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Research Article

THE EFFECTS OF COQ-10 SUPPLEMENTATION ON OXIDATIVE STRESS AND INFLAMMATORY MARKERS IN IRAQI TYPE 2 DIABETIC PATIENTS

AHMED SALIH SAHIB*

Department of Pharmacology, College of Pharmacy, University of Karbala, Karbala, Iraq. Email: ahmedsalih73@yahoo.com

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ABSTRACT

Objective: This study was aimed to determine the effects of coenzyme Q10 (CoQ10) administration on glucose homeostasis parameters, oxidative stress parameters, and biomarkers of inflammation among patients with Type 2 diabetes mellitus (T2DM).

Methods: A total of 28 T2DM patients (18 female [64.29%] and 10 male) of age range from 35 to 60 years old and mean±standard deviation age 46.76±7.89 years. Participants were randomly allocated into two groups. Group A (n=14) received placebo and Group B (n=14) received 150 mg CoQ10 supplements for 12 weeks in addition to the already given oral hypoglycemic agent (glibenclamide) and dietary control. In addition, 25 age and sex-matched healthy volunteers were included in the study as a control group. Fasting blood samples were taken at the beginning of the study and after 6 and 12 weeks intervention to quantify glucose homeostasis parameters, oxidative stress, and biomarkers of inflammation.

Results: Compared with the placebo, CoQ10 supplementation resulted in a significant reduction in fasting blood glucose, glycosylated hemoglobin, improvement in antioxidant status, and reduction of inflammatory biomarkers.

Conclusion: Daily administration of 150 mg CoQ10 supplements for Type 2 diabetic patients for 12 weeks had beneficial effects on glycemic control, oxidative stress parameters, and inflammatory markers.

Keywords: Coenzyme Q10, Type 2 diabetes, Oxidative stress, Inflammation.

INTRODUCTION

The prevalence of Type 2 diabetes mellitus (T2DM) worldwide mandate continuous research to explore the mechanisms contributing to complications of the disease and at the same time fast and comprehensive scanning of old agents and investigation of new agents that acting by different mechanisms of action which may be beneficial to prevent or slow the appearance of diabetic complications [1]. Targeting of complications like oxidative stress and inflammation in T2DM represent interesting strategy that may delay the appearance of micro- and macro-vascular complication along with the main goal which is good glycemic control [2].

The patients with Type 2 diabetes are vulnerable to increased oxidative stress due to the excessive production of free radicals especially reactive oxygen species (ROS) and impaired antioxidant defense mechanism [3]. Poorly glycemic control leads to hyperglycemia which results in increased production of ROS which causes membrane damage due to the peroxidation of membrane lipids and protein glycation [4]; for this reason, the targeting of oxidative stress is necessary in diabetic patients. Many studies have shown that the use of antioxidants, as well as herbal agents, might help control the oxidative stress [5]. Many studies suggest a central role for oxidative stress in the pathogenesis of this multifaceted metabolic disorder. This has prompted investigations in the use of antioxidants as a complementary therapeutic approach [6].

Many studies reporting the relation between inflammation and T2DM have showed the role of inflammation in the development of insulin resistance and other pathogenic processes of T2DM [7]. It has been shown that the proinflammatory cytokine tumor necrosis factor-α (TNF-α) was able to induce insulin resistance [8]. It has been suggested that abnormal levels of chemokines released by adipose tissue activate monocytes and increase the secretion of pro-inflammatory adipokines. Such cytokines, in turn, enhance insulin resistance in adipose and other tissues, thereby increasing the risk for T2DM [9].

Exposure to exogenous factors triggers the release of pro-inflammatory cytokines like TNF-α and other interleukins, these cytokines are derived primarily from macrophages and can directly enhance insulin resistance in adipocytes, muscle and liver cells [10]. Cytokines also act on the liver to increase the production of very-low density lipoproteins (LDLs), leading to diabetic dyslipidemia [11], furthermore, cytokines deactivate the liver X receptors, resulting in an increased rate of cholesterol accumulation [12], and ultimately trigger the hepatic production and secretion of acute-phase proteins such as C-reactive protein (CRP); The synthesis of acute-phase reactants following the cytokine release characterizes the early stages of T2DM and exhibits graded increases as the disease progresses and clinical complications ensue [13,14].

