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Diabetes phenomena can not affect serum ghrelin in obese individuals

Torabi Mohsen*, Baghery Hadi, Falah Ahmad

Department of Physical Education and Sport Science, Shahre Rey Branch, Islamic Azad University, Tehran, Iran

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Abstract

Ghrelin is an acylated 28-amino-acid peptide plays role in glucose homeostasis, although the molecular basis of this relationship is not fully known yet. This study aimed to compare serum ghrelin between diabetes and no diabetes population and to determine relation between ghrelin with glucose in diabetes patient. For these purpose, fasting serum ghrelin, insulin, glucose and insulin sensitivity were measured in twelve adult obese men with or without type II diabetes. Independent student t test was used for between groups comparison. Pearson correlations were used to establish the relationship between serum ghrelin with glucose and insulin sensitivity in diabetic patients. A p-value less than 0.05 were considered statistically significant. No significant differences were observed in anthropometrical markers between two groups ($p \geq 0.05$). Serum ghrelin was not difference between two groups ($p = 0.385$). Fasting glucose was significant higher ($p < 0.001$) and insulin sensitivity was significant lower ($p < 0.001$) in diabetes subjects. Positive correlation was observed between serum ghrelin and glucose concentration in studied patients ($p = 0.006$, $r = 0.74$). Based on these data, we conclude that diabetes phenomena can not affect serum ghrelin in obese individuals.

* **Corresponding Author:** Torabi Mohsen ✉ mt.1358@yahoo.com

Introduction

In 1980 World Health Organization reported obesity as the most important risk factor for diabetes (Fauntuzi *et al.*, 1999). Type-2 diabetes is the most common type of diabetes that occurs in more than 90% of diabetic patients (Boyle *et al.*, 2001). The prevalence of obesity and its related diseases has been the subject of numerous studies on factors affecting energy balance and weight control. Recent research evidence supports the existence of some peptide hormones of different physiological and pathophysiological characteristics that affect appetite and satiety in animals and humans (Kevin *et al.*, 2006). Among them is ghrelin, a 28-aminoacid hormone secreted by the stomach and pancreas that is effective in hunger and the long term regulation of and body weight. Plasma ghrelin levels increase shortly before meals and decrease immediately after satiety (Date *et al.*, 2000). Research studies have state that long-term use of ghrelin increases body weight and adiposity in rats (Guo *et al.*, 2007). Also changes in ghrelin levels can affect the degree of insulin resistance (Vincent *et al.*, 2008).

Measuring ghrelin levels in patients with Type 2 diabetes seems to provide important information about the role of this peptide hormone in the pathophysiology of the disease. In this context, recent studies suggest that ghrelin levels increase in diabetic patients (Vancea *et al.*, 2009). Studies suggest that obesity affects the regulation of ghrelin secretion in diabetic patients. In contrast to these findings, a recent study showed that long-term increase in blood sugar, or hyperglycemia would reduce ghrelin secretion (Ariga *et al.*, 2008).

Some literature also suggests that changes in ghrelin levels are effective in quantifying insulin resistance (Vincent *et al.*, 2008). Decreased insulin resistance, subsequent to decrease in ghrelin levels in diabetic patients, has been observed in some studies (Katsuki *et al.*, 2004). However, in another study no reciprocal relationship was observed between serum ghrelin levels and energy metabolism regulation in diabetic patients (Reinehr *et al.*, 2005). Since most patients with type-2 diabetes are categorized as obese, it is not clear whether the increase in ghrelin levels in these patients compared to non-diabetic individuals is due to the presence of obesity in these people or that this disease directly affects the release of ghrelin or blood ghrelin levels. Hence, this study aims to compare blood ghrelin levels in diabetic and non-diabetic obese subjects.

