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Are Ghrelin Levels Directly Related with Ishemic Heart Disease ?

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ABSTRACT

The aim of the study was to determine whether plasma ghrelin levels influence ischemic heart disease.
Methods. We conducted an analytical transversal study of 88 patients submitted in the Cardiology Department of the Rehabilitation Hospital, Cluj-Napoca, Romania. The patients were divided in two groups: 37 patients (42.04%) with ischemic heart disease (group A) and 51 patients (57.95%) without this disease (group B). For the statistical analysis we used the SPSS 16.0, p value and Pearson correlation index.
Results. Plasma ghrelin levels were significantly lower in group A (38.65± 25.96 pg/ml) than in group B (40.45±13.21 pg/ml, p=0.04) and in patients diagnosed with chronic heart failure (31.44±13.2 pg/ml). In group B we found a negative correlation between circulating ghrelin and waist circumference (p=0.031, r=-0.303) and BMI (p=0.046, r=-0.281) too.
Conclusion. Our study showed a strong correlation between ischemic heart disease and plasma ghrelin levels, especially in patients diagnosed with chronic heart failure.

Keywords : ghrelin, ischemic heart disease, heart failure

Introduction

Ghrelin is a bioactive peptide secreted by the oxyntic mucosa of the stomach with important growth hormone (GH) releasing effects [1, 2]. Recent studies have shown that ghrelin is involved in the modulation of cardiovascular functions as well as in the fat and glucose metabolism [3]. It was thus proved that higher ghrelin levels may determine a decrease in blood pressure, atherosclerosis, regression as well as cardioprotective effects chiefly in ischemia, necrosis and cardiac remodeling [4].

Under these circumstances, the aim of our study was to determine whether plasma ghrelin levels influence the most important cardiovascular risk factors and cardiovascular pathology.

Materials and methods

We conducted a cross-sectional study of 88 consecutive patients admitted in the Cardiology Department of the Rehabilitation Hospital, Cluj-Napoca, Romania. Inclusion criteria were the presence of cardiovascular risk factors and/or cardiovascular pathology. We have excluded patients without these clinical conditions and those who did not express their consent. The selected patients were informed about the study protocol and gave their signed informed consent. The institutional ethics committee of "Iuliu Hatieganu" University of Medicine and Pharmacy approved the study protocol. The age of the subjects ranged between 38 and 89 years with a mean of 61.7 ± 10.33 years, and 26.14% of them were men. The subjects were divided into two groups: 37 patients (42.04%), who were diagnosed with ischemic heart disease (group A), and 51 patients (57.95%) without coronary heart disease (group B). All patients were assessed for the presence of cardiovascular risk factors (obesity, arterial hypertension (HTN), fasting plasma glucose levels, metabolic syndrome, smoking and plasma levels of LDL, cholesterol and triglycerides). Blood glucose was measured by the glucose oxidase method, and serum lipids, total cholesterol, triglycerides, high density cholesterol weremeasured using commercially available kits. Low density cholesterol was estimated using the Friedewald's formula. Blood pressure was measured according to standard protocol as the mean of two readings after the participant was at rest for 5 min in a sitting position. Metabolic syndrome was defined using the International Diabetes Federation (IDF) criteria [5]. Plasma ghrelin levels were determined with a Commercial ELISA kit and the results were measured in pg/ml. Statistical analysis was carried out by using the SPSS 16.0 software for Windows (Demo Version), p value (Student test) and Pearson correlation index.

Results

The incidence of cardiovascular risk factors in both groups (A and B) is summarized in Table 1.

Table 1 about here.

Table1. Age-Adjusted Mean _ SD or Prevalence of Risk Factors

Variables	Group A (37 patients)	Group B (51 patients)	P value
Age (years)	64.86±10.69	59.41±9.52	0.014
Females (%)	70.27% (26 patients)	76.47% (39 patients)	0.871
Smokers (%)	10.81% (4 patients)	21.56% (11 patients)	0.3
BMI (kg/m2)	29.11±4.53	29±4.26	0.908

Waist circumferences (cm)	99.65±12.47	97.80±9.37	0.430
Glycemia (mg/dl)	109.7±45.01	93.39±23	0.029
Total Co (mg/dl)	211.03±58.73	214.37±46.99	0.767
LDL-Co (mg/dl)	137.46± 43.07	136.73±39.37	0.934
HDL-Co (mg/dl)	40.46±9.46	44.53±8.4	0.036
TG (mg/dl)	165.62±83.4	145.76±56.49	0.186
Hypertension (%)	94.59% (35 patients)	68.62% (35 patients)	0.003
Diabetes (%)	43.24% (16 patients)	15.68% (8 patients)	0.004
Metabolic syndrome (%)	83.78% (31 patients)	66.66% (34 patients)	0.07
Ghrelin (pg/ml)	38.65±25.96	40.45± 13.21	0.03

