The Study of SAD1/UNC-84 Domain Protein 1 in Muscle of Diabetic Male Wistar Rats

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Received: 10 July 2018

Accepted: 21 September 2018

Published in May 2019

Abstract

Objective: The purpose of this study was to measure the changes of the SUN1 protein levels on soleus muscle in diabetic male wistar rats.

Materials and Methods: Twenty male Wistar rats with 10 weeks old and weighing 200-250 grams were selected. After two weeks, the rats were divided into two groups (diabetic group and healthy group). After 12 hours fasting, diabetes was induced by intraperitoneally injection of streptozotocin (STZ). At the end of sixth week, the soleus muscle was removed and kept at a temperature of -80 degrees to evaluate the difference of SUN1 protein between two groups.

Results: there was not significant difference in SUN1 protein levels between diabetic and control groups (*P*-value: 0.525).

Conclusion: Although in most of laminopathies, the SUN1 protein that located in the inner nuclear membrane changed, but it seems the proteins in the inner membrane, are not affected by diabetes.

Keywords: LINC complex, SUN proteins, Diabetes mellitus, Soleus muscle, Rats

Introduction

The LINC complex is composed of SUN proteins (sad 1 and UNC-84) in internal nuclear membrane and KASH proteins (Klarsicht, ANC-1, Syne/ nesprin-1, 2 Homology) in external nuclear membrane (1). At least, five distinct isoforms of SUN protein (SUN1-5) were identified in the mammalian genome (2).

Nuclear positioning in muscle cells regulated by the connection of LINC complex and Cytoskeleton (3-5). Improper nuclear positioning often is associated with the cell dysfunction and it may have various clinical results (6,3).

Previous studies showed that diabetes mellitus causes various changes in the structure and function of skeletal muscle such as the muscle atrophy (7), changing in the fiber type (8), muscle weakness and decrease in energy metabolism(9). Several muscle diseases were

associated with inappropriate positioning of myonuclear (10-11,3) and the proper positioning and anchoring of nuclei is essential for normal functioning of skeletal muscle. Therefore, the study of the LINC complex proteins in diabetes is important. There are some studies about the relationship between mass and functional, growth, development, muscle restoration and metabolic activity of the skeletal muscles in various types of diabetes mellitus. The purpose of this study was to measure the changes of the SUN1 protein levels on soleus muscle in diabetic male wistar rats

Materials and Methods

This research was a semi-experimental study. In this research, 20 male Wistar rats with ten weeks old and 200- 250 grams weight were prepared from animals care center of Lorastan University of Medical Science and after two weeks the rats were divided into two groups, diabetic group (DG) which included 10 male Wistar rats and healthy group (HG).

After 12 hours fasting, diabetes was induced by intraperitoneally injection of streptozotocin (STZ/ 50mg/kg solved in 0.5 mol/L fresh citrate buffer with 4.5 PH). Then 48 hours after the diabetes induction, using a small lesion by lancet a small drop of blood from the tail vein was placed on the glucometer tape and was measured by glucometer device (Glucotrend 2, Roche Germany). The rats with blood glucose levels higher than 300 mg/dL were considered as diabetic. At the end of the sixth week, all of the rats were anaesthetized and then dissected. the soleus muscle was removed and kept at a temperature of -80 C instantly. It should be noted that 6-8 samples from each group were studied to perform a molecular tests of measuring the expression of SUN1 protein. The ELISA method with kits produced by Cusabio-Japan company was used for SUN1 protein levels measurment.

Data analysis was performed using a SPSS-21. To evaluate the difference of SUN1 protein between two studied groups the independent t-test were used at a significant level of P <0.05.

It should be noted that the ethical code of this research is LUNS.REC.1395.170 from the Lorestan University of Medical Sciences. The proposal for this thesis has been approved in 1395/10/25 to number 969.

Results

The results of this study showed that there was no significant difference in the amount of SUN1 protein in the soleus muscle between DG and HG (P= 0.525) (Figure 1).

Discussion

SUN1 proteins are affected in many diseases. In the present study, diabetes had no effect on the expression of SUN1 protein. Since, this protein is one of the proteins that related to lamina; it seems that diabetes does not have significantly disturbed lamina proteins.

SUN1 protein expression reduction or its

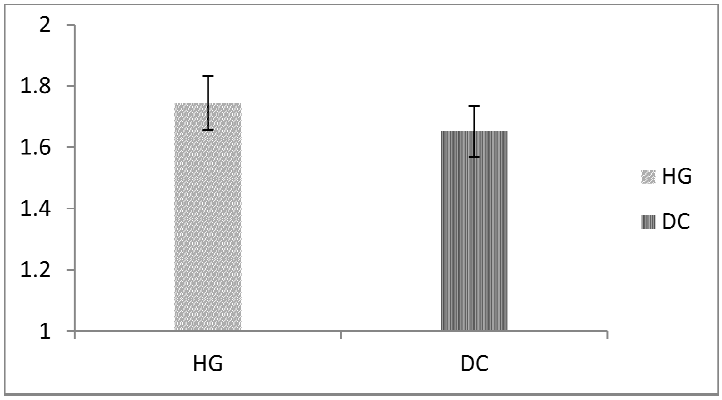

Figure 1. The SUN1 protein level in soleus muscle of HG and DG groups

accumulation in the nucleus membrane leads to the some changes, such as disruption in anchoring of the muscle nucleus, decrease in the connection and mechanical sense between the nucleus and cytoskeleton, and also the destruction of DNA. In the present study unchanged SUN1 protein may be attributed to the no effect of diabetes on mechanical responses.

SUN 1 protein is essential to maintain a normal distance between the internal and external membranes of the nucleus, especially in muscle cells that are under the mechanical pressure (12). According to the results of present study, there were not significant changes in level of SUN1 protein between two studied groups.

SUN proteins play important roles in a wide range of the cellular functions. Depletion of SUN1 and SUN2 in mice caused death shortly after birth due to the of respiratory system failure. The past studies on mice with SUN1 deficiency indicated that the disruption in SUN1 proteins prevents the telomeres joining to the nuclear membrane. An increase in apoptosis and DNA degradation has also been observed with SUN1 protein depletion in mice. Also, SUN proteins play an important role in breaking down DNA strings and thus maintaining the stability of the genome. (13-15). However, in the present study, we did not find the significant change in the SUN1 protein expression in the soleus muscle of diabetic group.

Conclusions

The LINC complex proteins are affected in many of laminopathies. In the present research which studied the changes in the inner nuclear membrane protein (SUN1) in diabetic rats, it was shown that, in contrast with other types of laminopathies, diabetes does not affect SUN1 protein. Since identifying the factors that involved in diabetes and its related proteins can provide a setting for a more complete understanding of diabetes, the studying of proteins that located in the outer membrane nucleus can exactly explain the changes of the LINC complex in diabetes.

Acknowledgments

This research is a part of PhD thesis which has been approved by the Lorestan University of medical sciences. We would like to thank the personnel of Razi laboratory in Khorramabad and all those who helped us for accomplishment of the present study.

Funding

The authors received financial support for the research from Lorestan University of medical sciences.

Conflict of Interest

The authors declare that there are no conflicts of interest.

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