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Research Article

Effects of Coenzyme Q10 on Biochemical Markers of Hepatic Necroinflammation in Patients with Nonalcoholic Fatty Liver

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Abstract

Background: Non-Alcoholic Fatty Liver Disease (NAFLD) is a common metabolic liver disorder that can progress to cirrhosis. Up to now, there is no established treatment for this disease. **Methods:** We randomly assigned 55 adults with NAFLD to receive Coenzyme Q10 (CoQ10) 60 mg daily (30 subjects) or vitamin E 800 unit daily (25 subjects) for 3 months to assess the effect of CoQ10 versus vitamin E on BMI, ALT, AST, ALK-P, PT, Bilirubine, ALB, Ferritin, TG, Total Cholestrol, FBS, Serum Insuline, LDL, HDL, Total Anti Oxidant Capacity (TAC) before and after intervention. **Results:** In CoQ10 group there was a significant improvement in AST, ALT, TAC (P value<0.0001), Ferritin, Total bilirubin, GGT (p value<0.01), HDL (p value<0.05). In vitamin E group there was a significant improvement in AST, ALT, TAC, Ferritin, GGT, HDL (p value<0.01). There was not significant improvement in FBS, Insulin resistance and other lipid profile in both groups. **Conclusion:** Our study assigned that 60 mg CoQ10 is effective on improvement of noninvasive liver parameters in NAFLD. We suggest longer duration treatment and with larger dosage. We also suggest a large study with biopsy control for the assessment the effect of CoQ10 in NAFLD.

Keywords: Coenzyme Q10; Nonalcoholic fatty liver; Biochemical markers; Hepatic necroinflammation

Introduction

Non-alcoholic fatty liver disease (NAFLD), a condition in which lipid accumulation substitute normal liver tissue, is the most prevalent metabolic liver disease in world and an important risk factor for chronic liver disease, cirrhosis and hepatocellular carcinoma [1]. Caloric overconsumptions, insulin resistance that cause metabolic syndrome are the major risk factors for this rapidly rising hepatic disorder [2,3]. Treatment of NAFLD rely on life-style modifications including nutrition and exercise but there are many drugs that investigate for treatment [4]. Coenzyme Q10 (CoQ10) as a lipid-soluble component of virtually all cell membranes has an important role in respiratory metabolism by interfere in the mitochondrial electron transport chain [5]. Recently, CoQ10 has been demonstrated as an antioxidant that not only protects the cells by preventing lipid peroxidation but also by regenerating other antioxidants [6]. Some studies showed that CoQ10 protects liver tissue against toxin and enhanced antioxidant protection of liver membranes in long-lived rats and depletion of antioxidants such as CoQ10 may occur in NAFLD [7-9]. Therefore, we propose that COQ10 might be effective in treatment of NAFLD. According to our best knowledge, up to now, the effects of dietary CoQ10 on NAFLD have not been investigated in humans.

Patient and Method

Method

This was a single-blinded randomized clinical trial that patients with NAFLD were randomized to receive CoQ10 60 mg or Vitamin E 800 IU for three months.

Step 1 American Heart Association diet and encouragement to walk or jog at least 30 minutes daily advice to both groups. Blood was obtained in the fasting state at entry and the end of study for: Fasting Blood Sugar (FBS), Triglyceride (TG), Total Cholesterol, LDL, HDL, Serum Insulin, Albumin(ALB), PT, Ferritin, Bilirubin total and direct (BILI T/D), Gamma Glutamyl Transpeptidase (GGT), AST, ALT, and ALP.

Two cc of serum sent to a research center for measurement of serum total anti-oxidant capacity (TAC) with FRAP (Ferric reducing Ability of plasma) that is a rapid and simple method [10].

Patients

Inclusion criteria: Patients were including if they had:

1- At least one of these metabolic disorder (Diabetes Mellitus, hyperlipidemia, obesity) and,

2- Persistent abnormal transaminase for at least 6 months and,

3- Negative serologic markers for known chronic liver disease (antinuclear antibody, smooth muscle antibody, anti LKM antibody, anti-mitochondrial antibody, hepatitis B surface antigen, anti HBc antibody, anti-hepatitis C virus anti-body, ceruloplasmin and iron profile) and,

4- Age between 18 to 65 years and,

5- Sonography was compatible to fatty liver disease.

