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An Open, Pilot Study to Evaluate the Potential Benefits of Coenzyme Q10 Combined with *Ginkgo Biloba* extract in Fibromyalgia Syndrome

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An open, uncontrolled study was undertaken to measure the subjective effects of coenzyme Q10 combined with a *Ginkgo biloba* extract in volunteer subjects with clinically diagnosed fibromyalgia syndrome. Anecdotal reports from patients with fibromyalgia syndrome have claimed benefits from the use of these supplements. The aim of this study was to determine if these reports could be substantiated in a pilot clinical trial. Patient questioning had determined that poor quality of life was a major factor in the condition and a quality-of-life questionnaire was used to measure potential benefit. Subjects were given oral doses of 200 mg coenzyme Q10 and 200 mg *Ginkgo biloba* extract daily for 84 days. Quality of life was measured, using the well-validated Dartmouth Primary Care Cooperative Information Project/World Organization of Family Doctors (COOP/WONCA) questionnaire that measures seven different subjective responses, at 0-, 4-, 8- and 12-week intervals. The subjects were asked for an overall self-rating at the end of the study. A progressive improvement in the quality-of-life scores was observed over the study period and at the end, the scores showed a significant difference from those at the start. This was matched by an improvement in self-rating with 64% claiming to be better and only 9% claiming to feel worse. Adverse effects were minor. A controlled study is now planned.

KEY WORDS: FIBROMYALGIA; COENZYME Q10; *GINKGO BILOBA* EXTRACT; QUALITY OF LIFE

Introduction

Fibromyalgia syndrome (FMS) is a disabling disorder characterized by generalized musculoskeletal pain with diffuse tenderness at discrete anatomical sites. Secondary symptoms include general fatigue, depression, disturbed sleep, headaches, vasomotor instability, gastrointestinal upsets and paraesthesias. FMS affects both the central nervous system and the peripheral neuromuscular system. Its prevalence is believed to be about 10 – 20 per thousand of the adult population and about 90% of sufferers are female. The cause of FMS is unknown but the development of the condition follows soft-tissue injury in about 25% of cases. There is no known cure and treatment is aimed at ameliorating symptoms; this may be in the form of

rehabilitative therapy, such as physiotherapy and graded exercise; drug treatment with anti-depressants or corticosteroids; localized infusion of local anaesthetics; administration of growth hormone; or nutritional intervention that may improve muscle or vascular function. There is no treatment that is universally effective, and in some cases the adverse effects of drug therapy, e.g. with corticosteroids, may outweigh the benefits.

Some members of the Fibromyalgia Association, the UK patient support group, have claimed that they have obtained benefit from various nutritional supplements. Two that they claim to be effective are coenzyme Q10 (Ubiquinone) and a standardized formulation of *Ginkgo biloba* extract. It has been suggested that some of the symptoms of FMS may be due to the presence of excess oxygen-derived free radicals. These are known to be capable of inducing pain and inflammation and impair muscle function. Both coenzyme Q10 and *Ginkgo biloba* extract possess anti-oxidant properties and this property may account for some of the benefits attributed to these agents. Coenzyme Q10 can also improve muscle function[1] and *Ginkgo biloba* extract can improve vascular function.[2] Some clinicians believe that chronic fatigue syndrome (CFS) and FMS may have some aetiological factors in common; recent studies have shown that coenzyme Q10 can provide significant benefits in some patients with CFS.[1]

The objective of this pilot study was to assess the subjective effects of coenzyme Q10 plus *Ginkgo biloba* extract given daily for a period of 3 months in volunteer subjects with clinically determined FMS.

Subjects and methods

SUBJECTS

Twenty-five volunteer subjects of either sex, recruited from members of the Christchurch and District Fibromyalgia Support Group in the UK were entered into the trial. They had all been diagnosed clinically with FMS and had obtained the approval of their general medical practitioners to participate in the study. Written, informed consent was obtained before subjects would be considered for entry into the trial. Subjects were permitted to continue with prescribed medication but were discouraged from taking additional nutritional supplements; only subjects considered competent to complete the questionnaires were admitted.

TEST AGENTS

The test agents were coenzyme Q10 (Bio-Quinone Q10®, Pharma Nord, Morpeth, UK) 100 mg in gelatine capsules and 100 mg tablets of *Ginkgo biloba* standardized to contain 24 mg flavone glycosides and 6 mg terpene lactones (Bio-Biloba®, Pharma Nord). The subjects were instructed to take two capsules of coenzyme Q10 and two tablets of *Ginkgo biloba* daily at the same time each day. Both test agents were provided by Pharma Nord.

STUDY DESIGN

Subjects were asked to complete case-record forms that included a Dartmouth Primary Care Cooperative Information Project/World Organization of Family Doctors (COOP/WONCA) Quality of Life questionnaire before starting the investigational treatment and at 4-weekly intervals. The responses at each 4-week interval were evaluated blind and compared with those obtained at day 0. The study complied with Good Clinical Practice guidelines and the current Declaration of Helsinki.

