The impact of coenzyme Q10 on systolic function in patients with chronic heart failure
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CRD summary
The authors concluded that coenzyme Q10 improves systolic function in patients with heart failure, but the effects may be less in patients taking concomitant angiotensin-converting enzyme inhibitors. Poor reporting of review methods and study quality makes it difficult to comment on the strength of the evidence underpinning the authors’ conclusions.

Authors' objectives
To evaluate the effects of coenzyme Q10 (CoQ10) on systolic function in patients with heart failure.

Searching
MEDLINE, EMBASE, CINAHL and the Cochrane CENTRAL Register were searched from inception (1966) to June 2005 using the reported search terms. In addition, reference lists of identified trials and reviews and presentations were screened. Only English language reports were eligible.

Study selection
Study designs of evaluations included in the review
Double-blind, placebo-controlled parallel or crossover randomised controlled trials (RCTs) were eligible for inclusion in the review.

Specific interventions included in the review
Studies that compared CoQ10 with placebo were eligible for inclusion. Studies that evaluated combinations of supplements that included CoQ10 were excluded. The included studies evaluated 60 to 200 mg CoQ10 per day for periods ranging from 1 to 6 months. Some patients in some of the included studies were taking concomitant angiotensin-converting enzyme inhibitors (ACEIs), while in other studies no patients were taking concomitant ACEIs. Varying proportions of patients were treated with a variety of other concomitant medications for heart failure (e.g. digoxin, diuretics, nitro derivatives, hydralazine and vasodilators).

Participants included in the review
Studies of patients with heart failure were eligible for inclusion. The patients in the included studies had New York Heart Association class I to IV heart failure due to a variety of causes (including ischaemic, nonischaemic, idiopathic, hypertensive, dilated and valvular). The mean age of the patients ranged from 50 to 67 years.

Outcomes assessed in the review
Studies that evaluated ejection fraction (EF; the primary review outcome), cardiac output, cardiac index, stroke volume or stroke index were eligible for inclusion in the review.

How were decisions on the relevance of primary studies made?
Three reviewers conducted the searches but it was not clear whether the studies were selected independently or not.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.
Data were extracted directly from published reports or through contact with the authors. For parallel-group RCTs, mean differences in changes from baseline between treatment groups were calculated. For crossover RCTs, mean treatment differences at the end of the treatment and control periods were calculated or estimated from graphs. Crossover studies in which mean treatment differences were not reported were treated as two separate parallel trials. Where not reported, variances were calculated using reported statistics.

**Methods of synthesis**

How were the studies combined?

Pooled odds ratios with 95% confidence intervals (CIs) were calculated using DerSimonian and Laird random-effects models. A funnel plot was used to assess publication bias.

How were differences between studies investigated?

Statistical heterogeneity was assessed using the Breslow-Day test (p<0.10). Subgroup analysis was used to examine the effect of CoQ10 in patients with class IV heart failure, the inclusion of patients with idiopathic cardiomyopathy), concomitant use of ACEIs and the exclusion of crossover studies without a ‘proper’ washout period. The meta-analysis was repeated using a fixed-effect model.

**Results of the review**

Eleven RCTs (n=297) were included: 5 parallel-group RCTs and 6 crossover RCTs.

The EF was significantly improved in patients who received CoQ10 compared with placebo: net improvement of 3.68% (95% CI: 1.59, 5.77; based on 10 studies). Significant heterogeneity was found (p<0.00001; I-squared 86%).

The improvement in EF was greater when only patients not taking concomitant ACEIs were analysed: improvement 6.74% (95% CI: 2.63, 10.86; based on 4 studies). In patients taking ACEIs, there was no significant difference between CoQ10 and placebo in terms of the EF (based on 6 studies).

Compared with placebo, CoQ10 was associated with increased cardiac output (0.28 L/minute, 95% CI: 0.03, 0.53; based on 2 studies) and stroke index (reported as 5.80, 95% CI: 0.84, 10.75 in forest plot based on 2 studies). No significant heterogeneity was found. There was no significant difference between CoQ10 and placebo in cardiac index (0.32, 95% CI: -0.07, 0.70; based on 3 studies) or stroke volume (6.68, 95% CI: -0.41, 13.78; based on 3 studies). Significant heterogeneity was found.

The funnel plot appeared symmetrical, suggesting a low probability of publication bias.

**Authors’ conclusions**

CoQ10 improves systolic function in patients with heart failure, but the effects may be less in patients taking concomitant ACEIs.

**CRD commentary**

The review addressed a clear question that was defined in terms of the participants, intervention, outcomes and study design. Several relevant sources were searched but no attempts were made to minimise language bias. In addition, no specific attempts to minimise publication bias were reported, although no strong evidence of bias was found in the funnel plot. The methods used to select the studies and extract the data were not described in full, so it was not clear whether adequate attempts were made to reduce the potential for reviewer bias and error. Study validity was not assessed, thus the results from these studies and any synthesis might not be reliable. In particular, in view of the variety of concomitant drugs, there was no information about changes in drug doses over the duration of individual studies that might have influenced treatment effects.

Statistical heterogeneity was assessed and found to be significant for some analyses; this suggests that the pooling of studies might not always have been appropriate. Lack of reporting of review methods and study quality makes it difficult to comment on the strength of the evidence underpinning the authors’ conclusions.
Implications of the review for practice and research
Practice: The authors did not state any implications for practice. Research: The authors stated the need for further long-term studies to confirm the effects of CoQ10 as an adjunctive or alternative treatment for patients with heart failure and to identify the characteristics of those patients who benefit. Further examination of the effect of CoQ10 in patients taking and not taking concomitant ACEIs is also required.

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