Research methods and procedures

subjects

Twelve non-trained adult obese men with or without type 2 diabetes matched for age (40 ± 4.3) and weight (95.6 ± 6.4) were participated in the study. All subjects had a body mass index (BMI) greater than 30 kg/m^2. Participants were included if they had not been involved in regular physical activity/diet in the previous 6 months. Participants were non-smokers and non-alcoholics. The exclusion criteria were infections, renal diseases, hepatic disorders, use of alcohol, having history of known hyperlipidemia, coronary artery disease peripheral artery disease. Those that were unable to avoid taking drugs for 12 hours before blood sampling were also barred from participating in the study. Each participant received written and verbal explanations about the nature of the study before signing an informed consent form.

Anthropometry

After introduction and awareness of the subjects of the objectives of the study and once they had completed consent forms, the process of test implementation began. Height was measured without shoes on standing while the shoulders were tangent with the wall. Body weight was measured in duplicate in the morning following a 12-h fast. Obesity was measured by body mass index (BMI). Body mass index was calculated as body mass (in kilograms) divided by height squared (in square meters). Abdominal circumference and hip circumference were measured in the most condensed part using a non-elastic cloth meter.

Laboratory measurements

All blood samples were taken following an overnight

12-hour fast. Fasting serum ghrelin, insulin and insulin were measured and insulin sensitivity was determined using the homeostasis model assessment insulin sensitivity index (HOMA-IS) (Katz *et al.*, 2000). Insulin was determined by ELISA method (Demeditec, Germany). Glucose was determined by the oxidase method (Pars Azmoon kit, Tehran). Samples were centrifuged immediately for 10 minutes with 3500 rpm in +4°C in order to measure serum ghrelin levels. The intra-assay and inter-assay coefficient of variation of ghrelin (Biovendor, Austria) were 8.10% and 8.3% respectively.

Statistical methods

Statistic analysis was done with SPSS 16.0 for Windows. Normal distribution of data was analyzed by the Kolmogorov-Smirnov normality test. Independent student t test was used for between groups comparison. Pearson correlations were used to establish the relationship between serum ghrelin with glucose and insulin sensitivity in diabetic patients. A p-value less than 0.05 were considered statistically significant.

Results

Table 1 presents the circulating ghrelin and anthropometrical characteristics in diabetes and non-diabetes group. Results are reported as group mean, standard deviation and standard error mean. There were no differences in all anthropometrical markers between two groups ($p \geq 0.05$). We also did not observe significant change in serum ghrelin between two groups ($p = 0.385$, Fig 1). Fasting glucose was significant higher ($p < 0.001$) and insulin sensitivity was significant lower ($p < 0.001$) in diabetes subjects than non-diabetes individuals. A strong positive correlation was observed between serum ghrelin and glucose concentration in studied patients ($p = 0.006$, $r = 0.74$, Fig 2).

Table 1. Mean, standard deviation and standard error of ghrelin and anthropometrical markers in diabetes and non-diabetes subjects.

	Diabetic group=1, non-diabetic group=2	Mean	Std. Deviation	Std. Error Mean
Weight (kg)	1	95.00	5.187	1.497
	2	96.50	6.908	1.994
Abdominal (cm)	1	107.00	5.673	1.638
	2	106.67	5.466	1.578
Hip (cm)	1	104.08	2.503	.723
	2	104.83	5.114	1.476
BMI (kg/m2)	1	31.75	2.006	.579
	2	31.17	1.899	.548
Body Fat (%)	1	30.17	2.079	.600
	2	31.92	4.078	1.177
Glucose (mg/dl)	1	224.83	66.956	19.328
	2	101.33	9.277	2.678
Insulin sesitivity	1	.5033	.03525	.01018
	2	.6133	.07088	.02046
Ghrelin (pg/ml)	1	60.08	10.466	3.021
	2	56.42	9.774	2.822

Discussion

The main finding of this study is the absence of a significant difference in ghrelin levels between diabetic and non-diabetic subjects. In fact, since in this study, both diabetic and non-diabetic groups were categorized as obese, the findings suggest that the presence of diabetes in these patients does not affect the blood ghrelin secretion or levels but that compared with healthy individuals, increased levels of ghrelin in these patients are a function of overweight and obesity.

