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

Thy B. Nguyen, Katherine Kuhn, Angela Fought, Shannon Pretzel, Rosemary McDonald, Andrew P. Bradford, PhD, and Nannette Santoro, MD

University of Colorado Anschutz Medical Campus, Aurora, CO, US.

University of Colorado Anschutz Medical Campus

Background

- Obesity in women is associated with decreased fertility, adverse pregnancy outcomes and relative hypogonadotropic 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), total T3 (tT3), cortisol, GH, prolactin (PRL), IGF-1, high molecular weight adiponectin, and leptin were measured by immunoassay.
- Wilcoxon signed-rank tests were used to compare hormone levels before and after the HFD intervention.

Table 1: Demographics

Parameter	Mean ± SD
Total Enrollment	19
Age (y)	29.37 ± 6.02
BMI (kg/m^2)	21.49 ± 1.93
Weight (kg)	60.43 ± 9.48
Height (cm)	167.41 ± 9.35
Cycle Length (days)	28.5 ± 2.36
HbA1c (%)	5.04 ± 0.23
TSH (mIU/ml)	1.87 ± 1.11
Prolactin (ng/ml)	12.69 ± 6.32
Triglycerides	83.11 ± 39.00
Cholesterol	162.47 ± 32.26

Abbreviations; Body Mass Index (BMI), Thyroid Stimulating Hormone (TSH)

Figure 1: Study Design, Participant Timetable, and Procedures

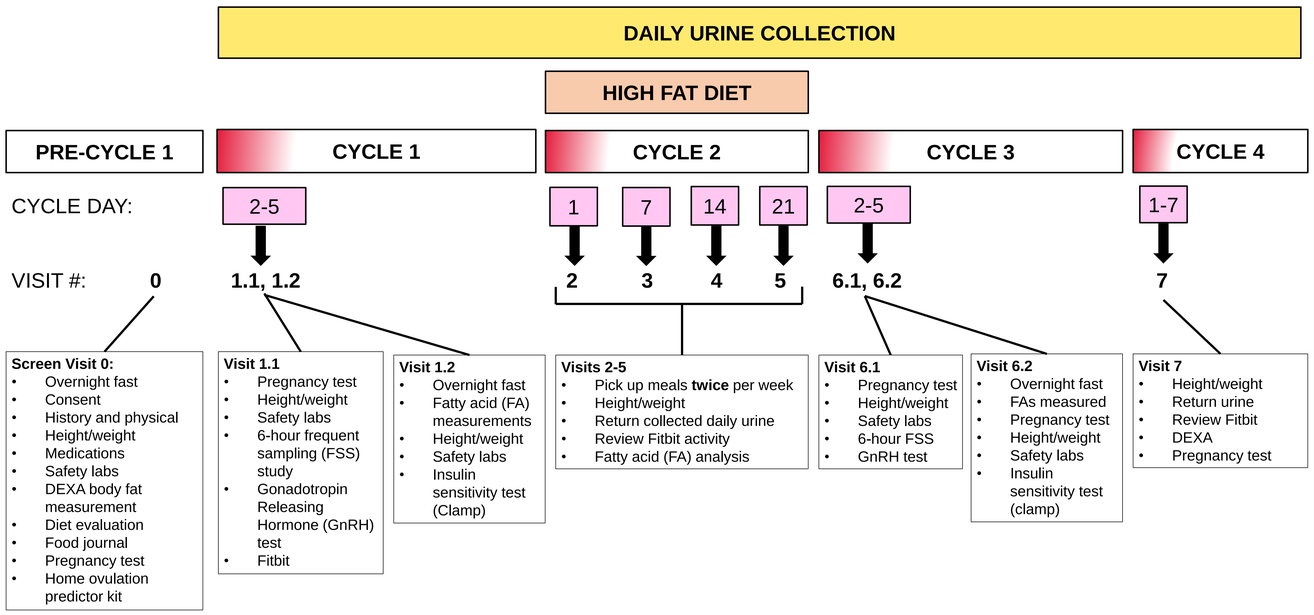

Table 2: Hormone and Adipocytokine Levels Pre- and Post-HFD

	Pre-Diet		Post-HFD		
Characteristic	**N**	**Median (IQR)**	**N**	**Median (IQR)**	**P value**
Adiponectin (ng/mL)	17	0.44 (0.34, 0.61)	17	0.41 (0.34, 0.51)	0.33
Cortisol (µg/dL)	**17**	**9.92 (6.96, 10.80)**	**17**	**7.36 (6.29, 8.50)**	**0.02**
fT4 (ng/dL)	17	1.34 (1.14, 1.40)	17	1.34 (1.24, 1.43)	0.55
GH (ng/mL)	17	0.72 (0.38, 1.14)	17	1.37 (0.83, 1.69)	0.22
IGF-1 (ng/mL)	16	2078.31 (1654.85, 3559.21)	17	2221.83 (1864.64, 2693.08)	0.86
Leptin (ng/mL)	17	7.73 (5.32, 14.27)	17	6.33 (4.88, 13.80)	0.13
Prolactin (ng/mL)	17	8.13 (6.06, 9.34)	17	7.25 (6.50, 9.00)	0.71
TSH (µIU/mL)	17	1.17 (0.87, 1.40)	17	1.08 (0.91, 1.43)	0.85
tT3 (ng/mL)	**17**	**1.09 (1.03, 1.17)**	**17**	**1.04 (0.97, 1.11)**	**0.01**

Abbreviations; Free T4 (fT4), Growth Hormone (GH), Insulin-like Growth Factor 1 (IGF-1), Thyroid Stimulating Hormone (TSH), Total T3 (tT3). IQR: interquartile range (25th, 75th percentiles)

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 tT3 (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

1. Chosich J, Bradford AP, Allshouse AA, Reusch JE, Santoro N, Schauer IE. Acute recapitulation of the hyperinsulinemia and hyperlipidemia characteristic of metabolic syndrome suppresses gonadotropins. Obesity (Silver Spring) 2017; 25:553-560.
2. Santoro N, Schauer I, Kuhn K, Fought A, Babcock-Gilbert S, Bradford AP. Gonadotropin response to insulin and lipid infusion reproduces the reprometabolic syndrome of obesity in lean eumenorrheic women: A randomized crossover trial. Fertility and Sterility 2021; 116(2):566-574.

Disclosures

- We have no disclosures to report.