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Original Article

Circulating irisin is increased in type 2 diabetes mellitus and correlates with fasting glucose levels

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ABSTRACT

Background/aims: Irisin is a hormone expressed in muscle, which is an exercise-induced myokine triggering browning of white adipose tissue and increases metabolic genes expression.
Methods: We investigated the irisin levels in 39 type 2 diabetes mellitus patients (T2D) compared to 39 control individuals.
Results: Irisin plasma levels were higher in T2D patients when compared with the control group ($p < 0.0001$). Non-obese T2D individuals presented higher irisin levels when compared with non-obese and obese controls ($p < 0.0001$ and $p = 0.011$, respectively). Obese T2D individuals showed higher irisin levels when compared with non-obese control ($p = 0.003$), but no difference was observed when compared with obese controls ($p > 0.05$). A positive correlation was observed between irisin and fasting glucose levels in the T2D group ($r = 0.341$, $p = 0.033$). No difference regarding irisin levels was found when T2D individuals who practice physical activity and sedentary individuals were compared ($p = 0.632$).
Conclusion: This result indicates that T2D is associated with an irisin release in order to compensate the insulin resistance observed in the skeletal muscle on diabetes, and that the poor glycaemic control contributes for enhancement of this state.

1. Introduction

Irisin is a glycosylated polypeptide hormone expressed in muscle as the type 1 membrane precursor protein FNDC5 (fibronectin type III domain containing 5), which is proteolytically cleaved and secreted.[1] This protein has been described as an exercise-induced myokine triggering browning of white adipose tissue and increasing metabolic genes expression.[1,2] Moreover, it is produced in response to activation of peroxisome proliferator activated receptor-c coactivator-1 α (PGC-1 α).[3]

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Some studies have demonstrated that irisin causes increase in total body energy expenditure, enhanced thermogenesis, increased oxidative metabolism, weight loss, besides improvement in glucose tolerance and insulin resistance.[1,4–6] Circulating irisin levels have been evaluated in cross-sectional studies involving type 2 diabetes (T2D) patients,[7–12] but its association with the disease is still conflicting.

In this study, the irisin plasma levels in T2D patients were evaluated comparing with a control group, as well as the association with anthropometric and laboratory parameters.

2. Material and methods

2.1. Subjects

This cross-sectional study was conducted with 39 patients with clinical and laboratory diagnosis of T2D [33 women and 6 men; 61 (9) years; BMI 27.5 ± 4.4 kg/m^2] and 39 non-diabetic controls [28 women and 11 men; 53 (11) years; BMI 26.7 ± 4.2 kg/m^2]. T2D diagnosis was based on the American Diabetes Association criteria.[13] The patient group was recruited from Santa Casa Hospital (Belo Horizonte, Minas Gerais, Brazil) and control group from the local community, in the period of June 2012–September 2013.

This study was approved by the Ethics Committee of the Federal University of Minas Gerais and Santa Casa Hospital. Informed consent was obtained from all the patients.

Anthropometric and laboratory data were obtained from medical records. The controls showed normal levels of fasting glucose (60–99 mg/dL) and no use of hypoglycaemic drugs. The exclusion criteria adopted were individuals older than 70 years, with history of cardiovascular diseases, cancer, autoimmune disease, with current or recent infectious process, and with treatment of anti-inflammatory drugs.

2.2. Clinical and laboratorial data

Clinical data (gender, age, and BMI) were obtained for all the subjects through interviews or medical records. The fasting glucose was measured in serum samples after eight hours fasting. The serum samples were centrifuged at 3,500 rpm for 20 min at 25 °C and the assays performed immediately. The tests were performed using enzyme-colorimetric method, BTR 811 spectrophotometer (Biotron, Minas Gerais, Brazil) and Glucose-PP kit (Gold Analisa, Minas Gerais, Brazil), following the manufacturer's instructions. The concentrations of fasting glucose were expressed in mg/dL. The irisin levels (Irisin Competitive ELISA Kit, AdipoGen®, Switzerland) were measured in heparin plasma samples (centrifuged at 1,100 × g for 20 min at 25 °C and stored at −70 °C until analysis) by ELISA, according to the manufacturer's instructions.

2.3. Statistical analysis

All of the statistical analyses were performed with Statistical Package of the Social Sciences (SPSS) version 17.0. The analysis of normality was performed by Shapiro–Wilk test. Data are presented as ''mean ± (standard deviation – SD)'' (parametric variables) or ''median (interquartile range – IQR)'' (non-parametric variables). Comparisons between two groups were made by Student's t-test for parametric variables and Mann–Whitney test for non-parametric variables. Comparisons of non-parametric variables were performed by Kruskal–Wallis test between the three groups. When differences were detected, they were compared in pairs by the Mann–Whitney method, followed by Bonferroni's correction. Spearman's correlations were computed in the T2D patient group to assess correlations between irisin plasma levels and fasting glucose. A p-value <0.05 was considered statistically significant.

3. Results

The groups were matched by gender (Chi-square test, $p = 0.329$) and BMI (Student t-test, $p = 0.391$).

Irisin plasma levels were higher in T2D patients [3.54 (3.01) μg/mL] when compared with the control group [2.01 (1.44) μg/mL] – Mann–Whitney test: $p < 0.0001$ (Fig. 1).

It was also observed that irisin levels are different between T2D and control groups (Kruskal–Wallis test, $p < 0.0001$) when weight criteria were considered: BMI < 30 kg/m^2 as non-obese and BMI ≥ 30 kg/m^2 as obese. Non-obese T2D individuals presented higher irisin levels [4.08 (3.76) μg/mL] when compared with non-obese [2.08 (1.33) μg/mL] and obese controls [1.70 (2.52) μg/mL] – Mann–Whitney test with Bonferroni correction: $p < 0.0001$ and $p = 0.011$, respectively. Furthermore, obese T2D individuals showed higher irisin levels [2.89 (1.06) μg/mL] when compared with non-obese control [2.08 (1.33) μg/mL] – Mann–Whitney test with Bonferroni correction: $p = 0.003$ (Fig. 2) – but no difference when compared with obese controls ($p > 0.013$ after correction). No statistical difference was observed when irisin levels in both non-obese and obese individuals considering the same group (patients or control) were compared.

A positive correlation was observed between irisin and fasting glucose levels in the T2D group (Spearman's correlation, $r = 0.341$, $p = 0.033$ – Fig. 3).

No difference regarding irisin levels was found when individuals who practice physical activity – at least three times a week, for 30 min [48.72% total group, irisin = 2.81 (2.35) μg/mL or 46.15% for T2D patients, irisin = 3.38 (3.71) μg/mL] – and

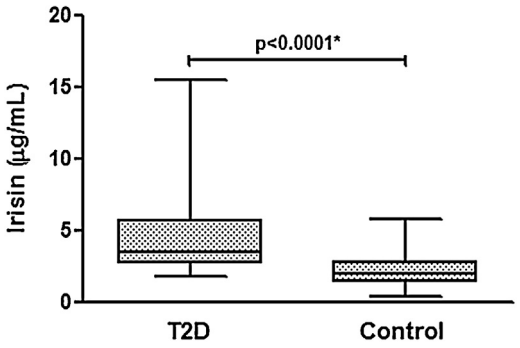

Fig. 1 – Irisin plasma levels in type 2 diabetes (T2D) patients and controls – *Mann–Whitney test, $p < 0.05$ was considered significant.

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