



STUDYING INSULIN LOWERING DIETS FOR TREATMENT OF POLYCYSTIC OVARIAN SYNDROME



Lynda Frassetto MD, Umesh Masharani MD, Nik Lenhart, Ashley Mason PhD, Heather Huddleston MD;
University of California, San Francisco CA, USA

Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine disorder [1-3] with a complex phenotype and poorly understood etiology. Criteria for diagnosing PCOS is not uniform. The Rotterdam criteria requires two of the three signs:

- oligo/anovulation
- Hyperandrogenism; clinical (hirsutism or male pattern alopecia) or biochemical (raised free androgen index or free testosterone)
- polycystic ovaries on ultrasound while the NIH criteria requires all three.

Elevated insulin levels due to the insulin resistant state contribute to the disruption of ovarian function. Interventions that lower circulating insulin levels such as physical activity, weight loss, and drugs such as metformin and thiazolidinediones have been shown to improve ovulation rates and fertility [4-6].

Medication interventions are not universally effective, and are accompanied by the potential for significant negative side effects, such as vomiting, diarrhea, weight gain, and fracture risk [7,8]. Weight loss is difficult to sustain.

Methods and Materials

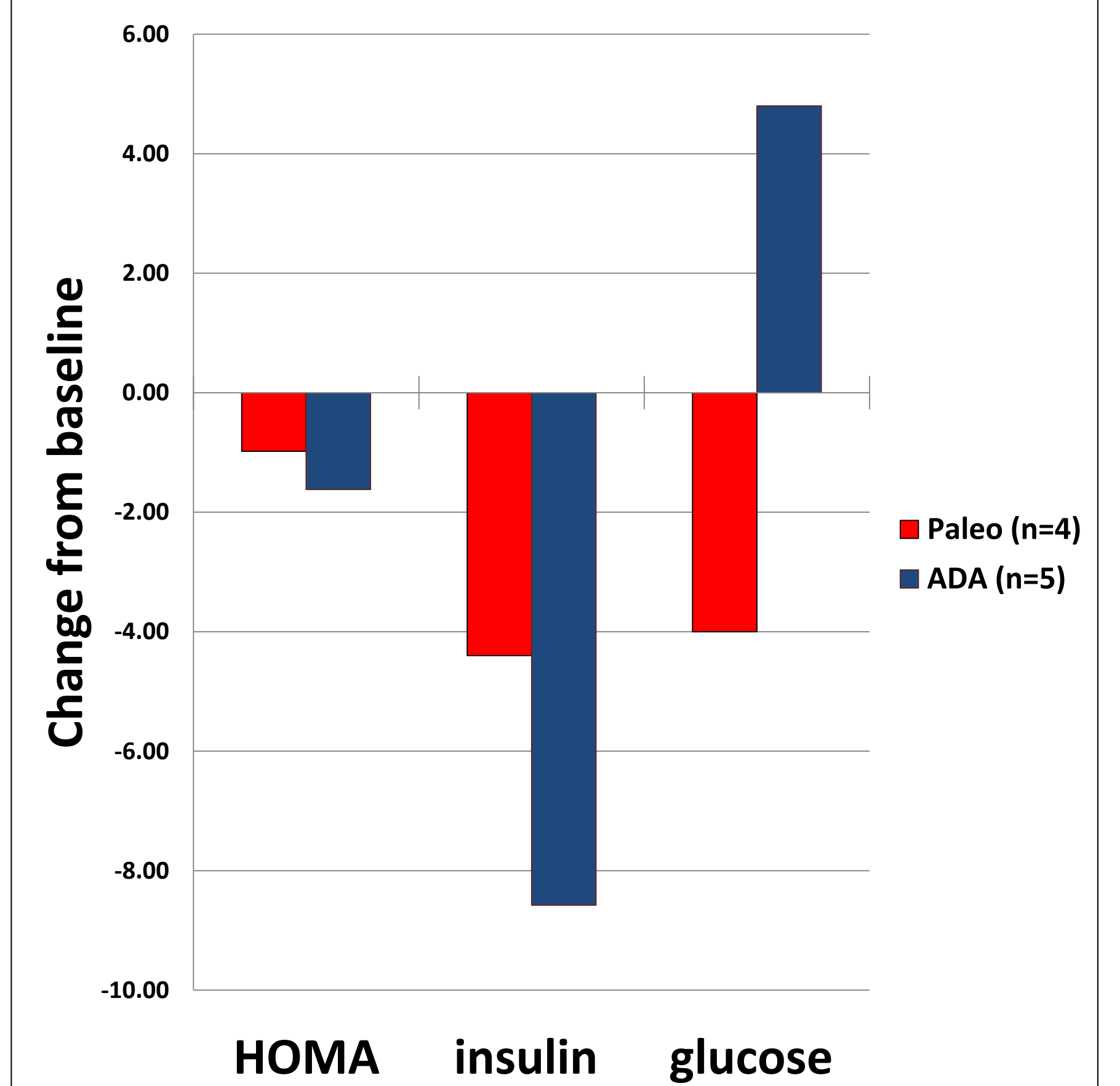
This is a prospective, open labeled, randomized diet intervention study done on adult participants with biochemical and physical signs of PCOS. All subjects had ≤ 8 menstrual cycles/year. After a run in period of 2 weeks on an ADA diet, participants are randomized to one of two arms:

