



Preventive Effect of Fasting In the Alloxan-Induced Diabetic Rats

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ABSTRACT

Diabetes is a metabolic disorder due to the defect in insulin secretion or function. Many people in the world are affected by this disease. The present study investigates the preventive effect of fasting in Alloxan-Induced diabetic rats. Eighteen adult male wistar rats weighing 180 to 230 g were randomly divided into 3 equal groups including: (experimental, diabetic and non-diabetic controls) and housed in single cages. Each group consisted of 6 rats. Twenty five days before blood glucose test, the rats of the experimental group were exposed to fasting so that in 24 hours only 6 hours (6 pm to 12 pm) to chow and water were accessed and at other times they were hungry but had free access to water. This case continued for 10 days then free access to food was provided and water for all groups during second 10 days. On day 21, the non-diabetic control group was given an injection of normal saline. The experimental and diabetic control groups was given an injection of Alloxan (130 mg/kg, i.p) Data were evaluated using parametric test by one-way analysis of variance followed by Tukey post-test and non-parametric analysis Kruskal-Wallis. Results showed that fasting has a significant effect on the prevention of diabetes.

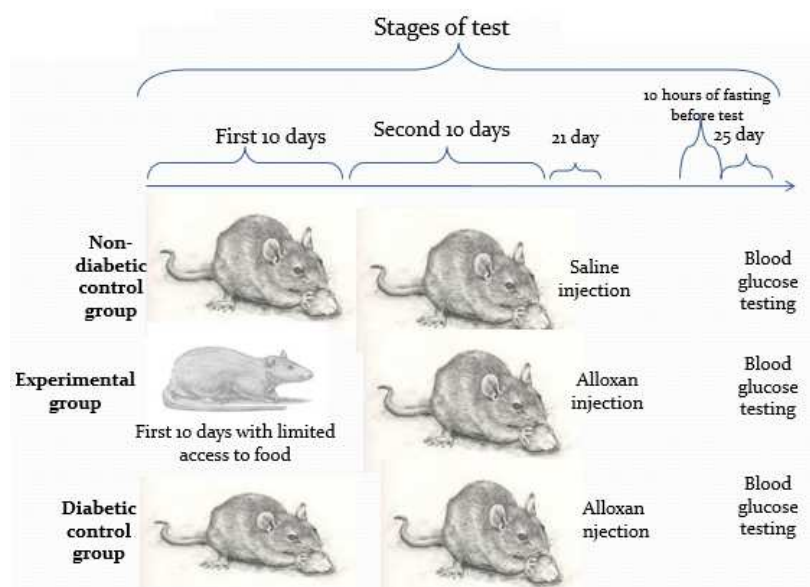
Key words: Diabetes, Fasting, Alloxan, Glucose

INTRODUCTION

Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The total number of people with diabetes is projected to increase from 171 million in 2000 to 366 million in 2030[1] Type 1 diabetes (T1D), an autoimmune disease once thought to be mediated exclusively by β cell-specific CD4+ T cells, is now recognized as one in which autoreactive CD8+ T cells play a fundamental role. In the non-obese diabetic (NOD) mouse model, CD8+ T effector cells take center stage in the destruction of pancreatic β cells and contribute to sustaining islet inflammation. [2]. Insulin resistance alone does not result in the development of type 2 diabetes; progressive dysfunction of pancreatic islet α and β cells, which results in inadequate control of hyperglycemia, must be present for the disease to develop. Because of these defects, meal stimulated insulin secretion from β cells is reduced and fails to meet the demands of the insulin resistant state [3]. The present study was conducted on the effects of fasting on the prevention of diabetes. Fasting is one of the important spiritual aspects of many religions such as Islam and Judaism. And it is believed that fasting has many benefits for the body. During fasting, the body consumes the storage of glucose and then break down body fat. The use of fat stored in the body as an energy source in the long run can reduce cholesterol levels, blood pressure, and weight decrease. Therefore, in this study the effect of fasting in the prevention of diabetes was evaluated.

