DISTURBED SERUM ADIPOKINES LEVELS IN NORMAL-WEIGHT, NORMOINSULINEMIC FOUR PHENOTYPES OF POLYCYSTIC OVARY SYNDROME

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Study question:

Altered adipose tissue secretion plays a central role in the metabolic abnormalities observed in PCOS. This study was observed to determine the concentrations of adipokines in different phenotypes of PCOS women, hypothesizing that normal-weight, normoinsulinemic PCOS women, with mildest phenotype also present with changes in adipokine secretion compared to controls.

Summary answer:

There was no difference in adipokines serum levels between different PCOS phenotypes. Lower levels of adiponectin and ghrelin, and higher levels of leptin and resistin were observed in all lean PCOS phenotypes compared to controls suggesting that other intrinsic PCOS factor is in the culprit of these abnormalities.

What is already known:

Women with PCOS have significantly elevated leptin and resistin, and lower adiponectin and ghrelin serum levels compared to healthy women. Whether these abnormalities are secondary to obesity/abdominal fat distribution/hyperandrogenism/hyperinsulinemia or represents the intrinsic PCOS abnormality is yet to be determined. There is a limited data on the adipokine serum levels in four main PCOS phenotypes defined by the Rotterdam Criteria. The majority of them observed positive association of serum adipokine concentrations and PCOS phenotype severity.

Study design, size, duration:

Observational, prospective study of 186 women with PCOS fulfilling Rotterdam criteria and 162 weight and age-matched women was conducted from 2009 to 2013. Five groups were created: phenotype A) O (Oligoovulation) + H (Hyperandrogenism) +P (Polycystic ovaries) (n=102); phenotype B) O+H (Oligoovulation) +H (Hyperandrogenism) +P (Polycystic ovaries) (n=27); phenotype C) H+P (Hyperandrogenism) +P (Hyperandrogenism) +P (Polycystic ovaries) (n=15); phenotype D) H+P (Hyperandrogenism) +P (Polycystic ovaries) (n=42) and E) control group (n=162).

Participants, setting, methods:

Body mass index (BMI), waist/hip ratio (WHR) and hirsuitism were evaluated. Serum concentrations of a leptin, adiponectin, resistin, ghrelin, androgens, sex hormone binding globulin (SHBG), glucose and insulin were measured. Free testosterone and homeostatic model assessment of insulin resistance (HOMA-IR) were calculated. Data are presented as mean±standard deviation. Comparisons of variables across the four groups were performed using analysis of variance (ANOVA). Tukey HSD post hoc test was used to determine significant differences between the groups. Results were analyzed using SPSS 17 for Windows.

Results

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>Control Group E</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>22.3±1.7</td>
<td>19.7±1.6</td>
<td>21.7±1.5</td>
<td>22.2±1.6</td>
<td>21.8±1.8</td>
</tr>
<tr>
<td>WHR</td>
<td>0.77±0.04</td>
<td>0.74±0.05</td>
<td>0.77±0.05</td>
<td>0.74±0.07</td>
<td>0.78±0.03</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>1.8±0.5</td>
<td>1.5±0.7</td>
<td>1.7±0.6</td>
<td>1.4±0.7</td>
<td>1.3±0.5</td>
</tr>
<tr>
<td>Ghrelin (pg/ml)</td>
<td>1167.4±203.5</td>
<td>1399.0±212.5</td>
<td>1254.0±179.6</td>
<td>1193.1±203.6</td>
<td>1690.4±239.0</td>
</tr>
<tr>
<td>Adiponectin (µg/ml)</td>
<td>9.4±1.6</td>
<td>9.8±0.8</td>
<td>10.1±1.3</td>
<td>9.3±1.4</td>
<td>13.5±1.5</td>
</tr>
<tr>
<td>Leptin (ng/ml)</td>
<td>11.2±1.4</td>
<td>10.6±1.5</td>
<td>10.6±1.2</td>
<td>10.9±1.5</td>
<td>8.4±1.9</td>
</tr>
<tr>
<td>Resistin (ng/ml)</td>
<td>11.6±1.8</td>
<td>11.9±2.4</td>
<td>11.6±2.2</td>
<td>12.1±2.8</td>
<td>9.0±1.7</td>
</tr>
</tbody>
</table>

Main results and role of chance:

No association was found between the leptin, resistin, adiponectin and ghrelin serum levels with severity of PCOS, where all PCOS phenotypes compared to control group (all p<0.001). The most prominent finding was the lower adiponectin (p<0.001) and ghrelin (p<0.001) serum levels and higher levels of leptin (p<0.001) and resistin (p<0.001) in lean PCOS patients without hyperandrogenemia and insulin resistance (phenotype D) compared to healthy controls (group E).

Limitations and role of caution:

Small sample size in group B. HOMA-IR was used instead of more reliable but technically difficult hyperinsulinemic-euglycemic clamp technique. With significant variations in PCOS presentation seen in different ethnic populations, generalizing data obtained from any single ethnic group to other population groups should be approached with caution.

Wider implications of the findings:

Although the O+P phenotype itself is under dispute, our data show that the normal-weight, normoinsulinemic PCOS women, who share this phenotype present with alterations in adipokines metabolism, the finding that was previously observed in PCOS women in general. This may suggest that some other intrinsic PCOS factor other than obesity, hyperandrogenism or hyperinsulinemia modulates the adipose tissue dysfunction which merit further research.

References: