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LETTER TO THE EDITOR

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Effect of Coenzyme Q_{10} on Psychopathological Symptoms in Fibromyalgia Patients

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Fibromyalgia (FM) is a common chronic pain syndrome accompanied by a myriad of variable physical and psychopathological symptoms such as fatigue, muscle stiffness, sleep disorders, morning tiredness, cognitive complaints, as well as depression and anxiety [1]. Despite the fact that it affects up to 5% of the general population worldwide, its pathogenic mechanism remains elusive. Recently, the hypothesis that oxidative stress and mitochondrial dysfunction are important events in the pathogenesis of FM [2] was proposed. Furthermore, coenzyme Q_{10} (CoQ_{10}) deficiency has been described in patients with FM [3]. CoQ_{10} plays a critical role in the mitochondrial ATP production and cellular metabolism. CoQ_{10} also regulates mitochondrial uncoupling proteins, mitochondrial permeability transition pore, and ROS production [2]. Recently, preliminary data showed an interesting improvement in clinical symptoms in patients with FM after oral supplementation with CoQ_{10} [4,5], including the control of the depressive symptom with the regulation of the serotoninergic system [6].

In addition to biological and clinical parameters, other psychopathological events have been involved in the pathophysiology of FM. Psychological factors, a high prevalence of depression and anxiety symptoms have been widely reported [7]. Following our earlier work about the therapeutic effects of CoQ_{10} on FM in a clinical trial (ISRCTN 21164124) [5], here we show the effect of 40 days of CoQ_{10} versus placebo supplementation in psychopathological profiles from patients with FM using a multidimensional psychological screening instrument, namely the Symptom Checklist-90-R' (SCL-90-R). The study protocol was reviewed and approved by the Ethical Committee of the University of Sevilla. All the participants to 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 reference 5. Data in tables are given as means ± SD. Data between different groups were analyzed statistically using ANOVA on Ranks with SigmaPlot and SigmaStat statistical software (SPSS for Windows, 19, 2010, SPSS, Inc). A value of $P < 0.05$ was considered significant. To compare the trial results from patients treated with CoQ_{10} or placebo, a two-way variance (ANOVA) analysis was used. 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 (age: 44.3 ± 9.7 years) received CoQ_{10} (Pharma Nord, Vejle, Denmark) in soft gel capsules for 40 days (300 mg/day CoQ_{10} divided into three daily doses), while another group of ten subjects (age: 55 ± 5 years) with similar characteristics received a matching placebo (Table 1). After 40 days, no changes were observed about BMI in the patients (baseline: 27.6 ± 4 kg/m^2 vs. placebo: 27.3 ± 4.8 kg/m^2 or CoQ_{10} group: 26 ± 4.8 kg/m^2). However, important molecular changes were induced by CoQ_{10} after treatment such as increment in mitochondrial biogenesis and antioxidants gene expression and reduction in inflammation accompanied by an improvement in the clinical symptoms determined by Fibromyalgia Impact Questionnaire (FIQ), Pittsburgh Sleep Quality Index (PSQI) and tender points [5] and corroborated in other studies [4,6]. After evaluating the effect of CoQ_{10} on the

Table 1 Characteristics of the patients with FM pre- and posttreatments

Parameter	Baseline N = 20	Placebo N = 10	CoQ_{10} N = 10
Age (years)	49 ± 9	55 ± 5	44 ± 9.7
Duration of Diseases (years)	6.9 ± 3.3	6.6 ± 3	7.1 ± 3.8
Systole BP, mm Hg	134 ± 19.4	136 ± 23.5	126 ± 21.7
Diastole BP, mm Hg	76.9 ± 9.6	78 ± 13.7	80.5 ± 12.5
Pulse rate, bpm	74.2 ± 10.3	69 ± 6.8	78.8 ± 14.5
Weight (Kg)	70.5 ± 11.2	73.2 ± 13.8	67.8 ± 13.7
BMI (kg/m^2)	27.6 ± 4	27.3 ± 4.8	26 ± 4.8

BMI, body mass index. Values are means ± SD.

Table 2 Symptom checklist revised changes in patients with FM pre- and posttreatment with CoQ_{10}

Parameter	Baseline N = 20	Placebo N = 10	CoQ_{10} N = 10
Somatization	2.06 ± 0.8	1.95 ± 0.6	1.39 ± 0.8*
Obsessive–compulsive	1.69 ± 0.9	1.58 ± 0.7	1 ± 0.2*
Interpersonal sensitivity	1.59 ± 0.6	1.51 ± 0.3	0.4 ± 0.2***
Depression	1.79 ± 0.3	1.73 ± 0.4	0.8 ± 0.2***
Anxiety	1.9 ± 0.6	1.84 ± 0.5	0.7 ± 0.2***
Hostility	1.75 ± 0.3	1.9 ± 0.5	0.4 ± 0.2***
Phobic anxiety	0.68 ± 0.5	0.78 ± 0.4	0.27 ± 0.2*
Paranoid ideation	0.78 ± 0.1	0.68 ± 0.4	0.2 ± 0.07**
Psychoticism	0.69 ± 0.3	0.55 ± 0.5	0.2 ± 0.05***

Values are means ± SD. *$P < 0.05$, **$P < 0.01$, and ***$P < 0.001$ between pre- and posttreatment.

psychopathological symptoms, a clinically significant improvement was observed in all subscores from SCL-90-R, being statistically significant for the reduction in interpersonal sensitivity ($P < 0.001$), depression ($P < 0.001$), anxiety ($P < 0.001$), hostility ($P < 0.001$), and psychoticism ($P < 0.001$) items, and a moderate statistical significance in somatization ($P < 0.05$) and obsessive–compulsive ($P < 0.05$; Table 2).

Previously, SCL-90-R has been used to determinate the emotional distress and show psychological distress and maladaptive emotional responses in these patients [8]. Interestingly, we show a very important improvement in psychological events highly implicated in the pathophysiology of FM. Indeed, CoQ_{10} has been implicated in one of the most important psychological symptom in FM, depression, and it has been recommended the oral use in these patients [9]. This has been argued because of the high levels of oxidative stress and mitochondrial damage [9]. Mitochondrial dysfunction and the resultant reduced bioenergetic production have been involved in somatization and depression [9,10], two of the symptoms highly shown by patients with FM. So, our preliminary data show a possible biological implication of the psychological symptoms in FM. On the other hand, it has been known since early on that patients with CoQ_{10} benefit from oral CoQ_{10} supplementation [9,10]. According to this, CoQ_{10} has been shown to be a potential drug candidate in the treatment of FM for different reasons. First, it is a mitochondrial cofactor with the potential to improve mitochondrial functions and respiration. Second, CoQ_{10} is a powerful free radical scavenger that can mitigate oxidative stress [5]. Now, our study has shown a new perspective about the treatment in patients with FM using CoQ_{10}. Because psychopathological symptoms and psychological distress are highly involved in the pathophysiology of FM and modulate the perception of the disease from the patients, the effect of CoQ_{10} in this clinical dimension proposes a biological and psychological approach from the same treatment. Furthermore, this study has appointed a new path toward understanding of FM.

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

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Conflict of Interest

The authors declare no conflict of interest.

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