



The Effect of coenzyme Q10 on serum levels of renal function indicators in diabetic rats induced by Alloxan

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ABSTRACT

The present study was conducted in order to evaluate the protective effects of Q10 on serum levels of renal function indicators in diabetic rats induced by Alloxan. The experimental model of diabetes type I in rats was created by intraperitoneally injection of 120 mg Alloxan monohydrate mg/kg. FBS within 120-250 mg/dl was considered as diabetic in the present study. Control group rats received buffer citrate 0.05 M with pH 4.5 intraperitoneally. Q10 Treatment group received 75 mg/kg Q10 via gavage for one month. The fourth group (combined intervention group) at first the rats was diabetic then they received 75 mg/kg Q10 by gavage. The data were expressed as Mean±SE. ANOVA statistical analysis method was used. The results of the present study show that induction of type I diabetes using Alloxan increases blood sugar meaningfully and the administration of Q10 in diabetic group doesn't decrease blood sugar. As a result, Q10 is affectless in type I diabetics to decrease blood sugar. In the present study, Alloxan caused a meaningful increase in the Urea, Uric acid, and Creatinine levels compared with the normal group. The obtained results of the administration of Q10 + Alloxan in diabetics, in the present study, show a meaningful difference in decreased level of Urea, Uric acid, and Creatinine. This means that the Q10 antioxidant characteristics can prevent nephropathy damages caused by disorders in renal function indicators. Then, blood glucose control is not enough by itself to postpone the process of diabetic nephropathy.

Key Words: Alloxan, Diabetic rats, Q10, Renal.

INTRODUCTION

Type I Diabetes, has been always as a problem in worldwide health and has been continued to increase, also it is the most common type of diabetes. Although the pathogenesis of type I diabetes is not clear perfectly, glucose and fat metabolism are involved in the problem) McGarry, 1992) There are most evidences suggesting its oxidative stress role and following it the production of free radicals in diabetic people and their involvement in diabetes pathogenesis (Kaneto et

al. 2007).It has been cleared that Hyperglycemia causes increased active oxygen and leads to sever oxidative tensions in cells. (Signoriniet al. 2002) The researches have been demonstrated that free radicals removing enzymatic and non-enzymatic defensive systems are attenuated in diabetic people and the lipid peroxidation rate increases in cells (Wohaiebet al. 1987) Accordingly, several and sever damages occur in different organs of diabetic people; such that, renal failure has been known as a

main factor of diabetics mortality (Pickup et al. 1997). Significant improvement have been obtained in the area of diabetes control using synthetic drugs, but the diabetic people demand to use natural products with anti-diabetes characteristics are increasing continuously due to adverse effects of insulin and hypoglycemic medicines (Rao et al. 2007). So, attempts to find natural agents to deal with the disease have an important clinical value. Plants have been used widely and it has been demonstrated that some plants can decrease complications of diabetes with or without decreasing the blood sugar (Neefet al. 1995). There are more than several hundreds of plant species that have anti diabetic effects. However, only a few of them have been studied (Noel et al. 1997).

Q10 was discovered in 1957 by Fredrick L. Crane. Q10 is considered as a vitamin or a vitamin-like substance and is found in food resources naturally as other vitamins, but its amount is very in food resources (Dhanasekaran et al. 2005). Q10 is synthesized in all tissues. Its biosynthesis is a multistage process that needs at least eight vitamins and several rare minerals. Q10 is soluble in fat and found in all cells of the body. It acts also as a coenzyme in most of important enzymatic stages to produce intra cell energy. The maximum amount of it is found in liver, kidney, heart, muscle, and brain. Another function of Q10 is as an antioxidant. Internal synthesis of vitamin and also its absorption through food caused normal rate maintenance of Q10 in a healthy person. The positive effects of Q10 in the treatment of Aids, cancer, gastric ulcers, obesity, muscular dystrophy, sensitivity, immune system function, and body physical strength have been studied (Dhanasekaran et al. 2005). The researchers' studies demonstrate that Q10 decreases in heart disease, muscular dystrophies, Parkinson, cancer, diabetes, and Aids. Furthermore, it protects membrane proteins from oxidative damages. In diabetes, cancer and heart diseases the decreased Q10 is observed (Dhanasekaran et al. 2005). Considering the various effects of Q10 especially hypoglycemic and antioxidant characteristics, it is assumed that Q10 can decrease diabetes nephropathy complications.