Coenzyme Q10 (CoQ10)

CoQ10 was first isolated in 1957 from beef mitochondria and is known to be highly concentrated in heart-muscle cells due to the high energy requirements of this cell type. It is a naturally occurring fat-soluble vitamin-like quinone. It is also called ubiquinone as it is ubiquitous or present in all eukaryotic cells [15]. CoQ10, also known as ubiquinone, and abbreviated at times to (CoQ10, Q10, where Q refers to the quinone chemical group, and 10 refers to the number of isoprenyl chemical subunits in its tail). This oil-soluble, vitamin-like substance is present in most eukaryotic cells, primarily in the mitochondria. It is a component of the electron transport chain and participates in aerobic cellular respiration, generating energy in the form of adenosine triphosphate [16]. CoQ10, or ubiquinone, is an endogenously synthesized lipid. Intracellular synthesis, which depends on the mevalonate pathway, is the major source of CoQ10. The mevalonate pathway is a sequence of cellular reactions leading to farnesyl pyrophosphate, the common substrate for the synthesis of cholesterol, and CoQ10. Cells synthesize CoQ10 *de novo* [17]. The well recognized biochemical functions of CoQ are mitochondrial energy coupling and its action as a primary regenerating antioxidant. Less well-established functions include oxidant action in the generation of signals and control of cellular redox state. By participation in transmembrane electron

transport, CoQ can carry reducing equivalents to the inside of vesicles or to the outside of cells. In addition, there is evidence that CoQ can take part in control of membrane structure and phospholipid status [18]. Serum CoQ10 levels in Type 2 diabetic patients are often decreased and may be associated with subclinical diabetic cardiomyopathy, reversible by CoQ10 supplementation [19].

The aim of this randomized, placebo-controlled clinical trial was to study the antioxidant and anti-inflammatory effect of CoQ10 supplementation in Iraqi patients with Type 2 diabetes.

METHODS

This is a prospective, placebo-controlled clinical trial carried out on patients with T2DM who attend the Specialized Center for Endocrinology and Diabetes-AL-Risafa, Directorate of Health-Baghdad. After getting Institutional Scientific and Ethical Committee approval, 28 patients with Type 2 diabetes mellitus were participated in this study, 18 female (64.29%) and 10 male (35.71%) of age range from 35 to 60 years old and mean±standard deviation (SD) age 46.76±7.89 years. 25 age and sex-matched healthy volunteers were included in the study as a control group, 17 female (68%) and 8 male (32%) of mean±SD age 46.40±7.71 years, respectively; an informed consent from each participant was done.

The inclusion criteria: Patients with Type 2 diabetes mellitus on a sulfonylurea (glibenclamide), and have disease duration of 5-10 years. The exclusion criteria: They should not have other associated chronic diseases like liver and kidney disorders and cardiovascular complications. The patients who are pregnant and breastfeeding are excluded. They should not be on insulin therapy or other antidiabetic drugs, or on antioxidant drugs, and any associated drugs should be considered. They should not take other hypolipidemic agent; anti-inflammatory or nonsteroidal anti-inflammatory drugs. Diabetic patients were assigned as follow:

1. Group A includes 14 patients treated with placebo in capsule dosage form in addition to the already given oral hypoglycemic agent (glibenclamide) and dietary control, for 12 weeks
2. Group B includes 14 patients treated with CoQ10 75 mg soft gelatin capsule twice daily (150 mg/day) in addition to the already given oral hypoglycemic agent (glibenclamide) and dietary control, for 12 weeks.

Sample collection and preparation

After 12 hrs fasting, blood samples were collected from all subjects by venepunture (10 ml), before starting drug treatment (as baseline samples) and then after 6 weeks and 12 weeks of treatment to follow the changes in the studied parameters.

Blood samples were divided into two tubes, one heparinized tube (1 ml of whole blood used for glycated hemoglobin [HbA1c] determination) and another part was collected in plane tube, then centrifuged at 3000 rpm for 10 minutes at 4°C. After centrifugation and isolation of cellular fraction, the obtained plasma fraction was divided into three parts in ependorff tubes and stored frozen until analysis performed.

Biochemical assay methods

Measurement of serum glucose level (fasting plasma glucose)

Serum glucose level was evaluated using a readymade kit for this purpose, according to the method [20], which is based on enzymatic oxidation of glucose to form glucuronic acid and hydrogen peroxide, and the reaction of the later with phenol and formation of quinonimine was followed spectrophotomertically at 505 nm. Results were expressed as mmol glucose/L, based on comparison with a standard glucose solution treated with the same method.