EXPERIMENTAL SECTION

Wistar rat of male sex, weighing about 180-230 g were used in the study. Animals were maintained under standard environmental conditions i.e. ambient temperature of $(22\pm 2)^{\circ}\text{C}$ and at 45%-55% relative humidity for 12 h, each of dark and light cycle and fed with a standard pellet rats diet obtained from Khorasan JavanehLtd,Iran and water was supplied ad libitum. Then the rats were randomly divided into three groups: non-diabetic, experimental, and diabetic control. Each group included 6 rats. On day 25 before blood glucose test, the rats of the experimental group were exposed to fasting so that in 24 hours only 6 hours (6 pm to 12 pm) to chow and water were accessed and at other times they were hungry but had free access to water. This case continued for 10 days. Then free access to food and water was provided for all groups during second 10 days. On day 21, the non-diabetic control group was given an injection of normal saline and the experimental and diabetic control groups were given an injection of Alloxan Monohydrate (130 mg/kg, i.p) in sterile saline. Three days after Alloxan injection, all groups were exposed to starving for 10 hours and at Twenty-fifth day, rats were anesthetized by intraperitoneal injection of ketamine (dose 75mg/kg) with acepromazine (dose 2.5mg/kg) and fasting blood glucose levels were measured in all groups. Blood glucose levels were measured using blood glucose test strips with Bioname glucometer. Blood glucose estimation and body weight measurement were done on day 0, 7 and 14 after alloxan injection. All values of results are presented as mean \pm standard error of mean (S.E.M.) The statistical analysis involving two groups was evaluated by means of Student 's t-test whereas one way analysis of variance (ANOVA) followed by Dunnet 's multiple comparison post-test was used for statistical comparison between control and various treated groups. Statistical significance was accepted at the $P<0.05$ values.



The figure 1 shows that the control group of diabetic rats with a dose 130 mg/kg Alloxan was induced by intraperitoneal injection with the use of significantly compared to non-diabetic control blood glucose levels showed the experimental group, however, increase in blood sugar is brief but significant decrease in serum glucose compared to diabetic control group shows. As the result of ANOVA, Tukey test showed significant differences ($P < 0/05$) between the experimental group and the control group of non-diabetic and diabetic control diabetes that is shown in (Figure 1). The body weight changes in three groups have been shown in fig 2. The mean body weight of diabetic control group was less on 7 days after the onset of diabetes, while weight in the experimental group did not change.

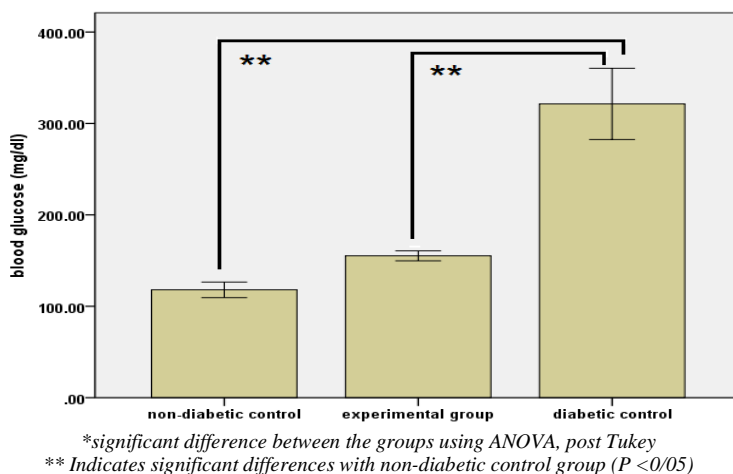
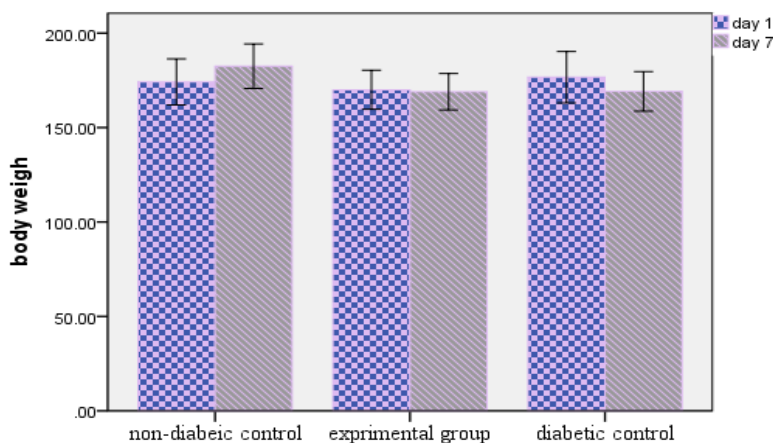