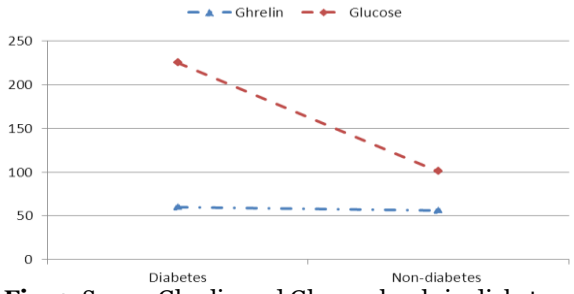

Fig. 1. Serum Ghrelin and Glucose levels in diabetes and non- diabetes subjects.

Ghrelin, leptin and adiponectin are three hormones

that are alternately related to metabolism, obesity and appetite (Tigno *et al.*, 2003).Ghrelin peptide hormone is a 28-aminoacid neuropeptide mainly secreted by the stomach (Tong *et al.*, 2010) stimulating growth hormone secretagogue receptors (Yada *et al.*, 2008). This hormone is one of the circulating peptides that stimulates appetite and regulates energy balance which is also identified as one of the candidates for obesity and type-2 diabetes (Pulkkinen *et al.*, 2010). Type-2 diabetes is the most common endocrine disorder in the world. Increased blood glucose and carbohydrate metabolism disorder are the main features of this disease (Kahn, 2000). Extensive studies point out that ghrelin plays a role in the development of metabolic syndrome and Type-2 diabetes. (Ukkola *et al.*, 2009). There are conflicting findings about the extent of blood ghrelin levels in healthy subjects or patients and normal-weight or obese individuals (Ariyasu *et al.*, 2002; Nakazato *et al.*, 2001; Hansen *et al.*, 2000).

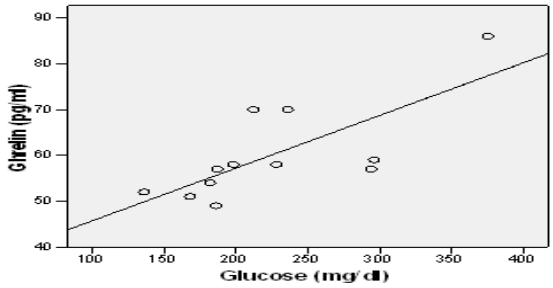

Fig. 2. Correlation between serum ghrelin and glucose concentration in diabetes subjects.

The present study showed that the serum ghrelin levels in diabetic patients are higher than their non-diabetic counterparts, but the difference is statistically insignificant. However, some studies have revealed that blood ghrelin levels increase in diabetic patients (Lazar, 2006). The findings of a recent study showed that serum ghrelin levels in diabetic patients are significantly higher than in healthy individuals (Ariga *et al.*, 2008). On the other hand, some studies on diabetics also suggest that ghrelin levels are similar in lean and obese Type-2 diabetic patients (Barazzoni *et al.*, 2007). Confirming this study, the findings of another study suggest similar levels of ghrelin levels in obese diabetic and non-diabetic individuals (Erdmann *et al.*, 2005).

Based on what was observed in the present study and according to the findings of other studies that report no significant difference in serum ghrelin levels in obese diabetics and non-diabetics it can be concluded that it is the phenomenon of obesity in these patients that affects blood ghrelin levels and the presence of diabetes in these patients is a secondary factor terms of the effect on ghrelin. However, since many previous studies emphasize the mutual association of ghrelin with insulin resistance or glucose levels in these patients, it seems that apart from effecting directly, blood ghrelin levels in these patients indirectly affect blood glucose and insulin secretion by affecting other hormonal mediators.

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