Determination of HbA1c

The variant HbA1c program utilizes the principles of ion exchange high-performance liquid chromatography for the automatic and accurate separation of HbA1c. Prepared samples are automatically injected into the analytical flow path and applied to the cation exchange column, where the hemoglobin is separated, based on the attraction of hemoglobin to the column material. The separated hemoglobin then passes through the flow cell of the filter photometer, where changes in the absorbance at 415 nm are measured. Samples are required to hemolyze the blood and remove schiff base. Samples are the first diluted with hemolysis reagent and then incubated at 18-28°C for a minimum of 15 minutes [21].

Measurement of serum malondialdehyde (S. MDA)

MDA is a by-product of lipid peroxidation and its measurement is based on the reaction of thiobarbituric acid (TBA) with MDA forming TBA-2MDA adducts. According to the standard method [22], which is modified by Gilbert *et al*. [23]. The method included the addition of 1.75 ml of saline azide to 0.25 ml plasma. Then, the mixture was centrifuged and 2 ml of supernatant was mixed with 0.5 ml of H_2O and 0.5 ml of 1% TBA in 0.05 M NaOH. The mixture was incubated in a boiling water bath for 15 minutes to achieve color development. The tubes were cooled under tap water, and the extent of MDA production was estimated from the absorbance at 532 nm. MDA concentration was calculated using a molar absortivity coefficient of $1.56 \times 105\ M^{-1}\ cm^{-1}$, and the results were expressed as µmol MDA/L.

Measurement of serum glutathione (S. GSH) levels

GSH contents (measured as total sulfhydryl groups) were measured according to the method [24]. 0.5 ml of serum was mixed with 206 ml of 3 mM dithionitrobenzene prepared in 0.1 M phosphate buffer (pH 8). The yellowish color chromophor formed was measured spectrophotometrically at 412 nm during 2 minutes and the concentration of GSH was calculated using a standard curve utilized for this purpose.

Measurement of serum superoxide dismutase (S. SOD) levels

SOD is one of the most important antioxidative enzymes. It catalyzes the dismutation of the superoxide anion into hydrogen peroxide and molecular oxygen. The sensitive SOD assay kit utilizes WST-1 that produces a water-soluble formazan dye on reduction with superoxide anion. The rate of the reduction with a superoxide anion is linearly related to the xanthine oxidase activity, and is inhibited by SOD. Therefore, the inhibition activity of SOD can be determined by a colorimetric method. Detection method-absorbance (450 nm) [25].

Measurement of serum oxidized LDL (S. Ox-LDL)

Measurement of Ox-LDL level in human serum done using an enzyme immunoassay (ELISA) kit for the quantitative determination of human autoantibodies (immunoglobulin G and immunoglobulin M) against Ox-LDL in human serum [26].

Measurement of serum TNF-α (S. TNF-α) level

TNF-α human ELISA is a sandwich assay for the determination of TNF-α in serum. During the first incubation period, TNF-α in patient serum samples is captured by the monoclonal antibody to human TNF-α coated on the wall of the microtiter wells. After washing away the unbound components from samples, a peroxidase-labeled second monoclonal antibody conjugate is added to each well and then incubated. After a second washing step, the bound enzymatic activity is detected by addition of tetramethylbenzidine (TMB) chromogen-substrate. Finally, the reaction is terminated with an acidic stop solution. The intensity of reaction color is directly proportional to the concentration of human TNF-α in the sample [27].

CRP

Microtiterstrips coated with anti-CRP are incubated with diluted standard sera and patient samples. During this incubation step, CRP is bound specifically to the wells. After removal of the unbound serum proteins by a washing procedure, the antigen-antibody complex in

each well is detected with specific peroxidase-conjugated antibodies. After removal of the unbound conjugate, the strips are incubated with a chromogen solution containing TMB and hydrogen peroxide; a blue color develops in proportion to the amount of immune complex bound to the wells of the strips. The enzymatic reaction is stopped by the addition of 1 N acidic solution, and the absorbance values at 450 nm are determined [28].

Statistical analysis

The results were expressed as mean±SD. Student's *t*-test for paired and unpaired sample and ANOVA test was used to examine the degree of significance, p<0.05 considered significant and <0.001 considered highly significant.

RESULTS

Comparison between healthy volunteers (control) and patients with diabetes in relation to laboratory parameters

Statistical comparison is done between healthy subjects (control group) and patients group at baseline (before treatment) for the studied parameters including fasting blood sugar (FBS), (bA1c, S. GSH, S. MDA, S. SOD, S. ox-LDL, S. TNF-α, and serum CRP (S. CRP).

