Effects of Coenzyme Q_{10} on Hemoglobin A_{1C}, Serum Urea and Creatinine in Alloxan-Induced Type 1 Diabetic Rats

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ABSTRACT

Coenzyme Q_{10} is a natural antioxidant and free radicals scavenger. In the present study, we examined effect of coenzyme Q_{10} on hemoglobin A_{1C}, serum urea and creatinine in alloxan-induced Type 1 diabetic rats. Thirty Sprague-Dawley male rats were divided into three groups randomly; group one as control, group two diabetic untreated, and group three treatments with coenzyme Q_{10} (15 mg/kg i.p daily), respectively. Diabetes was induced in the second and third groups by alloxan injection subcutaneously. After 8 weeks, animals were anaesthetized; blood samples were collected to measure the hemoglobin A_{1C}, serum glucose, urea and creatinine. Coenzyme Q_{10} significantly decreased hemoglobin A_{1C}, serum glucose, urea and creatinine. Coenzyme Q_{10} exerts beneficial effects on the hemoglobin A_{1C} and serum glucose in alloxan-induced type 1 diabetic rats.

Keywords: Diabetes, Hemoglobin A_{1C}, Serum, Glucose, Rat, Coenzyme Q_{10}

Hyperglycemia is confounded for the complications of diabetes because hyperglycemia directly causes glycation of proteins, lipids and nucleic acid that injures cells and induces lipid peroxidation [1]. Also, antioxidant and antioxidative enzyme activities are reduced due to glycation or increased lipid peroxidation products [2]. A number of natural antioxidant such as vitamin E and phenolic compounds are known to have hypoglycemic, hypolipidemic or both activities [3]. Chemical drugs have many side effects; therefore, screening for new antidiabetic sources from natural antioxidants is still attractive because they are mostly safe and are good alternative for treatment of diabetes mellitus. A growing body of research indicates that nutritional deficiencies such as antioxidants contribute to the development of diabetes.

Coenzyme Q_{10} is a natural human ubiquinone, and it has fundamental role in mitochondrial energy (ATP) production in the respiratory chain [4,5]. Coenzyme Q_{10} is also antioxidant, scavenging free radicals and inhibiting lipid peroxidation [6-8]. The antioxidant effect of coenzyme Q_{10} is greater than vitamin E [8]. Coenzyme Q_{10} is also known to enhance the availability of other antioxidants such as vitamin C, vitamin E and beta-carotene [9]. Since the protective effects of coenzyme Q_{10} on hyperglycemia and hemoglobin A_{1C} status in alloxan-induced type 1 diabetic rats have not previously been reported; the objectives of the present study were to investigate amelioration of altered glucose, hemoglobin A_{1C}, serum urea and creatinine by coenzyme Q_{10} in alloxan-induced type 1 diabetic rats.

MATERIALS AND METHODS

Experimental designee

Animals

Thirty mature Sprague–Dawley rats (180-200 g) were obtained from Pasteur Institute of Tehran and were allowed to adapt themselves with the new location for one week. This study was approved by the Animal
diabetes induction

Diabetes was induced after overnight fasting in the second and third groups by injection of alloxan monohydrate (120 mg/kg) subcutaneously [10]. Beta cell degradation by alloxan leads to release of more insulin. Because of acute hypoglycemia, the rats received 10% sucrose solution for 48 h instead of drinking water. Five days after induction of diabetes, blood samples were gathered from the end part of tails. Blood glucose was measured by glucometer and the rats with blood glucose level ≥300 mg/dl (16.7 mmol/L) were considered as diabetic [11-13]. During the first five days after diabetes induction, 1-3 rats per group died because of alloxan toxicity. The rats were kept at 12/12 dark/light period in 21±3 °C temperature. All animals were allowed free access to food and water ad libitum during the experiment. The third group was treated with coenzyme Q₁₀ by 15 mg/kg i.p daily [12]. The treatment was begun at the first day of diabetes induction. After 8 weeks treatment, animals were anesthetized (Nesdonal 50 mg/kg, i.p.), blood samples were obtained from hearts and allowed to clot for 20 minutes in laboratory temperature and then centrifuged at 3000 rpm for 10 minutes for serum separation [13]. Also, blood sample were used to measure the hemoglobin A₁C.

Level of hemoglobin A₁C, serum glucose, urea and creatinine

The hemoglobin A₁C was determined using a hemoglobin A₁C assay kit (Randox Lab., Ltd., UK) according to the manufacturer's protocol. Also glucose, urea and creatinine in the serum were determined by biochemical analyzer using commercial kits (Olympus AU-600, Tokyo, Japan).

