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Investigating the effects of using coenzyme Q10 in diabetic like conditions on Phosphor, Magnesium, Iron and ALP of blood serum and diet parameters of adult male rats.

Alireza Shahriary*, Masood Khakzadihe, and Yunes Panahi.

Chemical Injuries Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran.

ABSTRACT

High glucose range causes oxidative stress as a result of increased production of reactive oxygen species. Co Q10 inhibits certain enzymes involved in the formation of free radicals and hence attenuates oxidative stress. 45 male adult rats were selected and divided in to three groups. Control rats fed on normal diet ad libitum with i.p. injection of saline daily. Fructose fed control rat group fed on normal diet and supplemented by 10% fructose in drinking water ad libitum with i.p. injection of saline daily. Third group as Fructose fed rats treated with coenzyme Q10 (10 mg/kg i.p. daily). The food and water intake of Fructose Fed group was significantly higher than other two studied groups. The serum P levels were found significantly increased in CoQ10 treated fructose fed rats compared to the fructose fed rats. The serum ALP levels were found decreased in CoQ10 treated fructose fed rats compared to the fructose fed rats. There were no significant changes on serum Mg. using Coenzyme Q10 had protective effects on diabetic like conditions.

Keywords: Diabetes Mellitus, Co Q10, Biochemical, Serum, Food Intake, Water Intake, Rat

Corresponding author

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INTRODUCTION

Diabetes mellitus type II is a chronic metabolic disorder, results from defects in insulin secretion and/or insulin action [1]. High glucose range causes oxidative stress as a result of increased production of reactive oxygen species from mitochondria organized through oxidative phosphorylation, glycosylation, auto-oxidation and glycosamine pathways [2, 3]. High free fatty acids can result oxidative stress because of increase mitochondrial separate of oxidative phosphorylation and β-oxidation directing to an enhancement the production of reactive oxygen species [2, 4]. Recent molecules play an important role as signals to activate a cellular stress sensitive pathways that activation of these pathways is not only linked to the development of late complications of diabetes, but also to resistance of insulin, β-cell and endothelial dysfunctions [3, 4].

Coenzyme Q (Co Q) is 2, 3-dimethoxy, 5-methyl, 6-polyisoprene parabenzoquinone [5]. The well recognized functions of co enzyme Q10 (Co Q10) are in energy coupling of mitochondria and its action as a primary regenerating antioxidant [5, 6, 7]. Less well established functions include oxidant action in the generation of signals and control of cellular redox state. By participation in transmembrane electron transport Co Q can carry reducing equivalents to the inside of vesicles or to the outside of cells [5, 6, 8]. There is also evidence for a role in proton gradient formation in endomembranes and at the plasma membrane. In addition, there is evidence that Co Q can take part in control of membrane structure and phospholipid status [6, 8].

In diabetes condition, mitochondrial oxidative phosphorylation is considerably reduced; therefore production of Adenosine triphosphate is reduced along with decreased level of Co Q10 [1]. Moreover to helping transferring of electrons during oxidative phosphorylation, Co Q10 inhibits certain enzymes involved in the formation of free radicals and hence attenuates oxidative stress [3, 4, 5, 9].

Feeding fructose or sucrose, supplies a pattern of hyperglycemia, hyperlipidemia and insulin resistance through the highly synthesis of cholesterol, fatty acid and triglyceride in the liver [3, 9]. This research conducted to investigate however, CoQ10 can change the ALP, Magnesium, Phosphorous and Iron of diabetic rat blood serum and effects intake of water and food under these conditions.

MATERIAL AND METHODS

For this study 45 male adult rats were selected and divided in to three groups (n=15). They were caged in wire bottom galvanized metal wall boxes under controlled condition. There were no significant differences on weight (The average body weight 180 to 220 gram), age, appearance and environment of rats. The environment was exposed to 12-hour lighting and 12-hour dark during the experiment for each group (10 Lux). The room temperature was 22±2 Degrees Celsius during the experimental period with 58-62% relative humidity. Using fed was according to NRC and presented in table 1. The consumed water was the Tabriz city tap water which was re-refined using carbon and sand filters.

