ORIGINAL ARTICLE

Impact of Serum Adropin and Irisin in Iraqi patients with Congestive Heart Failure

MAHDE SALIH HAMAD[1], ENTEDHAR RIFAAT SARHAT[1*], THURAIA RIFAAT SARHAT[2], KASIM SAKRAN ABASS[3]
[1]*Department of Basic Medical Science, Dentistry College, University of Tikrit, Tikrit, Iraq*
[2]*College of Education, University of Tikrit, Tikrit, Iraq*
[3]*Department of Pharmacology and Toxicology, College of Pharmacy, University of Kirkuk, Kirkuk, Iraq*
Correspondence to Dr. Entedhar Rifaat Sarhat, Email: entedharr@tu.edu.iq

ABSTRACT

Background: The relations of adropin, and irisin concentrations to congestive heart failure (CHF) risk have not been comprehensively elucidated. We sought to study the markers of adropin, and irisin , both in control subjects and in CHF.
Methods: The study registered thirty four patients with CHF and thirty four healthy group. Fasting venous blood samples were collected from all cases. Serum adropin and irisin levels were analyzed using ELISA method. For all comparisons, statistical significance was defined by $p \leq .05$.
Results: Adropin, total cholesterol, and triglycerides parameters were found significantly high ($P< 0.001$) with the exception of irisin, and high-density lipoprotein- C which was significantly low ($P< 0.001$) in CHF patients.
Conclusion: The present work suggests a measurement of adropin and irisin level in serum samples is a potential marker for diagnosing of CHF.
Keywords: Adropin and irisin, congestive heart failure.

INTRODUCTION

Congestive heart failure (CHF) is a leading cause of cardiac morbidity and mortality, It is characterized by dyspnea, fatigue, and signs of volume overload, which may include peripheral edema and pulmonary rules Data from the National Health and Nutrition Examination Survey III (NHANES III) estimate that 4.7 million people in the United States are treated for CHF each year. CHF has a poor prognosis despite new improvements in its management. Activation of the sympathetic nervous system is one of the major pathophysiological abnormalities in HF patients. Myocardial ischemia may occur either from increased demand of oxygen by the myocardium, or decreased oxygen supply to the myocardium, or both[1-3].

The adipose tissue is a complex, essential, and highly active metabolic and endocrine organ[(4)]. that releases many metabolically active peptide hormones, bioactive cytokines ,chemokines and adipokines , including leptin, visfatin, resistin, apelin, omentin, sex steroids, and various growth factors are cell signaling proteins[5,6].

Apelin is a novel adipocytokine produced by white adipose tissue, that is synthesized by endothelial cells and exerts its functions through autocrine and paracrine pathways by binding to endogenous ligand of the G-protein coupled receptor expressed absolute presence in most types of cells in the heart, including myocytes, smooth muscle cells and fibroblasts[(5,7)]. The apelin and its receptor (APJ receptor) is one of the molecular systems which counteracts the negative effects of aldosterone on the myocardial cells and limits the inflammatory re- actions and the oxidative[8].

Adropin is a new peptide hormone , its expression in a human liver cell line (Hepg2) is suppressed following the activation of liver receptor (LXRa), suggesting sensitivity to carbohydrate and lipid metabolism[(9)], regulation of energy metabolism, insulin resistance, and endothelial functions, regulating angiogenesis and increasing blood flow and capillary density in a model of hind limb ischemia[10].

Energy metabolism and insulin resistance-related proteins, such as leptin, adiponectin, ghrelin and tumor necrosis alpha, have been well-studied, and recently an additional exercise-induced peptide known as irisin has been identified[11,12]. Irisin, with 112 amino acids (12587 Da), is a cleaved and secreted fragment of fibronectin type III domain containing 5 (FNDC5)[13], an adipokine and myokine, and exhibits autocrine and paracrine effects that is released from the liver, testis, spleen gut, kidney, heart, nerves ,skeletal muscles and skin. that plays a pivotal role in mitochondrial function , metabolic and energy expenditure regulation[14].

METHODS

Subject: One hindered fifty individuals with age ranged between (20-45) year were enrolled in this study. They were divided into two groups: group one (G1) consisted of 30 patients with CHF. group (G2) consisted of 30 healthy group. The patients attended the Tikrit Teaching Hospital / Tikrit / Iraq during June 2018 to August 2019. Echocardiographic measurements were performed according to guidelines and recommendations by the European Association of Echocardiography[15].

Blood Sample Collection

Five milliliters of blood samples were drawn from an antecubital vein by careful venipuncture using a 21-gauge needle without stasis between 08.00 and 10.00 a.m. after a resting time of 30 min and a fasting period of 12 h. Routine biochemical parameters were determined by standard methods.

Biochemical analyses: Adropin and irisin levels were analyzed using enzyme linked-immunosorbent assay (Catalog No. CK-E90905, Hangzhou East biopharm Co. Ltd.) was used to determine Irisin levels, following the manufacturer's instructions.. we also measured glucose, triglyceride, cholesterol, high-density lipoprotein (HDL),and

low-density lipoprotein levels in both patient and control groups.