Exclusion criteria:

1- Suspicious or history of drink any much alcohol for any time,

2- Evidence of chronic liver disease/Cirrhosis (ascites, esophageal varices, spider angioma, gynecomastia, serum albumin level less than 3.5 g/dl, international normalized ratio greater than or equal to 1.7, serum bilirubin level greater than 2 mg/dl, AST or ALT >300,

3- History of drug or illness that can impaired transaminase,

4- Any positive serology tests previously outlined or suspicious sexual contact or IV drug abusers,

5- Pregnant or barest feeding women,

6- Pervious Vit E or CoQ10 supplement within 3 month of study enrollment.

Statistics

Results were assessed using the student t- test and paired t- test where appropriate. Repeated -measures ANOVA was used to analyze data. A P value equal and less than 0.05 was considered statistically significant.

Results

Subjects were enrolled in the trial and were treated and followed for 3 months. Eighty-six patient (48 men and 38 women) ranging in age from 19 to 65 years were enrolled. 21 patients were excluded from the study for many reasons. Of the 65 subjects who underwent randomization 35 were assigned to receive CoQ10 and 30 were assigned to receive vitamin E (Figure 1).

The two groups were well matched according to demographic characteristics (weight, height, gender, age, diabetes, metformin and statin user) clinical and laboratory data (Table 1).

In CoQ10 group two and three patients take metformin and statin respectively. In Vit E group, four and five patients take metformin and statin respectively.

None of the patients in both group take fibrate and/or PPAR alpha and gamma agonists drugs.

Sub group analysis for all biochemical variable show no difference between two group before intervention. After 3 months of intervention two group assessment for demographic and laboratory variable was done (Tables 2-4).

In CoQ10 group there was improvement in weight and BMI (P value=0.001), AST, ALT, TAC (P value<0.0001), Ferritin, Total bilirubin, GGT (P value<0.01), HDL (P value<0.05) but no significant difference in FBS, TG, Total Cholestrol, LDL, FBS, Serum Insulin, ALB, PT, ALK-p parameters before and after treatment with CoQ10 (Table 2).

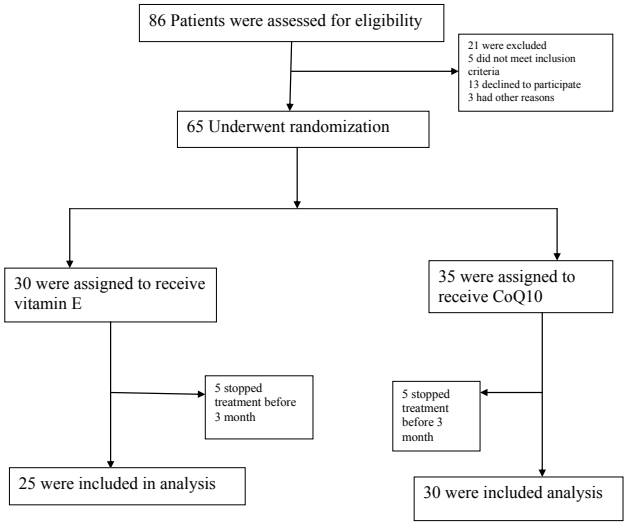

Figure 1: Screening, Randomization, and Follow-up of Study subjects.

In Vit E group there was a significant improvement in weight (p=0.05), AST, ALT, TAC, Ferritin, GGT, HDL (p value<0.01), but no significant difference in FBS, TG, Total Cholestrol, LDL, FBS, Serum Insulin, ALB, PT, ALK-p, total bilirubin parameters before and after treatment with vit E (Table 3).

There was no significant difference between CoQ10 and Vit E groups in improvement any demographic and biochemical parameters (Table 4).

Adverse Events

One event of mild dyspepsia and two event of mild headache were reported in CoQ10 group. No adverse event was seen in Vit E group.

Discussion

In this study, both CoQ10 and vitamin E groups show significant improvement in BMI, weight, ALT, AST, ferritin, TAC, HDL, bilirubin and GGT. Up to now, there is no published clinical trial about the role of CoQ10 in treatment of NAFLD in human, Ghada et al. cannot show a role for CoQ10 in treatment of rat liver steatosis [11] but two studies show CoQ10 reduce the hepatic oxidative stress and liver function in rats [12,13]. In our study, CoQ10 significantly improve ALT and AST. We think this effect may be correlated to antioxidant effect of CoQ10, since serum total antioxidant capacity significantly improves after intervention. Our study also shows the effect of CoQ10 in decrease serum ferritin level that is a significant marker for both inflammation and insulin resistance. We think this can be the effect of CoQ10 on inflammation. CoQ10 reduce serum CRP level, and reduce inflammatory stress in obese mice [14,15]. Weight loss is another mechanism that can explain improvement of liver enzyme in this study. Obesity maybe increase in oxidative stress and increased plasma level of oxidized low-density lipoprotein [16-18], but only few studies examined antioxidant systems such as CoQ10 in obesity [19-23]. Significant decrease in CoQ10 plasma level obese people was shown by Mehmetoglu et al. [20]. The potential effect of CoQ10 on increase fatty acid oxidation and suppression of adipocyte differentiation can be justify weight loss [24,25]. Moreover, due to reduction in lipolysis and plasma levels of circulating Apo-B containing lipoprotein, Weight loss cause increase the HDL plasma level [26,27].