In any case, considering that no study has been conducted so far on Q10 effects on renal tissue damages resulted of diabetes, the present study was conducted in order to evaluate the protective effects of Q10 on serum levels of renal function indicators in diabetic rats induced by Alloxan.

MATERIAL AND METHODS

The experimental model of diabetes type I in rats was created by intraperitoneally injection of 120 mg Alloxan monohydrate mg/kg and physiology serum was used as Alloxan solvent (Ugbenyen et

al., 2009) 72 hours after injection of Alloxan, glucometer was used to measure the animal FBS using glucometer (Lazos, 1986). FBS within 120-250 mg/dl was considered as diabetic in the present study (Gupta et al., 2005). ZiestChem glucometer kit made by Iran *zistchimi* was used.

Control group rats received buffer citrate 0.05 M with pH 4.5 intraperitoneally. Q10 Treatment group received 75 mg/kg Q10 via gavage for one month (Dhanasekaran et al., 2005). The fourth group (combined intervention group) at first the rats was diabetic then they received 75 mg/kg Q10 by gavage.

The keeping condition in other cases was considered equal for all groups. At the end of experiment period, following to 12 hour diet, 20 blood samples were obtained from the back of the eyeball in order to measure blood sugar and some biochemical indicators such as urea, uric acid, and Creatinine. The blood sera were centrifuged with 2500 RPM at 30°C for 15 min.

The data were expressed as Mean±Sem. ANOVA statistical analysis method was used for data analysis and Tukey test were used to compare the difference between groups. $P < 0.05$ was used to determine the significance level.

RESULTS AND DISCUSSION

Effect on Blood Sugar:

The mean blood sugar in normal, Q10, Alloxan, and Q10+Alloxan groups were 94.8 ± 3.88 , 94.2 ± 3.4 , 245.1 ± 2.1 , and 240.5 ± 9.26 mg/dl, respectively. The obtained results suggest no meaningful difference between Alloxan and Q10± Alloxan groups ($P > 0.05$) (Fig 1).

Effect on Blood Urea:

The mean urea in normal, Q10, Alloxan, and Q10+Alloxan groups were 52.25 ± 4.13 , 521.35 ± 3.4 , 128.35 ± 14.67 , and 94.75 ± 5.6 mg/dl, respectively. The obtained results suggest a meaningful difference between Alloxan and Q10± Alloxan groups ($P < 0.1$) (Fig 2).

Effect on Blood Uric acid:

The mean serum uric acid in normal, Q10, Alloxan, and Q10+Alloxan groups were 1.57 ± 0.15 , 1.87 ± 0.7 , 3.51 ± 0.46 , and 2.11 ± 0.38 mg/dl, respectively. The obtained results suggest a meaningful difference between Alloxan and Q10± Alloxan groups ($P < 0.1$) (Fig 3).

Effect on Blood Creatinine:

The mean serum creatinine in normal, Q10, Alloxan, and Q10+Alloxan groups were 1.07 ± 0.11 , 1.17 ± 0.13 , 2.34 ± 0.38 , and 1.83 ± 0.11 mg/dl, respectively. The obtained results suggest a meaningful difference among Alloxan, Q10± Alloxan, and Q10, groups ($P < 0.1$) (Fig 2).

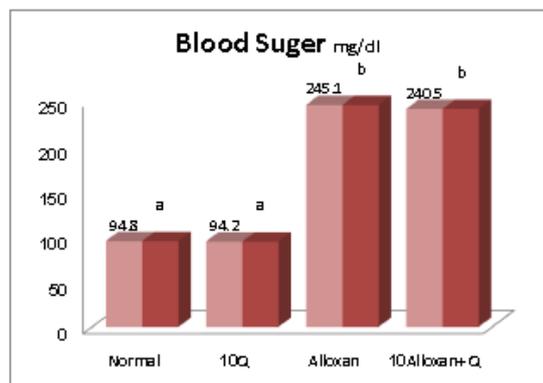


Fig 1: Comparison of Mean±SEM of blood sugar, followed by administration of Q10, Alloxan, and both of which coincidentally in rats in a one-month period. {The different letters show a meaningful difference of mean among groups ($P<0/01$)}