Analysis of *t*-test revealed high statistically significant changes (p<0.001) in the level of FBS, S. HbA1c, S. GSH, S. MDA, S. SOD, S. ox-LDL, S. TNF-α, and S. CRP in patients with diabetes in comparison with healthy group, Table 1.

Effect of CoQ10 on glycemic control in patients with Type 2 diabetes in comparison with baseline and placebo-treated group

This study demonstrated that in comparison with value at baseline in the same group, the level of FBS significantly decreased after 6 weeks in placebo and CoQ10 treated group. After 12 weeks, no significant difference in FBS level of placebo group, while a high significant decrease in FBS level of CoQ10 treated group was recorded. In comparison with a placebo-treated group at corresponding duration, after 6 weeks there is no significant difference in FBS in CoQ10 group.

Table 1: Baseline comparison of control group with Type 2 diabetic patients

Parameters	Control (n=25)	Patients (n=28)
FBS (mmol/l)	4.06+0.27	11.26+3.58**
HbA1c (%)	4.66+0.54	8.18+142**
S. GSH (µmol/l)	0.98+0.08	0.54+0.12**
S. MDA (µmol/l)	0.85+0.09	1.82+0.35**
S. SOD (µmol/l)	74.42+4.47	28.81+7.61**
S. ox-LDL (U/ml)	23.84+1.86	47.83+7.15**
S. TNF-α (pg/ml)	31.88+5.8	65.64+8.35**
S. CRP (µg/ml)	1.15+0.26	5.18+1.95**

FBS: Fasting blood sugar, HbA1c: Glycosylated hemoglobin, S. GSH: Serum glutathione, S. MDA: Serum malondialdehyde, S. SOD: Serum superoxide dismutase, S. ox-LDL: Serum oxidized low density lipoprotein; S. TNF-α: Serum tissue necrosis factor alpha, S. CRP: Serum C-reactive protein. Results represent mean±SD; **Highly significant difference (p<0.001) from control group

While after 12 weeks, there was a significant decrease in FBS level of CoQ10 group. Concerning glycosylated hemoglobin, Table 2 showed that in comparison with value at baseline in the same group after 6 weeks there was a significant decrease in HbA1c in placebo and CoQ10 groups. After 12 weeks, no significant difference in HbA1c in placebo group, and a high significant decrease in HbA1c in CoQ10 group. In comparison with a placebo-treated group at corresponding duration, after 6 weeks there is no significant difference in HbA1c in CoQ10 group. After 12 weeks, a significant decrease in HbA1c of CoQ10 group was seen (Table 2).

Effect of CoQ10 on oxidative stress parameters in patients with Type 2 diabetes in comparison with baseline and placebo-treated patients

CoQ-10 supplementation to Type 2 diabetic patients resulted in high significant increase in S. GSH compared with value at baseline in the same group after 6 weeks; there is a significant increase in S. GSH in the placebo group.

After 12 weeks, no significant difference in S. GSH in the placebo group and highly significant increase in S. GSH in CoQ10 group.

In comparison with a placebo-treated group at corresponding duration, after 6 weeks there is no significant difference in S. GSH level of CoQ10 group. After 12 weeks, there is high significant increase in S. GSH level in CoQ10 group.

In relation to S. MDA, in comparison with value at baseline in the same group after 6 weeks, there is no significant difference in S. MDA in placebo group and high significant decrease in S. MDA in CoQ10, group. After 12 weeks, no significant difference in S. MDA in placebo group and a high significant decrease in S. MDA in CoQ10 group. In comparison with a placebo-treated group at corresponding duration, after 6 weeks there is no significant difference in S. MDA in CoQ10 group, after 12 weeks, there is a high significant decrease in S. MDA in CoQ10.

Concerning S. SOD, in comparison with value at baseline in the same group after 6 weeks, there is no significant difference in S. SOD in placebo and CoQ10 groups, after 12 weeks, no significant difference in S. SOD in CoQ10 group, and significant increase in S. SOD in placebo group. In comparison with a placebo-treated group at corresponding duration, after 6 and 12 weeks, there is no significant difference in S, SOD in CoQ10 group. In relation to S. ox-LDL, in comparison with value at baseline in the same group after 6 and 12 weeks there is no significant difference in S. ox-LDL in placebo, and high significant decrease in S. ox-LDL in CoQ10 group. In comparison with a placebo-treated group at corresponding duration, after 6 weeks no significant difference in S. ox-LDL in CoQ10 group, after 12 weeks, high significant decrease in S. ox-LDL in CoQ10 group, (Table 3).

