CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.3819141

Available online at: http://www.iajps.com Research Article

EFFECT OF COENZYME Q 10 ON ADIPONECTIN, OXIDATIVE STRESS AND GLYCAEMIC CONTROL IN PATIENTS WITH TYPE II DIABETES MELLITUS

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Article Received: March 2020 **Accepted:** April 2020 **Published:** May 2020

Abstract:

Aim: *To evaluate the effect of coenzyme Q10 supplementation on glycemic control, oxidative stress and adiponectin levels in type 2 diabetic patients.*

Methods: *A randomized, single-blind, placebo-controlled study was conducted in people with type 2 diabetic patients. Patients and controls received 100 mg coenzyme Q10 or placebo twice daily for eight weeks. Various measurements were made at the beginning and end of the intervention. These include markers for measuring glycemic control (fasting blood sugar and glycated hemoglobin); an oxidative stress marker (malonic aldehyde); and anti-inflammatory marker (adiponectin). SPSS 18 was used for statistical analysis.*

Results: *Out of 52 patients, 28 (54%) were male and 24 (46%) were female, and the average age was 51.73 ± 7.34. In the intervention group there were 16 (62% men and 10 (39%) women), 12 (46%) men and 14 (54%) women in the control group, which resulted in a significant reduction of coenzyme Q10 and the difference was not significant (p> -0.05). In addition, fasting blood glucose, glycosylated hemoglobin and adiponectin did not show significant differences within or between groups (each p> 0.05).*

Conclusion: *Coenzyme supplementation may reduce oxidative stress in patients with type 2 diabetes, but may not have an effect on glycemic control and adiponectin levels.*

Key words: *coenzyme Q10, diabetes, blood sugar, oxidative stress, inflammation.*

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Please cite this article in press Zainab Hooria et al, ***Effect Of Coenzyme Q 10 On Adiponectin, Oxidative Stress And Glycaemic Control In Patients With Type Ii Diabetes Mellitus.,*** *Indo Am. J. P. Sci, 2020; 07(05).*

INTRODUCTION:

Diabetes mellitus (DM) is a chronic metabolic disorder that is characterized by hyperglycemia and insulin secretion, and / or impaired insulin function. It is considered one of the most common health problems around the world. Free radicals and oxidative stress (OS) have been shown to play an important role in the pathogenesis and development of diabetic complications. Diabetes-related hyperglycemia will lead to the development and maintenance of an oxidative environment[1-2]. Chronic inflammation is one of the other conditions associated with the pathogenesis of type 2 diabetes (DM2). In addition, systemic etiologic components such as abdominal obesity and insulin resistance have been reported to induce inflammation in T2DM.

The presence of OS in the body can be eliminated thanks to natural defense mechanisms, including enzymatic and non-enzymatic antioxidant pathways[3]. Some of the non-enzymatic antioxidants are vitamins C and E, α-lipoic acid and coenzyme Q10 (CoQ10). CoQ10 is a vitamin-like substance that is endogenously synthesized. It is a powerful lipophilic antioxidant in the form of ubiquin, reduced by its ability to regenerate other antioxidants[4-5]. It is also an important component of the electron transport chain in mitochondria and is therefore very important for the synthesis of adenosine triphosphate (ATP). CoQ10 has also been suggested to have anti-inflammatory properties through gene expression. Studies have been conducted on the various health effects of CoQ10 in a variety of disease states, including diabetes. However, the results are often inconsistent[6-7]. This highlights the need for further research. The current study plans to evaluate the effect of CoQ10 supplementation on glycemic control, OS and adiponectin levels in patients with TQDM. This is the first study to investigate the effect of CoQ10 on adiponectin levels in diabetic patients.

PATIENTS AND METHODS:

A randomized, single-blind, placebo-controlled study was held in the Medicine Unit of Holy Family Hospital Rawalpindi for 3 months duration from January 2019 to January 2020. The samples represented the diabetic population because people were taken from health centers at different socioeconomic levels in different parts of the city. The sample size was calculated from the previous study10 with a strength of 90% and a significance level of 0.05, based on the result of systolic blood pressure (SBP). Blood pressure and some other variables were also measured and the results were previously published. T2 diabetes and body mass index (BMI) aged 35–60 years, 20–30 kg / m2 were included. The endocrinologist confirmed the condition of diabetes. People with chronic gastrointestinal (GI) disorders, kidneys and liver, anticoagulant therapy, vitamin and mineral supplements, and smokers are excluded. Also excluded were those who changed the dose or type of hypoglycemic drugs during the intervention. After approval by the Ethics Committee, participants were provided with the purpose and procedures of the study and written informed consent was obtained from each of them. Block randomization was used to assign participants to two equal groups. One group contains 100 mg CoQ10 B.I.D. (200 mg / day) for the next eight weeks, microcrystalline cellulose B.I.D. During the same period, participants were blind to interventions at work.