In our study did not prove any effect in both group on FBS and serum insulin. DM is a condition of increased oxidative stress and impaired energy metabolism. Although Plasma levels of CoQ10 have been found to be lower in diabetic patients [27], CoQ10 supplementation did not improve glycemic control in some studies [28,29]. Our study did not show any effect on total cholesterol, LDL, TG in both group, but the effect of CoQ10 in improvement lipid profile has shown in some studies [29,30] Action on mitochondrial anti-oxidant defense may be the potential biochemical mechanism of this effect [31-33].

One event of mild dyspepsia and two event of mild headache were reported in CoQ10 group but improve spontaneously after continue to using. Up to now, CoQ10 consumption have not been associated to serious adverse effects in human. Dyspepsia, low appetite, nausea and diarrhea was the complication that was reported by Greenberg et al. [34]. Increase serum LDH and SGOT levels without hepatotoxicity was seen in doses Higher than 300 mg daily [35]. The major limitation of our survey was not performing liver biopsy that is not only gold standard test for diagnosis but also in response to treatment in NASH.

	Q10 group	Vitamin E group	P value
Age (years)	39.66 ± 13.04	43.20 ± 10.05	0.272
Weight (kg)	81.03 ± 10.82	83.12 ± 12.86	0.516
Hieght (cm)	168.36 ± 8.45	166.96 ± 7.31	0.517
BMI (kg/m^2)	28.59 ± 3.20	29.78 ± 4.16	0.235
FBS (mg/dl)	104.76 ± 20.80	114.64 ± 54.86	0.366
Triglyceride (mg/dl)	225.76 ± 146.92	238.32 ± 141.28	0.749
Total cholesterol (mg/dl)	200.90 ± 36.41	198.88 ± 50.74	0.864
HDL-c (mg/dl)	43.20 ± 6.97	40.12 ± 4.87	0.069
LDL-c (mg/dl)	107.40 ± 20.81	115.84 ± 29.92	0.224
Insulin (µU/mL)	17.47 ± 6.37	16.91 ± 8.87	0.789
total Billirubin (mg/dl)	0.70 ± 0.30	0.87 ± 0.80	0.281
Direct Billirubin (mg/dl)	0.25 ± 0.13	0.24 ± 0.13	0.864
AST (U/L)	41.70 ± 14.0	50.28 ± 45.69	0.334
ALT (U/L)	62.30 ± 28.86	72.40 ± 71.60	0.482
GGT (U/L)	47.36 ± 21.27	39.84 ± 23.90	0.222
Ferritin (mg/dl)	171.88 ± 180.13	253.60 ± 247.96	0.202
PT	11.78 ± 0.58	12.06 ± 0.61	0.094
Total antioxidant (µmol/L)	555.69 ± 142.92	555.92 ± 130.12	0.995
Albumin (mg/dl)	4.07 ± 0.40	4.212 ± 0.385	0.204

Table 1: Baseline Characteristics of the Study Subjects.

	Before treatment	After treatment	P value
Weight (kg)	81.03 ± 10.81	79.00 ± 9.87	0.001
BMI (kg/m^2)	28.59 ± 3.20	27.86 ± 2.81	0.001
FBS (mg/dl)	104.76 ± 20.80	99.93 ± 15.12	0.113
Triglyceride (mg/dl)	225.76 ± 146.92	204.00 ± 129.87	0.366
Total cholesterol (mg/dl)	200.90 ± 36.40	192.56 ± 32.97	0.189
HDL-c (mg/dl)	43.20 ± 6.97	46.40 ± 8.64	0.049
LDL-c (mg/dl)	107.40 ± 20.81	104.30 ± 18.17	0.440
Insulin (µU/L)	17.47 ± 6.37	19.76 ± 9.34	0.188
total Billirubin (mg/dl)	0.700 ± 0.300	0.57 ± 0.23	0.009
Direct Billirubin (mg/dl)	0.25 ± 0.12	0.20 ± 0.07	0.085
AST (U/L)	41.70 ± 14.06	30.10 ± 12.07	<0.0001
ALT (U/L)	62.30 ± 28.86	42.76 ± 24.72	<0.0001
GGT (U/L)	47.36 ± 21.27	37.45 ± 24.46	0.005
Ferritin (mg/dl)	171.88 ± 180.12	141.55 ± 159.99	0.007
PT	11.78 ± 0.58	11.66 ± 0.56	0.147
Total antioxidant (µmol/L)	555.69 ± 142.92	628.39 ± 89.16	<0.0001
Albumin (mg/dl)	4.07 ± 0.40	4.07 ± 0.34	0.941

Table 2: Difference in variable in CoQ10 group before and after treatment.

