body. CoQ\textsubscript{10} transfers electrons from complexes I and II to complex III in the mitochondrial respiratory chain and fulfills a critical role in mitochondrial ATP production, playing a crucial role in cellular metabolism; regulating uncoupling proteins, the transition pore, \(\beta\)-oxidation of fatty acids, and nucleotide pathway; and also limiting the production of reactive oxygen species (ROS) \cite{Turunen2004, Battino1999}. Many neurodegenerative, muscular, and cardiovascular disorders have been associated with low CoQ\textsubscript{10} levels, either as a primary or secondary event \cite{Littarru2010, Lodi1997}. Patients with all forms of CoQ\textsubscript{10} deficiency have shown clinical improvements after initiating oral CoQ\textsubscript{10} Supplementation, with observed decrease of muscle pain associated with statin treatment \cite{Caso2005} and a decrement of migraine symptom \cite{Sandor2007}.

Fibromyalgia (FM) is a common chronic pain syndrome accompanied by other symptoms such as fatigue, headache, sleep disturbances, and depression, only diagnosed by classification criteria established by the American College of Rheumatology \cite{Wolfe1990}. Pathophysiological mechanisms of FM are difficult to identify and current drug therapies demonstrate limited effectiveness, only focused to the management of single symptoms. Recently, we have observed CoQ\textsubscript{10} deficiency, mitochondrial dysfunction, oxidative stress and mitophagy activation in blood mononuclear cells (BMCs) from FM patients. BMCs from these patients showed a good response to treatment with CoQ\textsubscript{10} \cite{Cordero2010}. Therefore, could CoQ\textsubscript{10} be used as a novel therapeutic approach for FM? To this respect, in 2002, Lister reported beneficial effects of oral CoQ\textsubscript{10} supplementation in FM patients, although this could be also due to the presence of Ginkgo biloba in the treatment \cite{Lister2002}. Moreover, we have observed an important decrement on symptoms of mother and son with FM after oral CoQ\textsubscript{10} supplementation \cite{Cordero2011}. Herein, we report the benefit of CoQ\textsubscript{10} in five patients with FM and CoQ\textsubscript{10} deficiency.

2. Patients and methods

The patients, four women of 43, 59, 62 and 66 years old respectively, and one man of 21 years old, were diagnosed with FM by exclusion of other diseases and syndromes, and in accordance with the American College of Rheumatology criteria \cite{Wolfe1990}. All of
These patients had daily episodes of intense musculoskeletal pain and fatigue, stiffness, anxiety, sleep disturbance, and depression. Three of them had daily episodes of migraine. Routine laboratory test yields normal results (data not show). At the moment, they only use paracetamol to demand. All patients presented high score of Visual Analogical Scale of pain (VAS), and Fibromyalgia Impact Questionnaire (FIQ) (Table 1). In Patients 1, 2, and 3, Headache Impact Test (HIT 6) and Migraine Disability Assessment (MIDAS, little or no disability: 0–5; mild disability: 6–10; moderate disability: 11–20; severe disability: 21+) were 66, 63, and, 65 in HIT 6, and 73, 65, and 70 in MIDAS, respectively. After informed consent and the approval of the local ethical committee were obtained, the patients were treated orally with 300 mg daily CoQ10 divided in three doses. After nine months of treatment, the patients were evaluated.

Biochemical parameters were compared with BMCs and plasma obtained from healthy age- and sex-matched control subjects after informed consents were signed.

2.1. Blood mononuclear cells

BMCs from heparinized blood were purified with isopycnic centrifugation by using Histopaque-1119 and Histopaque-1077 (Sigma Chemical Co., St. Louis, MO, USA).

2.2. Measurement of CoQ10 levels

CoQ10 contents in BMCs were analyzed with HPLC (Beckman Coulter, Brea, CA, USA; 166-126 HPLC) with ultraviolet detection (275 nm), according to the method of Montero et al. (2008).

2.3. Lipid peroxidation

TBARS (thiobarbituric acid reactive substances) levels in plasma were determined by a method based on the reaction with thiobarbituric acid at 90–100 °C. Lipid peroxidation in cells was determined by analyzing the accumulation of lipoperoxides with a commercial kit from Cayman Chemical (Ann Arbor, Michigan, USA). TBARS are expressed in terms of malondialdehyde (MDA) levels. In these assays, a MDA standard is used to construct a standard curve against which unknown samples can be plotted.

2.4. Statistical analysis

The unpaired Student’s t test was used to evaluate the significance of differences between means of patients and controls. P values less than 0.05 were considered significant.

3. Results

The patients underwent a mitochondrial dysfunction analysis, showing, in BMCs, higher levels of mitochondrial ROS production and lipid peroxidation (LP), mitochondrial dysfunction, low levels of CoQ10, and higher levels of mitochondrial degradation (mitophagy). Oxidative stress and mitochondrial degradation were reduced by CoQ10 supplementation on BMCs of one representative patient (Patient 3 in this paper) (Cordero et al., 2010).

