Effects of a Eucaloric High Fat Diet on Anterior Pituitary Trophic Hormones, their Targets and Adipocytokines in Normal Weight Women

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Background

• Obesity in women is associated with decreased fertility, adverse pregnancy outcomes and relative hypergonadotropic hypogonadism, which we termed reprometabolic syndrome.¹

• We previously demonstrated that acute hyperlipidemia and hyperinsulinemia recapitulates this phenotype in normal weight women and exerts differential effects on the hypothalamic-pituitary-gonadal, adrenal and thyroid axes.²

• We hypothesized that a eucaloric high-fat diet (HFD) designed to elevate insulin and circulating free fatty acids would exert its primary impact on gonadotropes and have minimal or no impact on other pituitary hormones or adipocytokines (in the absence of weight change).

Methods

• 17 normal weight healthy, cycling women underwent frequent blood sampling (q10 min) in the early follicular phase (days 2-5) for 4 hours starting at 7 am, during a pre-diet cycle.

• They were subsequently provided a prescribed, eucaloric HFD (48% calories from fat) for the duration of their next menstrual cycle and the frequent blood sampling was repeated in their post-HFD cycle.

• Serum TSH, free T4 (fT4), PRL, GH, IGF-1, high molecular weight adiponectin, and leptin were measured by immunoassays.

• Wilcoxon signed-rank tests were used to compare hormone levels before and after the HFD intervention.

Table 1: Demographics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Enrollment</td>
<td>19</td>
</tr>
<tr>
<td>Age (y)</td>
<td>29.37 ± 6.02</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>21.49 ± 1.93</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>60.43 ± 9.48</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>167.41 ± 9.35</td>
</tr>
<tr>
<td>Cycle Length (days)</td>
<td>28.5 ± 2.36</td>
</tr>
<tr>
<td>Hba1c (%)</td>
<td>5.04 ± 0.23</td>
</tr>
<tr>
<td>TSH (mU/L)</td>
<td>1.87 ± 1.11</td>
</tr>
<tr>
<td>Prolactin (ng/ml)</td>
<td>12.69 ± 6.32</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>83.11 ± 39.00</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>162.47 ± 32.26</td>
</tr>
</tbody>
</table>

Table 2: Hormone and Adipocytokine Levels Pre- and Post-HFD

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pre-Diet</th>
<th>Post-HFD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adiponectin (ng/mL)</td>
<td>0.44 (0.34, 0.61)</td>
<td>0.41 (0.34, 0.51)</td>
<td>0.33</td>
</tr>
<tr>
<td>Cortisol (µg/dL)</td>
<td>9.92 (6.96, 10.80)</td>
<td>7.36 (6.29, 8.50)</td>
<td>0.02</td>
</tr>
<tr>
<td>fT4 (ng/dL)</td>
<td>1.34 (1.14, 1.40)</td>
<td>1.34 (1.24, 1.43)</td>
<td>0.55</td>
</tr>
<tr>
<td>GH (ng/mL)</td>
<td>0.72 (0.38, 1.14)</td>
<td>1.37 (0.83, 1.69)</td>
<td>0.22</td>
</tr>
<tr>
<td>IGF-1 (ng/mL)</td>
<td>2078.31 (1654.85, 3559.21)</td>
<td>2221.83 (1864.64, 2693.08)</td>
<td>0.86</td>
</tr>
<tr>
<td>Leptin (ng/mL)</td>
<td>7.73 (5.32, 14.27)</td>
<td>6.33 (4.88, 13.80)</td>
<td>0.13</td>
</tr>
<tr>
<td>Prolactin (ng/mL)</td>
<td>8.13 (6.06, 9.34)</td>
<td>7.25 (6.50, 9.00)</td>
<td>0.71</td>
</tr>
<tr>
<td>TSH (µU/mL)</td>
<td>1.17 (0.87, 1.40)</td>
<td>1.08 (0.91, 1.43)</td>
<td>0.85</td>
</tr>
<tr>
<td>T3 (ng/mL)</td>
<td>1.09 (1.03, 1.17)</td>
<td>1.04 (0.97, 1.11)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Table 2: Hormone and Adipocytokine Levels Pre- and Post-HFD

Figure 1: Study Design, Participant Timetable, and Procedures

DAILY URINE COLLECTION

HIGH FAT DIET

CYCLE 1

CYCLE 1

CYCLE 2

CYCLE 3

CYCLE 4

VISIT #:

SCREEN VISIT 0:

• Overnight fast
• Consult: History and physical
• Height/weight
• Medications
• Safety labs
• DXA body fat measurement
• Diet evaluation
• Food journal
• Pregnancy test
• Home ovulation predictor kit

VISIT 1.1

• Pregnancy test
• Height/weight
• Safety labs
• 6-hour frequent sampling (FSS)
• GnRH test
• Insulin sensitivity test (clamp)

VISIT 1.2

• Pregnancy test
• Height/weight
• Safety labs
• Return collected daily urine
• Review FSS
• Fatty acid (FA) analysis
• Fatty acid (FA) clamp test

VISIT 2-5

• Pregnancy test
• Height/weight
• Safety labs
• Review FSS
• GnRH test
• Insulin sensitivity test (clamp)

VISIT 6-2

• Pregnancy test
• Height/weight
• Safety labs
• Review FSS
• GnRH test
• Insulin sensitivity test (clamp)

VISIT 7

• Pregnancy test
• Height/weight
• Return urine
• Review FSS
• GnRH test
• Insulin sensitivity test (clamp)

Results

• No changes in TSH, fT4, PRL, GH, IGF-1, leptin, or adiponectin were observed in response to the HFD (Table 2).

• There was a small but significant decrease in T3 (p<0.01) and cortisol (p<0.02) after the HFD.

Conclusions

• A one-month eucaloric HFD, designed to reproduce the reprometabolic syndrome of obesity, did not affect non-gonadotropin pituitary hormones or adipocytokines.

• Small but statistically significant effects were observed for cortisol and rT3.

Acknowledgements

• This research was funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD): RO1 HD 087314

• University of Colorado Anschutz Medical Campus Research Track

References


Disclosures

• We have no disclosures to report.