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Comparison of Coenzyme Q10 Versus Placebo in Chronic Hearth Failure

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Abstract: Coenzyme Q10 is recommended in various disorders. One of this in congestive heart failure, the purpose of this study is to provide the efficacy of this drug in patients with hearth failure or not. To determine the effect of coenzyme Q10 on sign and symptom and ejection fraction. This 12 months randomized double blind placebo clinical trial was done in University of Mazandaran, we choose 100 patients who had congesting heart failure with New York Heart Association class II and III symptoms and ejection fraction = 40%, aged more than 40 years old, these patients divided into 2 groups, 50 patients received coenzyme Q10 (capsule 100 mg) the other 50 patients received placebo Left ventricular ejection fraction (measured by Echocardiography) and physical exam done each 3 months. Coenzyme Q10 administered orally has favorable actions on the sign and symptoms of patients with H.F in the beginning of study, SD (±) EF in the control group was 30±10.7 and in the case was 33.2±8.6 and after treatment EF increased in case groups ($p<0.05$). Coenzyme Q10 therapy in patients with CHF can be recommended as adjuvant therapy. Now we cannot use it as monotherapy until additional clinical trial demonstrate beneficial effects of it.

Key words: Coenzyme Q10, congestive heart failure, echocardiography, comparison, chronic hearth

INTRODUCTION

In several years ago, coenzyme Q10 was separated from mitochondria of beef heart. Later, identified its key role (in humans) in mitochondrial bioenergetics and its presence in other subcellurar fractions and in plasma and extensively investigated its antioxidant role (Greenberg and Frishman, 1990). Coenzyme Q10 (Co Q10) is an endogenously synthesized provitamin that serves as a lipid-soluble electron carrier in the mitochondrial electron transport. The other names, ubidecarenone and ubiquinon, meaning it's presence in all cells (Bresolin *et al*., 1990). These two functions of Co Q10 have been proposed as a treatment for congestive heart failure. Furthermore, recent data reveal that Co Q10 affects expression of genes involved in human cell signaling, metabolism and transport (Groneberg *et al*., 2005). The other forms of coenzyme such as Q8, Q7, are found in rats and mice (Mongthuong *et al*., 2001). Coenzyme Q10, Is prevalent in humans, with high endogenous concentrations found in the heart, liver, kidneys and pancreas. Supplementation with Co Q10 is common in Europe, Russia and Japan and was first introduced as an ethical drug for heart failure patients in Japan (Levien and Baker, 1998).

The few U.S. and European studies have had conflicting results. Some controlled studies showed no effect (Watson *et al*., 1999; Permanetter *et al*., 1992) but their limitations make the results inconclusive. Other trials noted improvement (Hofman-Bang *et al*., 1995; Judy *et al*., 1986) but concerns about end points, small numbers of patients and the lock of blinded have limited the acceptance of these studies.

MATERIALS AND METHODS

We performed a randomized placebo-controlled clinical trial to compare the effect of oral coenzyme Q10 (100 mg d^{-1}) and placebo.

We eligible 100 patients with New York Heart Association Functional class II, III for inclusion in this study, whom referred to heart center of Mazandaran University. All patients had ejection fraction = 40%, by Echocardiography and aged >40 years old (Table 1).

These criteria were used to selected symptomatic patients who would have the potential to improve.
They were separated into 2 groups (Co Q10 n = 50, placebo n = 50). Patients who had previously taken coenzyme Q10 were excluded.

Patients were randomly assigned to receive 100 mg Co Q10 per day or placebo addition to routine-treatment.

All patients were done echocardiography and visited each 3 months and patients were asked whether their symptoms were improved, worse, or the same.

The change in values of primary and secondary end pointes were compared by using (t-test) (case and control), pre and post interference by using, paired t-test.