EVALUATION

Assessment of efficacy used a quality-of-life, self-assessment questionnaire to determine overall quality of life. The Dartmouth

TABLE 1:
Quality-of-life scores[a] in fibromyalgia syndrome patients receiving coenzyme Q10 plus *Ginkgo biloba* extract

After day	0	28	56	84
Mean score[b]	26.6	24.4	22.9	22.3
SE	± 0.8	± 0.7	± 0.9	± 0.8

Day 0 versus day 84 $P < 0.02$

[a]Dartmouth Primary Care Cooperative Information Project/World Organization of Family Doctors (COOP/WONCA) Quality of Life questionnaire.
[b]The sums for each of the seven values, for each of the 23 subjects who completed the pilot study, were calculated and the totals for each 4-week period compared.

COOP/WONCA Quality of Life questionnaire was used.[3] This is a well-validated, figurative instrument that is used to assess seven qualities. Using a 5-point ordinal scale, subjects scored each quality measure: physical fitness; emotional feelings; daily activities; social activities; changes in health; overall health; and pain. Each of these measures may be affected in FMS. Subjects were asked to complete questionnaires on days 0, 28, 56 and 84. Assessments were made at 28-day intervals rather than the 14 days used by the original authors as there was evidence that the efffects of the two test agents could take more than 14 days to achieve maximal activity. In addition to the quality-of-life questionnaires, each subject was asked to provide an overall self-rating assessment at the end of the study to indicate how they felt compared with their situation at the start. They were also asked if they wished to continue with the supplements. Adverse events were recorded.

STATISTICAL ANALYSIS

The quality-of-life data were analysed using the non-parametric Wilcoxon signed-rank test. The scores for each of the seven measures were summed and the totals for each 4-week period compared. A difference with a value of $P < 0.05$ was considered significant.

Results

Twenty-three subjects completed the study. Two subjects withdrew for personal reasons, unrelated to the treatments.

The mean scores of subjects' quality-of-life questionnaires are shown in Table 1. Sixty-eight per cent of those who completed the trial expressed the view that they would like to continue with treatments. The overall subjective views of the patients, independent of quality-of-life scores, was that the majority (64%) felt the treatment was of some benefit (Table 2). Adverse events were reported by 42% of subjects but all were considered of little or no clinical significance and most were related to FMS.

Discussion

Fibromyalgia syndrome presents a real public health problem as it affects adults mainly during the most potentially productive years

TABLE 2:
Overall self-rating at day 84[a]

Better	64%
Worse	9%
Same	27%

[a]Patients were asked to complete a self-rated evaluation of how they felt at the end of the study period compared to how they felt at the start.

of their working lives, leading to significant disability. Different names may be used for the same condition, e.g. myofascial pain syndrome, fibrositis and fibromyositis. The terms fibromyalgia syndrome or primary fibromyalgia syndrome are now recognized as more encompassing and satisfactory.

An accurate estimate of the prevalence of FMS is difficult to determine as diagnostic criteria differ among clinicians and between cultural groups. A study from the USA found that the prevalence of fibromyalgia was 2.0% (95% confidence interval [95% CI] 1.4, 2.7) for both sexes, 3.4% (95% CI 2.3, 4.6) for women, and 0.5% (95% CI 0.0, 1.0) for men. The prevalence of the syndrome increased with age, with highest values attained between 60 years and 79 years.[4]

The aetiology of FMS is unknown but it is widely considered to be a multifactorial condition that involves the adreno-cortical axis, immune system, musculoskeletal system, peripheral and central nervous systems and psychosocial factors. The severity of each symptom can differ widely between patients and this accounts for the lack of any consistent changes in the scores between subjects in this study. Conventional treatments tend to concentrate on minimizing symptoms and those directed at pain management are widely applied. Pain relief can be attempted with established analgesics of both opioid and non-steroidal anti-inflammatory drug (NSAID) classes, and these may be used individually or combined; each can have serious adverse reactions of addiction and gastrointestinal toxicity, respectively. Injection of local anaesthetics at specific trigger sites can provide short-term relief but this approach is of limited value, as it must be given by a trained specialist. Anti-depressants, hypnotics, growth hormone and physiotherapy have proved helpful in some patients but no treatment is effective in all cases. This has led to a patient-centered approach that has proved effective in the management of FMS – patients are encouraged to try a variety of treatments to determine which is best for them.

Some FMS patients with muscle pains have found benefit from coenzyme Q10, while others with central nervous-system symptoms have found benefit from *Ginkgo biloba* extract. Coenzyme Q10 is essential for normal muscle activity and a deficiency in this coenzyme is thought to impair function.[5] *Ginkgo biloba* extract can improve vascular function in both muscle and brain.[2] Impairment of muscle activity and brain function have both been associated with oxidative stress,[6] although no evidence has been found that this is a factor in FMS. As both of these agents are anti-oxidants and free radical scavengers, it is possible that the benefit demonstrated in this study may be due, in part, to anti-oxidant activity.

Whatever the mechanisms involved, the finding that the combination of coenzyme Q10 and *Ginkgo biloba* extract can improve quality-of-life scores in patients with FMS justifies a larger scale clinical trial of these two agents and further investigations into the possible mechanisms of their actions.

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