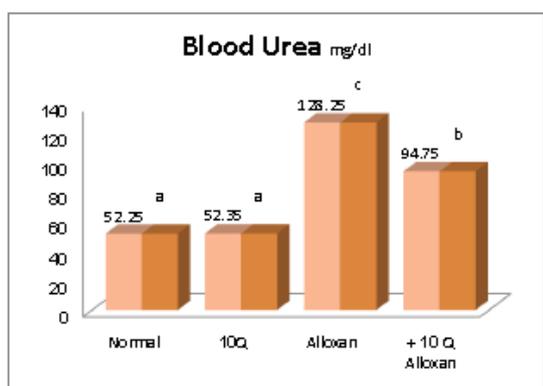


Fig 2: Comparison of Mean±SEM of urea followed by administration of Q10, Alloxan, and both of which coincidentally in rats in a one-month period. {The different letters show a meaningful difference of mean among groups ($P<0/01$)}

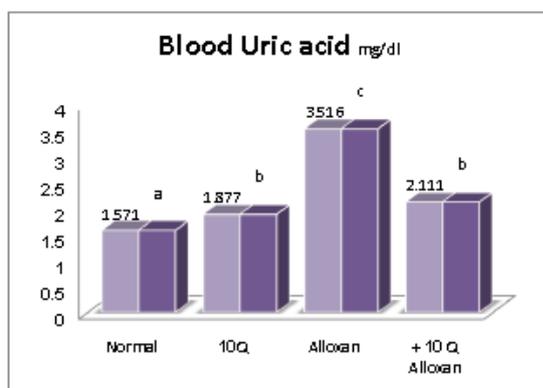


Fig 3: Comparison of Mean±SEM of blood uric acid followed by administration of Q10, Alloxan, and both of which coincidentally in rats in a one-month period. {The different letters show a meaningful difference of mean among groups ($P<0/01$)}

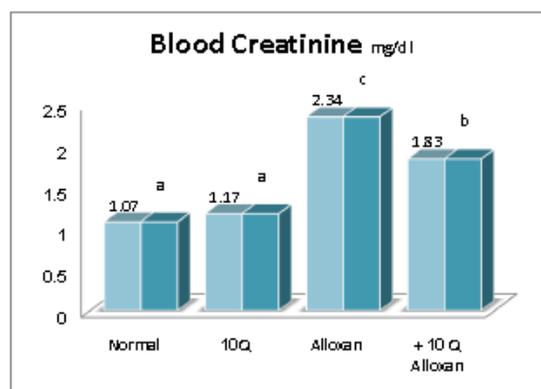


Fig 4: Comparison of Mean±SEM of blood Creatinine followed by administration of Q10, Alloxan, and both of which coincidentally in rats in a one-month period. {The different letters show a meaningful difference of mean among groups ($P<0/01$)}

DISCUSSION

The increased amount of free oxygen radical production, decreased antioxidant function, increased lipid peroxidation, and membrane damage are as the main factors of apoptosis or cell necrosis which are common in diabetes (Nwanjo *et al.*, 2006; Descoet *et al.*, 2002). The increased amount of urea has been observed in the blood serum of insulin-independent diabetics (Lehto *et al.* 1998). The increased urea has a close relationship with increased weight (Lee *et al.*, 1995), hypertension (Selby *et al.*, 1990), decreased hypertriglyceridemia (Wilson *et al.*, 1983), and decreased insulin sensitivity (Modanet *et al.*, 1987). Also, purine metabolism induced urea increase causes thrombosis increases (Visy *et al.*, 1991). There are evidences suggesting that increased urea caused hypertension, diabetes (Nakanishi *et al.*, 2003), heart attacks (Bos *et al.*, 2006), and cardiovascular diseases (Iseki *et al.*, 2001).