Experiment Groups

First group as control rats fed on normal diet and water ad libitum with i.p. injection of saline daily. Second group as Fructose fed control rat group (FFG) fed on normal diet and supplemented by 10% fructose in drinking water ad libitum with i.p. injection of saline daily. Third group as Fructose fed rats treated with coenzyme Q10 (10 mg/kg i.p. daily [3, 5, 10]) (F+CoQ10). The used coenzyme Q10 in this study was from metagenic company. The injection amount of saline in first and second groups was as same as coenzyme Q10 in third group.

Experiment Analysis

Daily changes of food and water intake were recorded (gram/rat/day). After 30 days (1month) at 30 day of treatment, all 45 rats were bled by head decapitation after overnight fasting. After blood collecting they kept in 24 degree Celsius for 30 minute for coagulating. After clotting, the blood was centrifuged with the speed of 3000 rpm for 10 minutes and the serum was removed. In this study magnesium review was performed using XilidiBlue method, phosphorus using U.V. method, iron using kinetik method and ALP using Kinetik method. All the introducing kits in this study are manufactured by Pars Azmoon Company.

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Table1: Ingredient - Diet used for rat breeding in this study

Ingredient	Diet
Basic Diet, g/kg diet	
Dried skim milk	50
Fish meal (60% protein)	100
Soybean meal (48% protein)	120
Alfalfa meal, dehydrated (17% protein)	40
Corn gluten meal (60% protein)	30
Ground #2 yellow shelled corn	245
Ground hard winter wheat	230
Ground whole oats	-
Wheat middlings	100
Brewer's dried yeast	20
Dry molasses	15
Soybean oil	25
Salt	5
Dicalcium phosphate	12.5
Ground limestone	5
Mineral premix	1.2
Vitamin premix	1.3
Mineral Premix, mg/kg diet	
Cobalt (as cobalt carbonate)	0.44
Copper (as copper sulfate)	4.4
Iron (as iron sulfate)	132.3
Manganese (as manganous oxide)	66.2
Zinc (as zinc oxide)	17.6
Iodine (as calcium iodate)	1.54
Vitamin Premix, per kg diet	
Stabilized vitamin A palmitate or stearate	6,060.00 IU
Vitamin D_3 (D-activated animal sterol)	5,070.00 IU
Vitamin K (menadione activity)	3.09 mg
All-rac-α-tocopheryl acetate	22.10 mg
Choline chloride	617.00 mg
Folic acid	2.43 mg
Niacin	33.10 mg
Ca-d-pantothenate	19.80 mg
Pyridoxine-HCl	1.87 mg
Riboflavin supplement	3.75 mg
Thiamin mononitrate	11.0 mg
d-Biotin	0.15 mg
Vitamin B12 supplement	0.004 mg

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Statistical Analysis

All raw data of this experiment was investigated by SPSS software version 15.00. The ANOVA and Duncans multiple range tests were used to analyze the data. Data with 5% level ($p<0.05$) of significance were considered.

RESULTS AND DISCUSSION

Results of the effects of co enzyme Q10 on food and water intake of rats in diabetic condition compared with control group presented in table 2. There were significant differences between Fructose Fed group with control and Fructose Fed+CoQ10 groups ($p<0.05$). The food and water intake of Fructose Fed group was significantly higher than other two studied groups. The percent of food and water intake changes presented in table 2. In chart 1 and 2 period of food and water intake changes, studied and compared with control group.

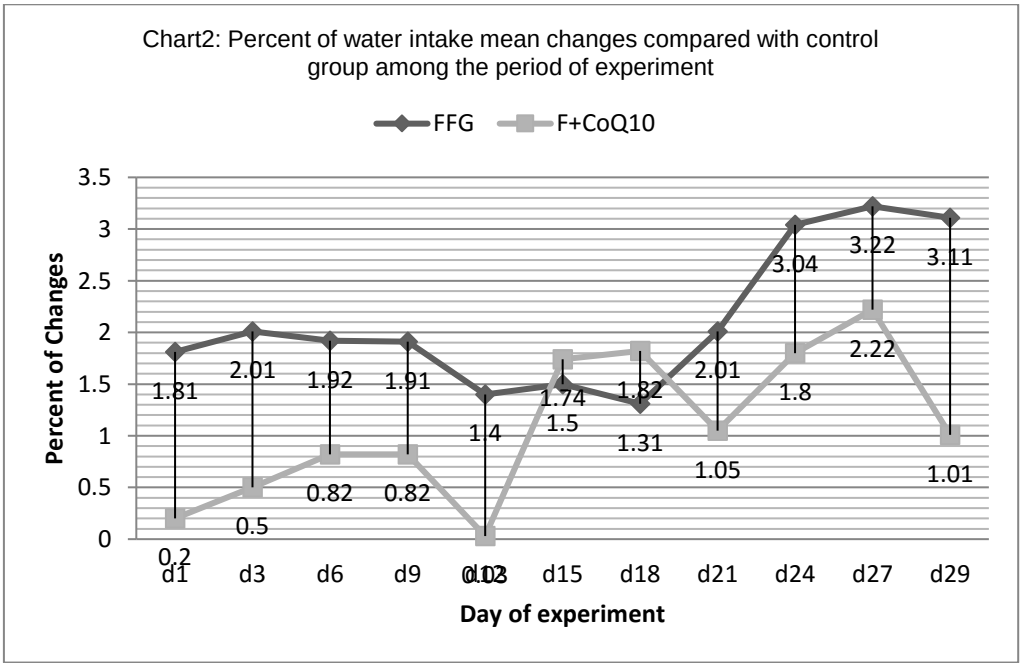
Table2: Effects of co enzyme Q10 on food and water intake of rats in diabetic condition