Plasma ghrelin levels were significantly lower in group A (38.65± 25.96 pg/ml) than in group B (40.45±13.21 pg/ml, p=0.03). Circulating ghrelin was significantly lower in patients diagnosed with chronic heart failure (31.44±13.2 pg/ml) than in those without chronic heart failure (42.34±20.3; p=0.03), especially in men (25.08±6.89 vs. 38.59±10.28; p=0.01) vs women (36.63±14.39 vs. 43.55±22.54; p=0.09). After the cardiovascular risk factors (hypertension, total cholesterol, LDL-cholesterol, triglycerides, HDL-cholesterol, BMI, glycemia, metabolic syndrome) were evaluated for all 88 patients, we found no statistically significant difference between ghrelin levels in the patients with and those without cardiovascular risk factors (p>0.05). In group B, ghrelin was negatively correlated with waist circumference (p=0.031, r= -0.303) and BMI (p=0.046, r=-0.281). Ghrelin levels were positively correlated with fasting plasma glucose - figure 1.

Figure 1 about here.

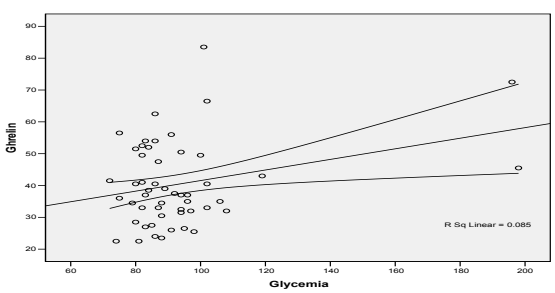

Fig. 1 The corellation between ghrelin and glycemia in ischemic heart disease patients.

DISCUSSION

Studies suggest that ghrelin protects the cardiovascular system against ischemia, improves the cardiac ejection fraction, decreases blood pressure and peripheral resistance, induces vasodilatation by increasing the oxid nitric production and decreasing the endhotelin-1 secretion, inhibits apoptosis and increases exercise capacity [6].

Our study showed that circulating ghrelin was decreased in patients with ischemic heart disease.

Ghrelin participates directly in the atherosclerotic development by having anti-inflammatory and anti-oxidative effects, improving endothelial dysfunction and the cardiac input [6].

Our study showed that circulating ghrelin was significantly lower in patients with ischemic heart disease in which the disease had progressed to the chronic heart failure stage. The fact that ghrelin levels are much lower in men with heart failure than in women and in men without heart failure can be explained by the prevalence of more severe forms of heart failure in men (heart failure with reduced ejection fraction).

Many researches have suggested that ghrelin has multi-protective effects on heart failure, such as: improvement of cardiac function [2,4,7,8,9] and ventricular remodeling [2,4], prevention or postponement of cardiac cachexia [2,4,10], inhibition of myocardial apoptosis [2,4,9], anti-neuroendocrine effects (suppression of the sympathetic system and decrease of norepinephrine concentration [2,4,10,11], anti-inflammatory and anti-oxidative actions [1,2,4,12].

As ghrelin exhibits anti-cachectic, anabolic and anti-inflammatory effects via both growth-hormone -dependent and -independent mechanisms, its administration may lead to improving the quality of life in chronic obstructive pulmonary disease, cancer, end-stage renal disease and severe stage of heart failure [13, 14]. Given these findings, ghrelin administration may improve the heart failure prognosis by increasing the cardiac output [17], improving the cachexia observed in end-stage patients and the ventricular remodeling [13, 14, 15, 16, 17].

Low plasma ghrelin levels were associated with obesity [18]; the assertion was in agreement with our study that showed a negative correlation of ghrelin with waist circumference and BMI in subjects without ischemic heart disease. Latest studies suggested that des-acyl ghrelin secretion in obese patients might be inhibited by hyperinsulinemia and hyperleptinemia [19].

In animal subjects, low circulating ghrelin was found to be in association with different insulin-resistant states, including type 2 diabetes [20]. Early studies on rats revealed reduced ghrelin plasma levels in the development of peripheral insulin resistance [20]. Our data recorded a positive correlation of ghrelin levels with fasting plasma glucose in patients with ischemic heart disease.

Although there is data substantiating ghrelin involvement in hypertension regulation, the precise mechanism is still unknown. In our study, ghrelin levels were not correlated with hypertension and neither with plasma lipid fractions. Undoubtedly, our study had certain limitations such as: the small size of the patient cohort and its heterogeneity.

Conclusion.

Our study showed a strong correlation between ischemic heart disease and plasma ghrelin levels, especially in patients diagnosed with chronic heart failure.

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