All patients reported an improvement in sleep and mental alertness, a marked decrease in joint pain, and decrement of episodes and intensity of headache in Patients 1, 2, and 3. After 9 months of treatment, the patients were evaluated and we observed an important decrease of tender points, VAS, FIQ, HIT-6 and MIDAS (Table 1). No serological alteration was detected after CoQ10 treatment: glucose 90.1 ± 12.6 mg/dL (normal values 76–110), urea 31.7 ± 9.13 mg/dL (n.v. 10–45), uric acid 3.11 ± 0.51 mg/dL (n.v. 2.5–7.5), total protein 8.25 ± 2.45 g/dL (n.v. 6.6–8.7), creatinine 0.71 ± 0.23 mg/dL (n.v. 0.5–1.1), aspartate aminotransferase 31.33 ± 10.31 mU/mL (n.v. 10–40), alanine aminotransferase 38 ± 11.07 mU/mL (n.v. 11–49), alkaline phosphatase 152 ± 21.44 mU/mL (n.v. 90–258), total cholesterol 201 ± 11.12 mg/dL (n.v. <220), HDL 59 ± 6.7 mg/dL (n.v. ≥35), LDL 128 ± 9.12 mg/dL (n.v. <150) and triglycerides 159 ± 21.52 mg/dL (n.v. 150–200). An important decrement of LP, both in plasma and BMCs was observed, and CoQ10 levels were restored in BMCs from all patients (Table 1).

4. Discussion

A large number of studies have shown high levels of oxidative stress markers, such as LP levels, in FM patients, suggesting that this process may have a role in the pathophysiology of this disease. Additionally, we have shown CoQ10 deficiency, mitochondrial ROS production, and LP in plasma and BMCs (Cordero et al., 2010).

Our results show that CoQ10 supplementation in FM patients decreased LP in plasma and BMCs, increased CoQ10 level in BMCs and improved clinical symptoms. It is known that LP indirectly reflects intracellular ROS generation, and ROS are known to be implicated in the etiology of pain, one of the most prominent symptoms in FM, by inducing peripheral and central hyperalgesia (Wang et al., 2004). Superoxide plays a major role in the development of pain through direct peripheral sensitization, the release of various cytokines (for example, TNF-α, IL-1β, and IL-6), the formation of peroxynitrite (ONOO–), and PARP activation (Wang et al., 2004).

It has been widely demonstrated that CoQ10 is essential for respiratory chain efficacy (Raučová et al., 1992), and as antioxidant. A decrease of muscle pain associated with statin treatment by CoQ10 supplementation (Casco et al., 2007), and a decrement of migraine and headache symptom by CoQ10 supplementation have been observed (Sandor et al., 2005). Furthermore, CoQ10 has showed anti-inflammatory and anti-nociceptive activities (Jung et al., 2009), regulating inflammatory gene expression as a pro-inflammatory cytokine TNF-alpha (Schmelzer et al., 2008), which role has been demonstrated in FM (Menzies and Lyon, 2010).

| Table 1 |

| Laboratory and clinical changes in FM patients pre and post treatment with CoQ10. |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                  | Pre/post        | Pre/post        | Pre/post        | Pre/post        | Pre/post        |
| Tender points    | 16/7            | 12/5            | 15/6            | 16/9            | 14/7            |
| VAS total score, range 0–10 | 7/3             | 6/2             | 5/2             | 7/3             | 6/3             |
| HQ total score, range 0–80 | 61/26           | 51/20           | 65/30           | 53/38           | 56/23           |
| HIT-6 total score, range 0–78 | 66/41           | 63/45           | 66/36           | No              | No              |
| MIDAS total score, range 0–21+ | 73/31           | 65/27           | 70/29           | No              | No              |
| LP in plasma (nmol/mL) | 18.4/4.1        | 17.1/3.8        | 17.7/2.3        | 16.2/3.3        | 17.9/4.6        |
| LP in BMCs (nmol/million cells) | 25.1/13.4       | 26.7/11.4       | 28.8/10.2       | 27.3/12.1       | 27.6/11.4       |
| CoQ10 (pmol/mg Protein) | 109.1/234.1    | 114.1/241.9     | 135.9/263.4     | 117.9/222.1     | 123.3/231.7     |

Pre/post: pretreatment and posttreatment with CoQ10; VAS: Visual Analogical Scale of pain; FIQ: Fibromyalgia Impact Questionnaire; HIT 6: Headache Impact Test; MIDAS: Migraine Disability Assessment; LP: lipid peroxidation; CoQ10: Coenzyme Q10.
The results of this study indicate that oxidative stress could be implicated in the severity of the clinical symptoms in FM and suggest that CoQ10 and antioxidant therapy needs to be examined as a treatment in FM.

References