Capsules were administered every two weeks to ensure compliance with the intervention and to check their regular intake. 24-hour diet withdrawal was completed for each patient before and after the study. Energy and macronutrient uptake (carbohydrates, proteins and fats) was obtained with Nutritionist IV version 3.5.2 and the percentage of energy derived from macronutrients was calculated. The same nutrition advice was given to both groups. Anthropometric data, including weight, height and BMI, were observed at the beginning of the study and at the end of the intervention. While the masses are measured using an analog scale (Seca), participants wear light clothing and shoes. The height was measured with a meter. The BMI is calculated by dividing the weight in kilograms by the squares of height in meters. After fasting overnight, blood samples were taken at the beginning and end of the intervention. They were analyzed for glucose, (HbA1c), malonic aldehyde (MDA) and adiponectin. Serum glucose was measured by an enzymatic colorimetric method in a BT1500 auto-analyzer. HbA1C was measured by high performance liquid chromatography (HPLC) using a C18 column (Agilent 1100 series, Germany) with a variable wavelength detector. Serum MDA level was determined using a thiobarbituric acid reagent method in a spectrophotometer. An enzyme immunoassay (ELISA) was used to determine adiponectin (Mediagnost, Germany).

Collected data were analyzed using SPSS 19. Results were expressed as mean ± standard deviation (SD) or frequency and percentage. To confirm the normality of the data, Kolmogorov-Smirnov and Shapiro-Wilk tests were used. When the data were correct, independent and paired t-tests were performed to make statistical comparisons between and between groups. Otherwise, Mann-Whitney and Wilcoxon tests were used. The chi-square test was also used for the distribution of groups by sex. $P < 0.05$ was considered statistically significant.

RESULTS:

Of the 52 patients, 28 (54%) were men and 24 (46%) were women, and their average age was 51.73 ± 7.34 (Table 1). In the intervention group there were 16 (62% men and 10 (39%) women), 12 (46%) men and 14 (54%) women in the control group, and the average BMI of the cases was 25.31 ± 2.14 kg / between controls 25.34 ± 2.39 kg / m2 While at the beginning of the experiment there was no significant difference between the two groups in terms of sex, age, duration of diabetes, anthropometric data, energy, carbohydrates and fat intake (the only exception was the percentage energy consumption from higher protein in the CoQ10 group (p = 0.007) There was no difference in the variables at the beginning (p> 0.05).

Table-1: Baseline parameters

Variable	CoQ10 Group (n=26) (mean ± SD)	Placebo Group (n=26) (mean ± SD)	P-value
Male/Female (n, %)	16 (31%) /10 (19%)	12 (23%) /14 (27%)	0.27
Age (year)	50.67±7.01	52.79±7.66	0.32
Duration of diabetes (year)	4.15±3.96	5.05±3.85	0.29
Height (m)	1.64±0.09	1.60±0.09	0.11
Weight (kg)	68.49±9.97	64.78±8.11	0.17
BMI (kg/m2)	25.31±2.14	25.34±2.39	0.96
Energy (Kcal)	1530±294	1558±498	0.83
Carbohydrate (%)	57.05±9.02	60.19±7.22	0.22
Protein (%)	16.95±4.19	13.9±2.76	0.007*
Fat (%)	25.91±6.92	25.95±6.58	0.98
Fasting Blood Glucose (mg/dl)	158.75±41.55	192.42±83.16	0.3
HbA1c (%) µ µ	7.32±1.01	8.13±1.99	0.09
MDA (mol/l)	12.68±5.98	11.24±2.66	0.76
Adiponectin (g/ml)	6.41±2.93	7.32±5.84	0.52

The average energy intake and percentage of calories from macronutrients did not differ significantly between groups after intervention, and CoQ10 supplementation did not affect mass and BMI (Table 2).

Table-2: Dietary intake components and anthropometric data.

Variable	CoQ10 Group		Placebo Group		P-value*
	(n=26) (mean ± SD)		(n=26) (mean ± SD)		
	Baseline	Final	Baseline	Final	
Energy (Kcal)	1530±294	1607±416	1558±498	1482±534	0.13
Carbohydrate (%)	57.05±9.02	63.00±8.28	60.19±7.22	63.52±8.69	0.73
Protein (%)	16.95±4.19	14.32±2.78	13.90±2.76	12.19±2.27	0.37
Fat (%)	25.91±6.92	22.59±6.7	25.95±6.58	24.19±8.55	0.49
Weight (kg)	68.49±9.97	68.65±9.87	64.78±8.11	65.43±8.16	0.09
BMI (kg/m^2)	25.31±2.14	25.38±2.14	25.34±2.39	25.6±2.46	0.07

The intervention resulted in a significant decrease in serum MDA levels in the CoQ10 group (p = 0.04), but the change between the groups was not significant. Fasting blood sugar and HbA1c levels did not change significantly between groups or between groups after intervention. In addition, serum adiponectin levels did not change significantly at the end of the intervention (Table 3).