Uric acid is as water soluble and non-enzymatic antioxidant (Anwar *et al.*, 2003) but high amounts of uric acid increases free radicals via an activating enzymatic system of xanthine oxidize. It has been found that uric acid amounts, increases in type I diabetic rats (Anwar *et al.*, 2003). Uric acid is the end product of purine metabolism. Increased uric acid is the result of its increased production or decreased secretion. Its increase is a risk factor of heart attack in insulin-independent diabetics; such that, the risk of heart attack is three times higher among people with high uric acid (Lehto *et al.*, 1998).

A study conducted the increased amount of Malondialdehyde in the renal tissue of diabetic rats induced by Alloxan it was demonstrated that oxidative stress caused by free radicals is one of the mechanisms involved in diabetic nephropathy (Tabrizi *et al.*, 1390).

Table 1. Comparison of mean on serum levels of renal function indicators in control and experimental groups. Dissimilar letters in each vertical column indicate a significant difference Mean±SD, (P<0/05).

Parameters	Control	Q10	Alloxan	Q10+Alloxan
Capsule thickness	3.87±0.175 ^a	4.33±0.183 ^a	16.57 ±0.849 ^c	8 ±0.527 ^b
Bowman capsule diagonal	108.37 ±3.77 ^a	108.12 ±3.47 ^a	59.16 ±2.1 ^c	73.95 ±2.5 ^b
Blood sugar	94.8 ±3.88 ^a	94.2 ±3.45 ^a	245.1 ±20.9 ^b	240.5 ±9.26 ^b
Urea	52.25 ±4.13 ^a	52.35 ±3.4 ^a	128 ±14.67 ^c	94.75 ±5.6 ^b
Uric acid	1.57 ±0.15 ^a	1.87 ±0.7 ^b	3.51 ±0.46 ^c	2.11 ±0.38 ^b
Creatinine ml/dl	1.07 ±0.11 ^a	1.17 ±0.13 ^a	2.34 ±0.38 ^c	1.83 ±0.11 ^b

The results of the present study show that induction of type I diabetes using Alloxan increases blood sugar meaningfully and the administration of Q10 in diabetic group doesn't decrease blood sugar. As a result, Q10 is affectless in type I diabetics to decrease blood sugar. The present result conforms to the results obtained by Tabrizi.

In the present study, Alloxan caused a meaningful increase in the Urea, Uric acid, and Creatinine levels compared with the normal group. Different researches about type I diabetes induction by Alloxan injection in rats show a meaningful increase in serum levels of renal function indicators like urea, uric acid, and creatinine (Tabrizi *et al.*, 1390; Kaneto *et al.*, 2007). On the other hand, in the studies conducted the induction of type I diabetes via streptozotocin (STZ) injection in rats caused a meaningful increase in the serum levels of renal function indicators like urea, uric acid, and creatinine (Pour Abouli *et al.*, 1393; Heidari *et al.*, 2011; Abdi *et al.*, 2006). Their reports conform to the results of the present study.

Based on the conducted studies, the rate of urea and creatinine in diabetics was 40 and 68 percent higher than the normal group (Demerdash *et al.*, 2005) that conforms highly to the results of the present study.

The obtained results of the administration of Q10 + Alloxan in diabetics, in the present study, show a meaningful difference in decreased level of Urea, Uric acid, and Creatinine. This means that the Q10 antioxidant characteristics can prevent nephropathy damages caused by disorders in renal function indicators.

In the studies conducted the meaningful changes in serum levels of renal function indicators have been attributed to diabetic renal damage (Pickup *et al.*, 1996; Burtis *et al.*, 1996). It is well known that diabetic nephropathy is caused by several factors which are not preventable by hyperglycemia and hypertension control. Although in the early stages of the disease the diabetic nephropathy changes are induced by hyperglycemia, the later injuries have no relationship to hyperglycemia (Liu *et al.*, 2008). Then, blood glucose control is not enough by itself to postpone the process of diabetic nephropathy.

CONCLUSION

It can be concluded from the discussion of the present study that type I diabetes causes a meaningful increase of in the serum levels of renal function indicators like urea, uric acid, and creatinine, and the administration of Q10 as an antioxidant in diabetics causes in some extent the decrease of renal function indicators and can decrease the side effects on the function of the vital organ.

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