	Before treatment	After treatment	P value
Weight (kg)	83.12 ± 12.86	81.72 ± 13.13	0.052
BMI (kg/m^2)	29.78 ± 4.16	29.27 ± 4.11	0.043
FBS (mg/dl)	114.64 ± 54.86	104.56 ± 28.69	0.409
Triglyceride (mg/dl)	238.32 ± 141.28	215.08 ± 133.87	0.112
Total cholesterol (mg/dl)	198.88 ± 50.74	199.64 ± 48.62	0.918
HDL-c (mg/dl)	40.12 ± 4.87	45.64 ± 9.84	0.004
LDL-c (mg/dl)	115.84 ± 29.92	109.72 ± 33.76	0.088
Insulin (µU/L)	16.91 ± 8.87	19.03 ± 14.15	0.422
total Billirubin (mg/dl)	0.87 ± 0.80	0.74 ± 0.55	0.213
Direct Billirubin (mg/dl)	0.24 ± 0.13	0.23 ± 0.12	0.574
AST (U/L)	50.28 ± 45.69	33.36 ± 20.46	0.010
ALT (U/L)	72.40 ± 71.60	45.68 ± 39.95	0.001
GGT (U/L)	39.84 ± 23.90	37.88 ± 33.98	0.586

Ferritin (mg/dl)	253.60 ± 247.96	200.68 ± 220.89	0.018
PT	12.06 ± 0.61	12.02 ± 0.56	0.647
Total antioxidant (µmol/L)	555.92 ± 130.11	697.08 ± 231.72	0.049
Albumin (mg/dl)	4.21 ± 0.38	4.08 ± 0.27	0.123

Table 3: Difference in variable in vit E group before and after treatment.

	CoQ10 group	Vitamin E group	P value
Weight (kg)	79.00 ± 9.87	81.72 ± 13.13	0.385
Hieght (cm)	168.36 ± 8.45	166.96 ± 7.31	0.517
BMI (kg/m^2)	27.87 ± 2.81	29.27 ± 4.11	0.141
FBS (mg/dl)	99.93 ± 15.12	104.56 ± 28.69	0.447
Triglyceride (mg/dl)	204.00 ± 129.87	215.08 ± 133.87	0.757
Total cholesterol (mg/dl)	192.56 ± 32.97	199.64 ± 48.62	0.525
HDL-c (mg/dl)	46.40 ± 8.64	45.64 ± 9.84	0.762
LDL-c (mg/dl)	104.30 ± 18.17	109.72 ± 33.77	0.452
Insulin (µU/mL)	19.76 ± 9.34	19.03 ± 14.15	0.821
total Billirubin (mg/dl)	0.57 ± .23	0.74 ± 0.55	0.137
Direct Billirubin (mg/dl)	0.20 ± .07	0.23 ± 0.12	0.249
AST (U/L)	30.10 ± 12.07	33.36 ± 20.46	0.466
ALT (U/L)	42.76 ± 24.72	45.68 ± 39.95	0.742
GGT (U/L)	37.45 ± 24.46	37.8800 ± 33.98936	0.957
Ferritin (mg/dl)	141.55 ± 159.99	200.68 ± 220.84	0.278
PT	11.66 ± 0.56	12.02 ± 0.56	0.025
Total antioxidant (µmol/L)	628.39 ± 89.16	697.08 ± 231.72	0.197
Albumin (mg/dl)	4.07 ± 0.34	4.08 ± 0.27	0.866

Table 4: Characteristics of the Study Subjects three months after intervention.

Although in our study 60 mg CoQ10 for 3 months improve biochemical markers of hepatic necroinflammation in patients with NASH but we recommend a study with higher dose and longer duration for assessment CoQ10 on insulin resistance and lipid profile.

Conclusion

In summary, our study assigned that 60 mg CoQ10 is effective on improvement of noninvasive liver parameters in NASH. Neither CoQ10 and nor vit E are effective in insulin resistance and lipid profile, but we suggest longer duration treatment and with larger dosage. We also suggest a larger study with biopsy control for the assessment the effect of CoQ10 in NASH.

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