Figure 1:

Table 1: Mean and Standard Error of Blood Glucose Groups

Groups	Mean	Standard Error
Non-diabetic control	118.3000	8.50098
Experimental group	155.1667	5.42474
Diabetic control	321.3333	38.9886



Comparative Effect of Fasting on Body Weight (g) After Alloxan (130mg/kg i.p.) Induced Diabetes In Rats Fig2.

RESULTS AND DISCUSSION

In this study, Anti- Diabetic Effects of Fasting on Male Rats were evaluated and it was shown that fasting has a preventive effect on the disease. In addition, studies have demonstrated that rats restricted in caloric intake exhibited extended life spans. Subsequently, calorie restriction (CR) was shown to extend life span in many animal models [4, 5]. Of the many effect of CR, two are widely accepted to be connected with extended longevity: redox changes and alterations in insulin signaling pathways [6-8] CR limits mitochondrial generation of reactive oxygen species (ROS), alters the expression and activity of antioxidant pathways, and prevents oxidative modifications of biomolecules during aging[7, 9, 10] . CR also prevents the loss of peripheral sensitivity to insulin, precluding many of the effects of aging associated with insulin resistance [6, 8].

Insulin regulates glucose uptake into cells by recruiting membrane vesicles containing the Glucose transporter type4 (GLUT4) from the interior of cells to the cell surface, where it allows glucose to enter cells by facultative diffusion.

Skeletal muscle accounts for at least 80% of the glucose uptake in human [11]. Furthermore, a close relationship between muscle GLUT-4 content and maximal insulin-stimulated glucose transport has been observed [12].

Realization has shown that blood glucose levels in rats fed a high-fat (HF) diet with alternate-day fasting (ADF) in response to exogenous insulin compared to the control group was not significant [13] However, this is not inconsistent with this study because the amount of enzyme GLUT4 in skeletal muscle may be an important determinant of whole body glucose disposal as well as skeletal muscle glucose transport capacity. It is therefore plausible that low-protein, high-fat diet cause the lower GLUT-4 expression counteracted the beneficial effect of the ADF. Fasting for 3 days resulted in a marked increase in insulin binding relative to ad libitum fed control rats. Over the 5-day refeeding period, the amount of insulin bound slowly returned to control values [14]

In this study one of the causes of the decline in blood glucose in experimental group than control group may be the increased sensitivity of insulin receptors to the small amounts of insulin in the blood.

CONCLUSION

The results of this study showed significant effects of Fasting in the Prevention of Diabetes and Improvement body weight in the Alloxan-Induced Diabetic Rats. Realization has shown that blood glucose levels in rats fed a high-fat (HF) diet with alternate-day fasting (ADF) in response to exogenous insulin compared to the control group was not significant [13] However, this is not inconsistent with this study because the amount of enzyme GLUT4 in skeletal muscle may be an important determinant of whole body glucose disposal as well as skeletal muscle glucose transport capacity. It is therefore plausible that low-protein, high-fat diet cause the lower GLUT-4 expression counteracted the beneficial effect of the ADF.

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