Effect of CoQ10 on inflammatory markers in patients with Type 2 diabetes in comparison with baseline and placebo-treated patients

This study demonstrated that in comparison with value at baseline in the same group after 6 weeks there is no significant difference in S. TNF-α in placebo group, while there is high significant difference in S. TNF-α level of CoQ10 group. After 12 weeks, there is a significant increase in S. TNF-α in placebo group, and high significant decrease in

Table 2: Comparison of FBS and HBA1c at different duration in each group

Group	FBS (mmol/l)			HbA1c (%)		
	Baseline	6 weeks	12 weeks	Baseline	6 weeks	12 weeks
Placebo (n=14)	11.68+3.64	10.62+2.94*	11.62+2.79	8.35+1.93	8.6+1.94	8.15+1.61
CoQ10 (n=14)	11.2+3.66	9.39+3.92*	8.56+2.95**[a]	7.81+1.49	7.11+2.25*	6.42+2.23**[a]

FBS: Fasting blood sugar, HbA1c: Glycosylated hemoglobin. Comparison is with baseline value *Significant difference from baseline (p<0.05), **Highly significant difference from baseline (p<0.001). [a]Significant difference (p<0.05) between drug group and placebo group at corresponding duration. [b]Highly significant difference (p<0.001) between drug group and placebo group at corresponding duration

Table 3: Comparison of oxidative stress parameters at different duration in each group

Group	S. GSH (µmol/l)			S. MDA (µmol/l)			S. SOD (µmol/l)			S. ox-LDL (U/ml)		
	Baseline	6 weeks	12 weeks	Baseline	6 weeks	12 weeks	Baseline	6 weeks	12 weeks	Baseline	6 weeks	12 weeks
Placebo (n=14)	0.49+0.05	0.56+0.12*	0.51+0.07	1.72+0.29	1.95+0.34	1.79+0.27	32.05+6.48	32.0+6.7	34.07+5.42*	45.69+7.95	42.69+6.33	45.85+9.43
CoQ10 (n=14)	0.52+0.12	0.62+0.15**	0.73+0.12**[b]	1.77+0.35	1.39+0.31**	1.14+0.24**[b]	32.2+5.8	33.91+4.81	33.69+9.2	53.71+5.66[a]	41.5+3.23**	34.79+4.0**[b]

S. GSH: Serum glutathione, S. MDA: Serum malondialdehyde, S. SOD: Serum superoxide dismutase, S. ox-LDL: Serum oxidized low density lipoprotein. Comparison is with baseline value. *Significant difference from baseline ($p<0.05$), **Highly Significant difference from baseline ($p<0.001$). [a]Significant difference ($p<0.05$) between drug group and placebo group at corresponding duration. [b]Highly significant difference ($p<0.001$) between drug group and placebo group at corresponding duration

S. TNF-α level of CoQ10 group. In comparison with a placebo-treated group at corresponding duration, after 6 weeks no significant difference in S. TNF-α in CoQ10 group, while after 12 weeks, significant decrease in S. TNF-α was seen in CoQ10 group.

In relation to S. CRP, in comparison with value at baseline in the same group after 6 and 12 weeks there is no significant difference in S. CRP in placebo group and high significant decrease in S. CRP in CoQ10, group.

In comparison with a placebo-treated group at corresponding duration, after 6 and 12 weeks, there is high significant decrease in S. CRP in CoQ10 group, (Table 4).

DISCUSSION

The data obtained in this study demonstrates the antioxidant and anti-inflammatory effects of CoQ10 supplementation 150 mg daily in combination with an oral hypoglycemic agent (glibenclamide) for Type 2 diabetic patients, the used dose was well tolerated by the patients and there was no any adverse effect appears during the treatment course.

In other clinical trials, a total of 194 Type 2 diabetic patients received 200 mg CoQ10 or a placebo daily for 12 weeks, resulted in good glycemic control [29]. CoQ10 supplementation in this population raised plasma CoQ10 levels, improved endothelial function in the brachial artery, significantly decreased both systolic and diastolic blood pressure, and decreased HbA1c. It has been demonstrated that 12 weeks supplementation with CoQ10 improves clinical outcomes and nerve conduction parameters of diabetic polyneuropathy; furthermore, it reduces oxidative stress without significant adverse events [30].