The results are expressed as mean ±S.D. and all statistical calculations were made by applying paired Student's t-test with the significance level at P<0.05.

RESULTS

Adropin, Irisin, and lipid profile of patients in CHD was significantly different from that of the controls; though within the desirable levels (Table 1).

The Apelin level in serum was substantially decreased in the CHF group as compared with the control group **(**1.2±0.73 vs2.7 ± 0.79 ng/ml: p < 0.001**).**

Serum adropin and **irisin,** levels were significantly elevated in CHF patients as compared to healthy controls (11.56±1.09 vs 5. 75 ± 1.27 ng/mL: p< 0.05), and **(**0.497 ± 0.145 vs 0.288 ± 0.138µg/mL:**)** respectively.

Table 1: Mean ±S.D. Adropin, Irisin, and lipid profile of patients in CHD

Parameter	Control	CHF	P value
Apelin (ng/ml)	2.7 ± 0.79	1.2± 0.73	< 0.001
Adropin (ng/mL)	5. 75 ± 1.27	11. 56 ± 1.09	< 0.05
Irisin (µg/mL**)**	0.288 ± 0.138	0.497± 0.145	<0.05
Total cholesterol(mmol/l)	4.35 ± 0.120	7.16 ±0.147	<0.0001
TG (mmol/l)	1.15 ±0.071	3.41 ±0.11	<0.0001
HDL-C(mmol/l)	1.09 ±0.035	0 .62 ±0.022	<0.0001

TC and TG levels showed a significant increase while HDL-C was significantly decreased among the cases. Mean and standard deviation values of TC in the cases was 7.16 ±0.147 mmol/l vs. 4.35 ± 0.120mmol/l in the controls (p< 0.0001). TG level in the cases was 3.41 ±0.11 mmol/l vs. 1.15 ±0.071 mmol/l in the controls (p<< 0.0001). HDL-C level in the cases was 0 .62 ±0.022 mmol/l compared to 1.09 ±0.035 mmol/l in the controls (p< 0.0001).

DISCUSSION

Biochemical changes in cardiac myocytes, interstitium, or both, associated with release of various biochemical markers like cytokines, neurohormones(renin-angiotensin-aldosterone and adrenergic nervous systems), enzymes, etc., which can be estimated in blood[16].

Under normal conditions apelin and APJ are expressed in cardiac myocytes. It have many actions ranging from inotropy to vasodilatory properties, both directly in a nitric oxide- and endothelium-dependent manner and indirectly through control of vasopressin release in the central nervous system[17,18].

Serum level of Apelin was found to be significantly reduced in patients with CHF compared to control group due to failing cardiac muscle could increase production of this powerful inotropic peptide as a compensatory mechanism to augment inotropic capacity and maintain cardiac output[19].

Adropin may be a novel and effective serum marker for the evaluation of endothelial function[20]. It increases nitric oxide release and activates eNOS, so it directly affects the endothelium and has a protective role for endothelium via up regulating eNOS[21].

Our study found a decrease in the activity of adropin could be due to endothelial dysfunction plays a crucial role in the maintenance of vascular homeostasis, and endothelial dysfunction contributes to the development and progression of cardiovascular diseases[22].Yu *et al*[23] have reported reduced adropin levels in cases of acute myocardial infarction and examined the role of adropin in MI.

Cardiac muscle produces more irisin than skeletal muscle. Irisin is mainly produced within heart and skeletal muscle[24],it is facilitate the conversion of brown adipose tissue that dissipates energy in the form of heat into white adipose tissue that serves as an energy depot[25].

In our study, however, we found statistically significant difference in irisin levels in the CHF patients and the control group (< 0.05).The exact mechanism by which irisin is involved in CHF is unclear. The elevated circulating irisin levels in patients with risk for cardiovascular diseases or MACE have been considered as a state of irisin-resistance. In addition, as heart might be a major producer of irisin, the uncoupling properties of irisin may result in more ATP loss and lead to poor prognosis of cardiovascular diseases[26]. Aronis *et al*[27].reported that increased irisin levels predict the development of major cardiovascular events, especially unstable angina, in patients with CAD after percutaneous intervention (PCI). Hanatani *et al*[28] also reported that irisin is a novel biomarker providing prognostic information in patients with heart failure with reduced ejection fraction.

Both basic science and clinical studies support the inverse relationship between HDL-C levels and atherosclerosis. HDL enhances the reverse cholesterol transport and has anti-oxidative, anti-inflammatory, antithrombotic, and vasoprotective effects[29].

This study demonstrated a significant increase in cholesterol, TG, LDL-C, with the exception of significant decrease in the HDL in CHD group. Elevated total cholesterol is related to increased blood pressure, increased arterial stiffness and decreased vascular compliance, and an increased left ventricular mass and wall thickness. Decreased HDL-C concentrations are associated with increased left ventricular mass, decreased diastolic function and a lower ejection fraction in people with both normal and stenosed coronary arteries[30,31].

CONCLUSION

These results revealed that adropin might represent as a potential biomarker for diagnosis of and severity CHF.

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