Parameters	Groups (Mean±SD)		
	Control	Fructose Fed	Fructose Fed+CoQ10
Food Intake (gram/rat/day)	22.40 ± 0.28^{A}	23.09 ± 0.44^{B}	22.93 ± 0.35^{A}
Water Intake (gram/rat/day)	50.1 ± 0.84^{A}	51.15 ± 0.94^{B}	50.61 ± 1.21^{A}

$^{A, B \text{ and } C}$ Sig at $p<0.05$ between groups in rows.

Table3: Percent of food and water changes compared with control group according to table 2

Parameters	Groups (% of Changes)		
	Control	Fructose Fed	Fructose Fed+CoQ10
Food Intake (%)	-	3.10	2.38
Water Intake (%)	-	2.11	1.02



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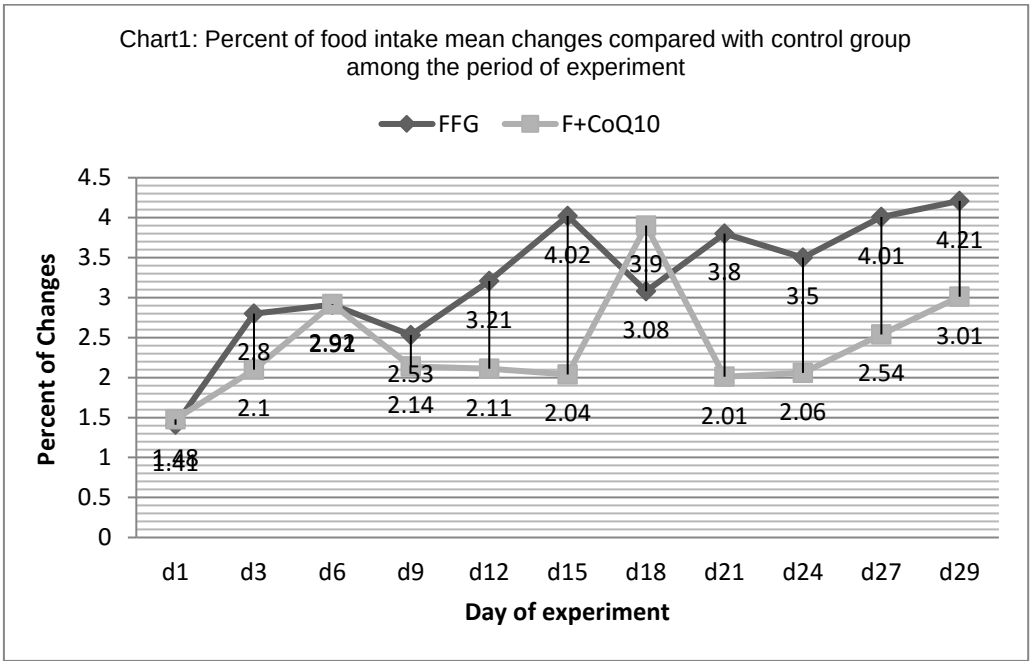

Effects of co enzyme Q10 on some biochemical parameters of rats in diabetic condition presented in table 3. The serum P levels were found significantly increased in CoQ10 treated fructose fed rats (9.36±1.99 mg/dl) compared to the fructose fed rats (7.56±2.56 mg/dl). The serum ALP levels were found significantly decreased in CoQ10 treated fructose fed rats (240.19±5.66 IU/L) compared to the fructose fed rats (260.36±6.38 IU/L). There were no significant changes on serum Mg levels between all groups.

