Effect Of Ghrelin, Obestatin Levels And The Ghrelin/Obestatin Ratio In Polycysticovary Syndrome

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Abstract:

Background: Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders among females. Central obesity has a close relationship with an altered secretion of some adipocytokines. Aim Of Study: investigate the relationship of Ghrelin and Obestatin with their body mass index and fasting insulin values in overweight females with PCOS.

Subjects And Methods: twenty four overweight females with PCOS age ranged between (20-45) years with (25) normal weight healthy female with age matched have been included in this study as a control group. BMI and WC were done for patients and controls as anthropometrical tests, while FSG was measured using spectrophotometric technique, but each of Ghrelin, obestatin and fasting insulin were measured using ELISA test.

Results: This study showed a significant decline in Ghrelin, Obestatin in patients with PCOS compared with controls, while BMI, WC, fasting Insulin, Ghrelin/Obestatin ratio were significantly higher in patients than that in control group.

Conclusion: Over weight patients with PCOS were at a high risk of the metabolic syndrome and accordingly Ghrelin and Obestatin can be used as a good predictor for PCOS overweight females.

I. Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders among females. PCOS produces symptoms in approximately 5% to 10% of women of reproductive age (approximately 12 to 45 years old). It is thought to be one of the leading causes of female subfertility, and the most frequent endocrine problem in women of reproductive age. Finding that the ovaries appear polycystic on ultrasound is common, but it is not an absolute requirement in all definitions of the disorder.

The most common immediate symptoms are anovulation, excess androgenic hormones, and insulin resistance. Anovulation results in irregular menstruation, amenorrhea, and ovulation-related infertility. Hormone imbalance generally causes acne and hirsutism. Insulin resistance in PCOS is associated with obesity, Type 2 diabetes, and high cholesterol levels. The symptoms and severity of the syndrome vary greatly among affected women.

Adiposity is observed in PCOS patients and plays an important role in their metabolic phenotype through the production of various adipocyte-derived cytokines and proteins known as adipokines. Central obesity has a close relationship with the altered secretion of some adipocytokines. Production of adipocytokines affects insulin sensitivity and is a predictor of metabolic syndrome.

Ghrelin is a peptide hormone produced by ghrelin cells in the gastrointestinal tract which acts as an aneuropeptide in the central nervous system. Beyond regulating hunger, ghrelin also plays a significant role in regulation and distribution the rate of use of energy by complex mechanisms for example energy homeostasis.

When the stomach is empty ghrelin is secreted, and when it is stretched secretion will stop. It acts on hypothalamic brain cells both to increase hunger, and to increase gastric acid secretion and gastrointestinal motility to prepare the body for food intake. The receptor for ghrelin is found on the same cells in the brain as the receptor for leptin, the satiety hormone that has opposite effects from ghrelin.
Obestatin: Obestatin is a 23-amino acid amidated peptide encoded by the ghrelin gene that is also released from the stomach. It has been shown to interact with the orphan receptor G-protein-coupled receptor 39, and oppose the stimulatory effect of ghrelin on food intake and gastrointestinal function. Studies in humans have shown that blood obestatin levels are significantly lower in obese subjects and correlate negatively with body mass index. (12)

In addition, obestatin has been shown to be positively correlated with ghrelin (13, 14); this suggests that levels of both obestatin and ghrelin may be altered in obesity and insulin resistance.

II. Aim of this study

The aim of the present study was to measure fasting plasma ghrelin and obestatin concentrations in obese PCOS females and control subjects and to investigate their relationship with their body mass index and fasting insulin values.

III. Subjects And Methods:

This study had included twenty four (24) overweight females with PCOS age ranged between (20-45) years with twenty five (25) normal weight healthy females with age matched had been included in this study as a control group who were attending the out patients consultation clinic of Gynecology in Baghdad Teaching Hospital / Medical City, in a period from October 2014- March 2015.  

- All patients and controls underwent complete general questionnaire.  
- Patients with suspected thyroid function disease were excluded from the study.  
- Body mass index (BMI) and waist circumference (WC) were done for patients and controls as anthropometrical tests, while fasting serum glucose (FSG) measured using spectrophotometric technique.  
- Each serum sample was analyzed for ghrelin hormone, obestatin hormone and fasting insulin using enzyme linked immune sorbent assay (ELISA).

IV. Statistical Analyses

Descriptive statistics for all data of each set were expressed as mean ± SD and the percent of abnormal value in any test was calculated as above or below the mean ± SD of the normal value for the matched control group, were compared using independent sample (t) test p<0.05 were considered statistically significant. (15)

The overall predictive values for the results in the studied groups were performed according to program of office xp.

V. Results

Table (1): Mean ± SD of all studied parameters in patients and control group.