Table 1: Demographic and baseline characters of patients

Clinical signs and symptoms	Case (%)	Control (%)	p–value (%)
Fc = II	22 (55%)	27 (54%)	66%
Fc = III	11 (27.5%)	13 (26%)	
Fc = IV	7 (17.5%)	10 (20%)	
Palpitation			
+	13 (29.3%)	16 (31.4%)	52%
–	29 (70.7%)	35 (68.6%)	
Peripheral edema			
+	3 (7.7%)	4 (8.5%)	89%
–	36 (92.3%)	43 (91.5%)	
Tachycardia			
+	3 (7.3%)	5 (10%)	65%
–	38 (92.7%)	45 (90%)	
S3 and S4			
+	24 (70.6%)	25 (52%)	0.9%
–	10 (29.4%)	23 (47.9%)	
Liver size			
Large	3 (7.3%)	48 (100%)	0.9%
normal	38 (92.7%)	0 (0%)	
LV volume			
> 3.7	29 (74.9%)	23 (69.7%)	66%
< 3.7	10 (25.6%)	10 (20.3%)	

For quantities changeable value in case and control groups we used Men mar test.

For significance, a p value less than 0.05 were required.

RESULTS AND DISCUSSION

One hundred patients were randomly assigned in our study. Six patients did not finish the study, 43 patients in the coenzyme Q10 group and 51 in placebo group. Placebo group were the same age, genus and functional class as, Co Q10 group. So they received Co Q10 and placebo addition to routine treatment. Baseline characterization did not differ between 2 group (Table1). The study sample consisted of 60 (63.8%) men and 34 (36.2%) women and the mean age in both groups was over 40 years (Fig. 1). All patients were categorized on being in New York Heart Association Class II and III and all of them were receiving digoxin and angiotensin converting enzyme inhibitors or other routine drugs. No adverse reactions were attributed to the study drug and no side effects occurred. In the beginning of the study, symptoms did not improve in the placebo or Co Q10 group.

But after the treatment symptoms improved in both groups especially in Coenzyme Q10 group. The ejection fraction at baseline 30±10.7% in Co Q10 group and 33.2±8.6% in placebo group. The difference between group, was not significant but after three-month treatment changed to 34.6±10.5 (Co Q10), 32.4±8.7 (placebo) which difference was significant ($p<0.05$).

After nine month treatment average of EF in both groups were 39±9 (in Co Q10) and 36.7±3% (in placebo).

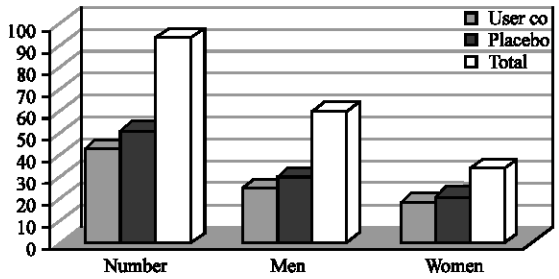

Fig. 1: Comparison of CoQ10 versus Placebo in men and women

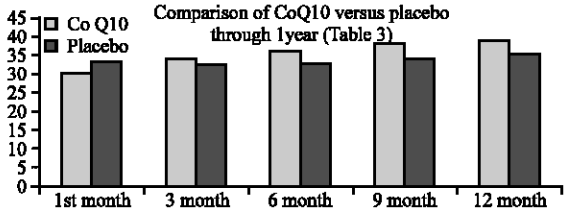

Fig. 2: Comparison of CoQ10 versus Placebo through one year

This result showed increased of EF in both groups after treatment but in Coenzyme Q10 group this difference was significant ($p<0.01$) and was not significant in placebo group (Fig. 2).

As classification of our patients on ejection fraction = 40%, we had 4 patients in Coenzyme Q10 group whom increased to 6 patients after treatment but in placebo groups there were 6 patients with EF = 40% whom decreased to 2 patients after treatment. As Chi-Square test, difference between pre and post treatment with Co Q10 was significant.

In this randomized, placebo-controlled clinical trial we detected objective benefit from Co Q10 administration in patients with heart failure. Cardiac ejection fraction and singe and symptoms changed with Coenzyme Q10. The use of Coenzyme Q10 for the treatment of heart failure has been advocated by physicians the studies cited to support its use have had major limitations. In addition to open-label studies with obvious susceptibility to unintentional bias (Tanaka *et al*., 1982; Langskoen *et al*., 1990), some studies have based their conclusions on evaluations of minimally symptomatic and inadequately treated patients (Permanetter *et al*., 1992) or on studies with noncom parable controls, subjective end points, poor statistics, or too few patients (Judi *et al*., 1986; Soja and Mortsensen, 1997). The few controlled studies have been contradictory. Our study was clinical trial and controlled and evaluated moderately ill patients with heart failure, who were receiving appropriate standard medical therapy. In addition the end points were objective and relevant.