Statistical analysis

All values were expressed as mean ± SEM. The data were compared between groups by Mann-Whitney U test. Statistical analyses were performed using the SPSS 13 for windows software. A p value of < 0.05 was considered statistically significant.

RESULTS

The level of hemoglobin A₁C in the untreated diabetic rats was significantly (1.58-fold) higher than that of control animals. The treatment of diabetic animal with coenzyme Q₁₀ could significantly (20%) inhibit the increase of hemoglobin A₁C in comparison with the untreated diabetic animals (Fig 1). The level of glucose in the untreated diabetic rats was significantly (4.5-fold) higher than that of control animals. The treatment of diabetic animal with coenzyme Q₁₀ could significantly (21%) inhibit the increase of glucose in comparison with the untreated diabetic animals (Fig 2). The level of urea in the untreated diabetic rats was significantly (1.5-fold) higher than that of control animals. The treatment of diabetic animal with coenzyme Q₁₀ could significantly (29.5%) inhibit the increase of urea in comparison with the untreated diabetic animals (Fig 3). The level of creatinine in the untreated diabetic rats was significantly (1.3-fold) higher than that of control animals. The treatment of diabetic animal with coenzyme Q₁₀ could significantly (14.5%) inhibit the increase of creatinine in comparison with the untreated diabetic animals (Fig 4).

DISCUSSION

Diabetes significantly increased serum urea and creatinine in comparison with the control group. Elevations of serum urea and creatinine were confirmed with development of diabetic nephropathy in the untreated diabetic rats [14]. Treatment of diabetic animals with coenzyme Q₁₀ significantly inhibited increase of serum urea and creatinine and progression of
In plasma, erythrocytes and platelets: rats. 20 Q [Neurobiol Dis] The effect of coenzyme as vitamin Higashikata T [1C can not be fully exp 1C, in alloxan such as superoxide can induce cell and Drissi A on Current views on type 2 diabetes. in alloxan progression of diabetic Menke T Bélanger MC, Mirault ME, Dewailly E, Berthiaume L, Julien P. J Endocrinol [Andler W [1C and prevent Littarru GP, Tiano L. Metabolism group. - serum urea Ahmadvand < 0.05 as compared with control group. diabetic nep hropathy. in comparison with the untreated diabetic animals. This study showed that coenzyme Q10 has beneficial effects, in reduction the increased hemoglobin A1C had protective effects on hyperglycemia in alloxan-induced diabetic rats. There are much evidence that oxidative stress play a key role in the most pathgenic pathway of diabetic injuries. Free radicals such as superoxide can induce cell and tissue injuries throughout lipid peroxidation and increase carcincogenesis, inflammation, early aging, cardiovascular diseases and tissue damage in diabetes [15,16]. Antioxidants such as vitamin E, coenzyme Q10 and antioxidant enzymes protect the cells against oxidative-stress-mediated cellular injuries by converting the toxic free radicals to non-toxic products [17,18]. There are reports that natural antioxidant such as vitamin E [19], caffeic acid [20,21], lipoic acid, quercetin [22], melatonin [23] and natural phenolic compounds have protective effects on hyperglycemia in diabetics disease [24,25]. Also, these compounds could reduce hemoglobin A1C level in diabetic patients [17-25]. There are reports that coenzyme Q10 have protective effects on lipid peroxidation and in vitro or in vivo LDL oxidation. The inhibitory effect of coenzyme Q10 on LDL oxidation is better than vitamin E [26]. Researchers showed coenzyme Q10 could reduce serum lipid peroxidation level in diabetic patients [26]. Moreover, researchers showed coenzyme Q10 could reduce serum lipid peroxidation level in patients with coronary artery diseases [27]. Results of our study are in accordance with other researchers’ study that showed coenzyme Q10 similar to others antioxidants such as vitamin E and lipoic acid could reduce hemoglobin A1C and prevent hyperglycemia. Therefore, natural antioxidant with protective effects on hyperglycemia could prevent or be helpful in reducing the complications that related to hyperglycemia in diabetes patients. Although the detailed molecular protective mechanisms of coenzyme Q10 can not be fully explained by our results, our results are satisfactory. Coenzyme Q10 as lipid soluble antioxidant with multi beneficial properties can be introduced to diabetic patients without diabetic nephropathy for inhibition of progression of diabetic nephropathy. This study showed that coenzyme Q10 has beneficial effects in decreasing the elevated hemoglobin A1C, urea and creatinine and protective effects on hyperglycemia in alloxan-induced diabetic rats. Hence, attenuation of hyperglycemia, hemoglobin A1C, urea and creatinine can decrease diabetic complication such as nephropathy in diabetic patients.

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**REFERENCES**

Effects of coenzyme Q10 on hemoglobin A1c


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