Table 3: Effects of co enzyme Q10 on some biochemical parameters of rats in diabetic condition

Biochemical Parameter	Groups (Mean±SD)			
	Control	Fructose Fed	Fructose Fed+CoQ10	Normal Range
P	4.28±2.35^{A}	7.56±2.56^{B}	9.36 ±1.99^{C}	3.11-11.0 mg/dl
Mg	2.55±0.48^{A}	2.95±0.25^{A}	2.88±0.26^{A}	1.6-4.44 mg/dl
Fe	171.38±47.85^{A}	160.22±36.25^{B}	169.58±22.69^{A}	60-200 mg/dl
ALP	230.48±5.33^{A}	260.36±6.38^{B}	240.19±5.66^{C}	-

$^{A, B \text{ and } C}$ Sig at $p<0.05$ between groups in rows.

The decreased biosynthesis of CoQ10 and its deficit in tissues is associated with degenerative changes of aging. Therefore, CoQ10 dietary supplementation has became helpful for organism and recently it is used for daily health care worldwide [5]. Recent studies found CoQ10 due to its antioxidant activity modified the biochemical changes occurred during experimental chemically induced diabetes [11], gentamicin nephrotoxicity [12], rhabdomyolysis [13] in rats.

Diabetes is well known pathologic condition that leads to bone loss. Nevertheless, the mechanisms that contribute to the loss vary. The low bone turnover that is associated with diabetes and the high bone turnover that is associated with estrogen deficit account for the variety of mechanisms [14].

Phosphate (P) is one of the most important ion species in nature and mammals body. Phosphate is present in every biological system [15, 16]. The serum P levels were found significantly increased in CoQ10

treated fructose fed rats (9.36±1.99 mg/dl) compared to the fructose fed rats (7.56±2.56 mg/dl). But the differences of serum P levels also were found within the normal physiological range.

Magnesium (Mg) is one of the most abundant and essential minerals in mammals and rat [15]. Magnesium is involved in more than 300 biochemical reactions in the mammal body and plays important roles in muscle and nerve functions, immune system, heart rhythm and bone formation [15, 16]. Magnesium deficiency may lead to muscle contractions, nausea, fatigue, hypocalcemia and hypokalemia (Cowell, 2004). There was no significant difference between all groups on serum magnesium levels. The normal range of blood serum magnesium reported 1.6-4.44 mg/dl in rats [15]. All groups' serum magnesium was in normal ranges.

Alkaline phosphatase (ALP) catalyzes the hydrolysis of phosphate esters in an alkaline environment, resulting in the formation of an organic radical and inorganic phosphate [17, 15]. In mammals and rat, this enzyme is found mainly in the both liver and bones tissue. Marked increase in serum ALP levels, a disease known as *Hyperalkalinephosphatasemia*, has been associated with malignant biliary obstruction, primary biliary cirrhosis, primary sclerosing cholangitis, hepatic lymphoma and sarcoidosis[17].

The serum Fe levels were found significantly decreased in fructose fed rats (160.22±36.25 mg/dl) compared to the other groups. But the differences of serum Fe levels also were found within the normal physiological range. Blood serum Fe decrease can be seen under stress condition [16]. High glucose level of blood serum can act as a major reason of Fe significant differences in fructose fed group.

Recent studies about this subjects shows our results can accept the CoQ10 properties. In a Heibashy et al. (2009) research assessment role of coenzyme q10 on some physiological and biochemical parameters in resembling type 2 diabetic rats were studied and reported using coenzyme Q10 can improve body antioxidant defense system. Also using co enzyme Q10 had significant difference on food intake but not on water intake [3].

In other research conducted by Kismali (2006) effects of Coenzyme Q10 on blood biochemistry in rats were studied. Kismali reported no major beneficial effects on the parameters investigated in study were observed following coenzyme Q10 treatment. In Kismali study were significant increase on P level and significant decrease on ALP level of blood serum after using Co Q10 [5].

CONCLUSION

Using Coenzyme Q10 in diabetic like condition can improve physiological activity in studied parameters as bone loss inhibition mechanism. Also it can regulate the food and water intake in hyperglycemia.

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