<table>
<thead>
<tr>
<th>Studied parameters</th>
<th>Patients (no=24)</th>
<th>Control (no=25)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>128.9±32.5</td>
<td>57.67±7.05</td>
<td>0.001(S)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>9.09±29.48</td>
<td>2.49±21.71</td>
<td>0.001(S)</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>103.90±9.87</td>
<td>79.56±5.20</td>
<td>0.002(S)</td>
</tr>
<tr>
<td>F.S.G. (mg/dl)</td>
<td>108.2±26.3</td>
<td>88.01±8.62</td>
<td>0.08(NS)</td>
</tr>
<tr>
<td>Ghrelin (pg/ml)</td>
<td>42.5±468</td>
<td>36.2±570.1</td>
<td>0.003(S)</td>
</tr>
<tr>
<td>Obestatin (pg/ml)</td>
<td>9.35±91.66</td>
<td>210.7±56.0</td>
<td>0.001(S)</td>
</tr>
<tr>
<td>Ghrelin/Obestatin ratio</td>
<td>0.573±5.148</td>
<td>0.816±2.900</td>
<td>0.001(S)</td>
</tr>
<tr>
<td>Insulin (MU/ml)</td>
<td>28.36±2.27</td>
<td>6.324±0.938</td>
<td>0.003(S)</td>
</tr>
</tbody>
</table>

Note: S: significant. NS: non-significant.

Results obtained in the present study showed that the serum levels of Ghrelin, Obestatin were significantly lower in patients with polycystic ovary than in healthy controls. While body weight, BMI, WC, fasting Insulin and Ghrelin \ Obestatin ratio were significantly higher in patients with polycystic ovary than in healthy controls, as they shown in table (1).  

Serum Ghrelin level and serum Obestatin were negatively correlated with BMI in females with PCOS as they shown in figure(1&2).
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**Fig (1): Correlation between ghrelin and BMI in PCOS.**

**Fig (2): Correlation between Obestatin and BMI in PCOS.**

In addition serum Ghrelin and Obestatin showed an inverse correlation with fasting serum Insulin in patients with PCOS, as they shown in figure (3&4).

**Fig (3): Correlation between serum Ghrelin and fasting Insulin values in PCOS.**
VI. Discussion

Obesity has become a major public health problem throughout the world and at least one-third of Arabs are obese, and this figure is rising steadily despite increased interest in fitness. Excess fat accumulation promotes the development of insulin resistance, glucose intolerance and type 2 diabetes mellitus. (16) A result obtained in the present study was found a highly significant decrease in Ghrelin level in PCOS women than the control group with negative correlation between Ghrelin and BMI. Although 21% of the obese subjects were non-insulin resistant, one cannot exclude the theory that obesity is associated with hyperinsulinemia and insulin resistance.

Supporting the hypothesis of a negative association between Ghrelin and risk factors of the metabolic syndrome, it’s found that there is a significantly inverse correlation between Ghrelin and Fasting Insulin in PCOS patients.

Mitkov et al. (17), Glintborg et al. (18), and Kamal et al. (19) published that serum ghrelin concentration was lower in the PCOS group than in healthy controls, while Wasko et al. (20) have reported elevated levels of plasma ghrelin in PCOS patients compared to healthy controls. This discrepancy of results may be explained by confounding factors, such as body weight, fat mass, age, hormonal status, and severity of disease. On the other hand, Daghestani et al. showed a significant inverse relationship between ghrelin and BMI in PCOS, it has been shown that ghrelin administration to healthy humans at pharmacological doses reduces insulin secretion, and conversely, insulin administration at high doses is capable of reducing ghrelin secretion. (21) In addition, to a negative correlation between Ghrelin and fasting Insulin hormone in females with PCOS which was conducted by Stepień and his co-workers. (22)

Extensive research on ghrelin has produced evidence that this peptide may have important positive effects on feeding, since exogenous ghrelin administration stimulates appetite and food intake in both rodents and humans. In addition, there is evidence that ghrelin reduces energy expenditure, fat catabolism, and lipolysis, and may promote adipogenesis. These findings contrast with the negative correlation between ghrelin levels and BMI. (23)

This study also found that serum levels of obestatin hormone were significantly lower in females with PCOS than in healthy control group which was agreed with Taskin MI et al. who demonstrated that serum obestatin levels were significantly lower in the obese PCOS group than they were in the non-obese and control groups (p<0.001). (24)

Obestatin levels were significantly reduced suggesting that the secretion of the Ghrelin and Obestatin is regulated in an opposing manner. This finding suggests that obestatin could modulate endogenous Ghrelin actions, and have shown that obestatin may inhibit jejunal activity and may suppress gastric emptying activity. (25)

This study showed an inverse relationship between Obestatin with BMI and with fasting Insulin which was disagreed by Yildiz Get al, who published that there was no correlation between obestatin levels and homeostasis model assessment-insulin resistance or BMI which suggest that distinct mechanisms play roles in the regulation of obestatin levels in case of high BMI. (25)

Changes in circulating ghrelin and obestatin levels may represent adaptive modifications to obesity development, rather than primary defects, and that their alteration in circulatory levels may reflect an imbalance of regulatory factors or mechanisms responsible, in turn, for their metabolic processes and action. (26)
VII. Conclusion

Polycystic ovary syndrome is a complex disorder, in which multiple genetic, metabolic and hormonal controls fail to interact properly and produce the hallmark symptoms of the disease. Obese PCOS patients demonstrated significantly lower Ghrelin and Obestatin levels than that of controls, thus suggesting this subgroup of patients to be at high risk for the metabolic syndrome and accordingly Ghrelin and Obestatin can be used as a good predictor for PCOS overweight females.

References