Results obtained by Mezawa *et al*. studied the effect of supplementation of the reduced form of CoQ10, ubiquinol, in addition to conventional glucose-lowering agents in nine subjects (3 males and 6 females) with Type 2 diabetes; the subjects were assigned to receive an oral dose of 200 mg ubiquinol daily for 12 weeks. The results obtained showed improvement in glycemic control by improving insulin secretion without any adverse effects [31].

Kolahdouz Mohammadi *et al*. reported in a randomized double-blind placebo-controlled trial, 64 Type 2 diabetic patients were randomly assigned to receive either 200 mg Q10 or placebo daily for 12 weeks, the results were improved glycemic control, total and LDL cholesterol while triglycerides and high-density lipoprotein cholesterol levels were no significantly improved [32].

Another study done by Zahedi *et al*. showed that supplementation of 150 mg CoQ10 or placebo daily for 12 weeks to 50 patients with diabetes who randomly allocated into two groups to receive either treatment resulted in significant lowering of fasting blood glucose level and HbA1c levels in CoQ10 treated group compared to placebo with which results obtained in this study are compatible [33].

The effect of supplementation of 150 mg CoQ10 to diabetic patients significantly improve the oxidative stress parameters after 12 weeks in this study, this finding can be seen in other studies, Shen and Pierce 2015, reported that the pathogenesis of Type 2 diabetes mellitus may be partly contributed to mitochondrial dysfunction secondary to oxidative stress, beside deficiency in CoQ10 which is often present among patients with Type 2 diabetes made CoQ10 a potent antioxidant to scavenge excessive ROS and provide protection to cells, especially mitochondria from oxidative damage. Leading to restoration of CoQ10 level among patients with T2DM and alleviate oxidative stress, preserve mitochondrial function, and eventually lead to improvement of glycemic control [34].

The previous study by El-ghoroury *et al*. revealed that plasma and platelet MDA level, as a marker of oxidative stress, were significantly higher in diabetic patients group compared to controls, and level of

Table 4: Comparison of inflammatory markers at different duration in each group

Group	S. TNF-α (pg/ml)			S. CRP (μg/ml)		
	Baseline	6 weeks	12 weeks	Baseline	6 weeks	12 weeks
Placebo (n=14)	65.92+9.25	69.0+8.18	69.46+9.42*	5.22+1.88	6.05+2.01	5.25+1.79
CoQ10 (n=14)	70.5+9.09	67.0+8.91**	60.64+8.79**[a]	4.66+2.28	3.19+1.55**[b]	2.61+1.48**[b]

TNF-α: Serum tissue necrosis factor alpha, S. CRP: Serum C-reactive protein. Comparison is with baseline value *Significant difference from baseline ($p<0.05$), **Highly significant difference from baseline ($p<0.001$). [a]Significant difference ($p<0.05$) between drug group and placebo group at corresponding duration. [b]Highly significant difference ($p<0.001$) between drug group and placebo group at corresponding duration

CoQ10, as antioxidant capacity, was significantly lower in diabetic patients than in controls. They showed that there was a negative correlation between plasma CoQ10 concentrations and glycosylated hemoglobin. They concluded that Type 2 diabetic patients are at increased risk of oxidative stress manifested by increased plasma MDA level as well as platelet MDA and decreased CoQ10 plasma level [35].

Montano *et al*. demonstrated that 12 weeks CoQ10 treatment significantly improved the extracellular redox balance in diabetic patients; they suggest that prolonged treatment may have beneficial effects also on clinical outcome in diabetes [36].

Raygan *et al*. showed that CoQ10 supplementation resulted in a significant reduction in serum insulin levels. In addition, the patients who received CoQ10 supplements had a significant increase in plasma total antioxidant capacity concentrations compared with the placebo group. In addition, compared with the placebo group, a significant positive change in plasma glutathione and a significant reduction in MDA were seen among patients who received CoQ10 supplement [37].

Akbari Fakhrabadi *et al*. study the effect of CoQ10 (200 mg/d) or placebo for 12 weeks on oxidative stress parameters, glycemic control and inflammation in 70 diabetic patients recruited for a double-blind randomized clinical trial, the mean insulin sensitivity and total antioxidant capacity concentration significantly increased in the CoQ10 group compared to the placebo after the trial. CRP significantly decreased in the intervention group compared to placebo after the trial [38]. The above-mentioned studies clearly support the findings obtained in this study, and conclusion can be made depending on obtained results that administration of CoQ10 (150 mg/day) as adjuvant therapy improve glycemic control, oxidative stress parameters, and inflammatory markers in Iraqi diabetic patients.

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