Our findings suggest that coenzyme Q10 should be recommended for treatment of heart failure. Evaluations of the effects of coenzyme Q10 on ejection fraction have been contradictory. In contrast to our study, one double-blind crossover study of 32 patients with function class III, IV heart failure receiving 100 mg of coenzyme Q10 per day reported that ejection fraction did not improved (Langsjoen *et al*., 1985). In a larger study of 79 patients resting or exercise ejection fraction did not improve according to radio nuclide measurement (Hofman-Bang *et al*., 1995).

In that study a minimal effect on ejection fraction was seen only during volume loading. Another double-blinded crossover study did not detect an effect of coenzyme Q10 on ejection fraction and quality of their life but the level of serum coenzyme Q10 was increased dramatically (Permanetter *et al*., 1992). Another study was done on patients with heart failure whom waiting for heart transplant. This study was placebo-controlled trial.

After 3 months treatment with Co Q10, their exercise capacity and Ejection fraction, ANF and TNF were elevated. However, the major disadvantage of this study was few patients, so this study was done on 32 patients and terminated with 27 (Berman *et al*., 2004). Few studied have evaluated the effect of coenzyme Q10 on maximal exercise. These studies present contradictory data, for example, maximal work load was reported to increase slightly in this study (Hofman-Bang *et al*., 1995) but was unchanged in an investigation of minimally impaired patients (Permanetter *et al*., 1992). Our study examined ejection fraction by echocardiography and sign and symptom in a randomized clinical trial.

We found trend toward an improvement. So coenzyme Q10 improve quality of (free of symptom) life in patients with heart failure. Many open- labels uncontrolled studies have shown a subjective improvement in clinical measures of heart failure (Baggio *et al*., 1994). Morisco *et al*. (1993) large randomized blinded trial detected a lower rate of hospitalization for heart failure among patients receiving coenzyme Q1o. However, this study also reported high rates of pulmonary edema and cardiac asthma in these patients. The effect on symptoms in other studies has been inconsistent (Watson *et al*., 1999; Hofman-Bang *et al*., 1995).

In our trial most patients reported significant change in symptoms. We studied patients who were receiving standard therapy for heart failure including (b- blocker and angiotensine converting enzyme inhibitor) (Lancet, 1999) for most patients. Consequently, our findings should be applicable to the contemporary treatment of heart failure.

In one blinded, randomized placebo controlled trial, detected no objective benefit from coenzyme Q10 on patients with heart failure (Kheiburtz, 2007). Cardiac performance (measured by ejection fraction) and maximal exercise (evaluated with oxygen consumption and test duration) did not change with Co Q10 (Baggio *et al*., 1994). Because of the relatively small size of our study, we can not definitively say that coenzyme Q10 has an effect in patients with heart failure.

However, the lack of any trend and the relatively narrow confidence intervals make it unlikely that Co Q10 exerts clinically important effects in patients already receiving well titrated standard medication. However, with a documented increase in serum concentrations, often treatment can be ascribed to adequate treatment.

CONCLUSION

Coenzyme Q10 administration orally has favorable actions in the described cardiovascular conditions and appears to be safe and well tolerated in the adult population. However, published clinical trials investigating the efficacy of CoQ10 in CHF, angina, hypertension, but produced inconsistent results (Hodgson *et al*., 2002).

It is difficult to draw definitive conclusion regarding the role of CoQ10 in the treatment of this disease without additional large-well-designed clinical trials. Present study shows benefit to adding coenzyme Q10 to the standard treatment of heart failure. Chronic illness motivates patients to seek out alternative therapy and it is not surprising that people have been willing to buy an expensive drug. This study supported in part by university of Mazandaran and Schedule Budget Organization.

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