- 1) an 8-month outpatient Paleo diet; or
- 2) a 4-month ADA diet followed by a Paleo diet for 4 months.

We will evaluate subjects for:

- 1) changes in reproductive function (menstrual cyclicity, ovarian volume, serum free and total testosterone) at 4 and 8 months;
- 2) changes in metabolic parameters (insulin sensitivity by HOMA-IR, lipids) pre- and post-intervention.
- 3) changes in psychological states (e.g., depression), psychological stress, and eating behavior, using validated questionnaires (CESD, Readiness Ruler, Three Factor Eating Questionnaire; Pittsburg-Sleep Quality Index; Perceived Stress Scale; Yale Food Addiction Scale; Binge Eating Scale; Reward-Based Eating Drive)

Comparison of Paleo & ADA diets after 8 weeks



Discussion

- 1) Enrollment for the study is slow, but ongoing.
- 2) We are also focusing on keeping the subjects we recruited, using personalized diet coaching to help the subjects adjust to the dietary changes.

Background

We have evidence that altering dietary composition can improve insulin resistance. Patients with type 2 diabetes and normoglycemic insulin resistant subjects consuming a *weight maintaining* diet consisting of lean meats, fruits and vegetables (Paleo-diet) had greater improvements in insulin sensitivity [9,10] blood pressure, and lipid levels when compared to subjects who followed a standard American Diabetes Association (ADA) diet.

The Paleo and ADA diets are similar in macronutrient composition but differ in that the Paleo-diet is lower in sodium content (1500 mg vs. 4000 mg) and higher in unsaturated fats, potassium, alkali salts, and antioxidants. The Paleo-diet also appears to be more satiating and is rich in micronutrients reported to have a positive effect on mood.

We hypothesized that an ad lib Paleo-diet would have greater benefit on reproductive function, metabolic parameters, satiety and mood than an ADA recommended diet.

Results

Screening: Over the last 28 months, we screened 196 women at the UCSF PCOS specialty clinic. Only 9% of the women seen qualified for the study. Thirty percent of the women did not have biochemical parameters for PCOS, 13% had normal menstrual cycles and 15% didn't have PCOS!

Recruitment: Nine women have been enrolled to date; 4 subjects have finished, 3 dropped out, and 2 are presently in the study.

At baseline, the average fasting glucose was normal, 86 ± 9 mg/dL, but fasting insulin and HOMA were elevated [22 ± 16 (normal < 19 μ IU); 4.4 ± 2.9 (normal < 3)], and 2 hour oral glucose tolerance tests were normal [11]. The women also had elevated total and free testosterone levels [100 ± 37 ng/mL (normal 2-45); 14 ± 6 pg/mL (normal 0.2-5.0)]. All the subjects had normal blood pressures, renal function and normal lipid profiles.

At week 8 on both diets, insulin decreased -7.4 ± 4.8 ($p=0.006$) and HOMA decreased -1.4 ± 1.1 ($p=0.014$).

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Contact

Professor Lynda Frassetto, MD
UCSF
Email: lynda.frassetto@ucsf.edu
Website: <http://www.pcosdietstudy.org/>
Phone: +01 415 476 6143