Table-3: Biochemical parameters.

Variable	CoQ10 Group (n=26) (mean ± SD)		Placebo Group (n=26) (mean ± SD)		P-value*
Baseline Final	Baseline	Final	Baseline	Final	
Fasting Blood Glucose (mg/dl)	158.75±41.55	154.92±41.49	192.42±83.16	199.17±87.02	0.22
P-value$^+$	0.34		0.48		
HbA1c (%)	7.32±1.01	7.25±1.04	8.13±1.99	8.18±2.02	0.55
P-valueµ	0.57	0.75			
MDA (mol/l)	12.68±5.98	10.43±3.13	11.24±2.66	11.68±5.14	0.19
P-value	0.04++		0.57		
Adiponectin (µg/ml)	6.41±2.93	6.85±4.88		6.77±3.88	0.74
P-value	0.66		0.48		

DISCUSSION:

Based on our results, CoQ10 did not affect fasting blood sugar and HbA1c compared to the placebo group. This is in line with the results obtained in some other studies. For example, 100-200 mg of CoQ10 did not significantly affect fasting blood sugar or HbA1c in patients with type 1 or type 2 diabetes, but CoQ10 did not improve glycemic control in some studies. Significant differences in fasting or HbA1c levels. For example, in a study of patients with hypertension with coronary artery disease and type 1 diabetes rats, CoQ10 significantly reduced blood sugar. In two other studies in patients with DM2, CoQ10 supplementation at 200 mg / day in the form of ubiquinone and ubiquinol resulted in a marked reduction in HbA1c.

Certain hypoglycemic drugs, such as glyburide, phenformin and tolazamide, have been reported to reduce the endogenous content of CoQ10. In diabetic patients with a relatively CoQ10 deficiency, CoQ10 supplementation may lead to an improvement in cell function. The glycerol-3-phosphate cycle is the main shuttle mechanism in pancreatic p cells. In this pendulum, the expression of mitochondrial glycerol-3-phosphate dehydrogenase is reduced in diabetic T2 cells. The activity of this enzyme is expected to be further exacerbated by the relative lack of CoQ10. In addition, there is a hypothesis that CoQ10 deficiency may lead to insulin resistance in muscle, the main tissue in which glucose is used. In this study, MDA in the participants' serum was measured as an OS marker. MDA is a highly toxic substance, the main peroxidation product of polyunsaturated fatty acids. Higher plasma MDA levels were observed in diabetic patients. In the current study, CoQ10 administration significantly reduced MDA levels in the intervention group. CoQ10's antioxidant properties outweigh other antioxidants in terms of quantity and effectiveness. CoQ10 can protect lipids, proteins and deoxyribonucleic acid (DNA) against oxidative events and is able to reproduce other antioxidants such as astocopherol and ascorbate. The presence of hyperglycemia in diabetes stimulates the increase in peroxide production in the mitochondrial electron transport chain. CoQ10 may inhibit the production of peroxide in mitochondria, which leads to a decrease in SG. In one study, water-soluble CoQ10 reduced OS with a change in MDA, thiobarbituric acid reagents (TBARS), diene conjugates and antioxidant vitamins in plasma of patients with coronary artery disease. Improvement in oxidation rates was also found in diabetic rats receiving CoQ10. However, two studies assessing the effect of CoQ10 on oxidation markers in diabetic patients (MDA modified low density lipoprotein (LDL 'or F2-isoprostane and 20-hydroxyyeicosetraenoic acid, respectively)) have not improved significantly. This study is the first to study the effect of CoQ10 on levels Adiponectin in patients with diabetes Adiponectin is an anti-inflammatory protein that is almost exclusively secreted by adipose tissue. Low levels of adiponectin in the circulation are associated with health problems such as insulin resistance and DM2. The presence of an oxidizing center has been proposed to suppress adiponectin expression. Adiponectin levels did not change significantly. This is similar to cross-study results in which CoQ10 supplementation does not change plasma adiponectin levels in well-established men. In addition, three months of CoQ10 administration to heart transplant candidates could not reduce tumor necrosis factor alpha (TNF-a) as an inflammatory marker. Various test features may explain the inconsistent results of studies on the effects of CoQ10 on diabetic metabolic parameters. These include differences in design, sample size, dose and timing of CoQ10 administration, and the use of specific medications. The different CoQ10 preparations used in the studies, and hence the variability in bioavailability, can also lead to inconsistent results. In this study, CoQ10 serum concentrations were not determined for participants. Also, the short duration of the intervention was a limitation of this clinical trial.

CONCLUSION:

Eight weeks of CoQ10 supplementation may reduce OS in patients with DM2. However, glycemic control and adiponectin levels may not change. More research is needed to confirm the impact on larger populations and longer periods.

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