Published in final edited form as:

Contraception. 2015 October ; 92(4): 298–300. doi:10.1016/j.contraception.2015.05.014.

Serum adipocytokines and adipose weight gain: a pilot study in adolescent females initiating depot medroxyprogesterone acetate

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Abstract

Objective—To evaluate whether serum adipocytokine concentrations, controlling for baseline adiposity, are predictive of adipose weight gain in adolescents initiating DMPA.

Methods—Percent body fat was measured at baseline and 6 months. Baseline serum adipocytokine concentrations were quantified.

Results—Mean percent body fat was 31.6% (± 7.6) at baseline and 33.5% (± 7.6) at 6 months. In multivariable linear regression modeling (adjusted for baseline percent body fat), Hispanic ethnicity and baseline serum adiponectin concentration were inversely associated ($p < 0.05$) with absolute change in percent body fat at 6 months.

Conclusions—Serum adiponectin concentration may be useful for assessing risk of DMPA-associated adipose gains.

Keywords

depot medroxyprogesterone acetate; adipose tissue; adipocytokines; weight gain; adolescents

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Conflict of Interest/Financial Disclosures: The authors have no conflicts of interest to disclose.

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Introduction

Risk of weight gain continues to concern adolescents initiating depot medroxyprogesterone acetate (DMPA). Approximately 1 in 4 adolescent females on DMPA gain excessive weight (> 10% over baseline) [1]. DMPA-associated weight gain is entirely composed of increases in total body fat mass [2, 3]. To date, clinical characteristics such as race and obesity status have not been found to consistently predict DMPA-associated weight gain [4–7]. Weight gain at 6 months has been shown to be the best predictor of continued excessive weight gain. Although 6-month weight gain is helpful, it would be more useful to be able to identify those at risk prior to initiating this method. The **objective** of this study was to evaluate whether baseline serum adipocytokine concentrations, controlling for baseline adiposity, are predictive of adipose weight gain in adolescent females initiating DMPA.

Methods

Healthy, post-menarcheal females, age 12–19 self-selecting to initiate DMPA, were recruited between 12/2007 – 08/2010 into a study evaluating the relationship between DMPA pharmacokinetics and weight gain. The methods and outcomes of the main study have been previously described [8]. Exclusion criteria included: 1) DMPA use within the past 12 months; 2) pregnancy within the past 6 months; 3) other hormonal contraceptive use within the past 3 months; 4) chronic disease affecting weight (e.g. diabetes); 5) medications affecting weight (e.g. corticosteroids); 6) weight exceeding the dual X-ray energy absorptiometry (DXA) scanner limit; and 7) need for confidential contraceptive care.

Subjects ≥ 18 years of age provided written informed consent. Subjects <18 years required written informed assent and written parent/guardian consent. The Institutional Review Boards of MetroHealth Medical Center and Nationwide Children's Hospital approved the study protocol.

Subjects received 150mg DMPA intramuscularly every 12 weeks. Baseline data collection occurred within 1 week prior to the first injection. Follow-up visits occurred at 3 and 6 months, and DMPA was given at the conclusion of each of these study visits.

Serum was collected at baseline for determination of adiponectin and leptin concentration by ELISA. Additional data collected at baseline, 3, and 6 months included: body mass index (BMI, kg/m²); total body fat (DXA, Hologic® QDR 4500W); daily caloric intake (24-hour dietary recall [9]); and daily exercise and sedentary time [10].

The primary outcome variable was absolute change in percent body fat at 6 months. Main predictors of interest included: baseline serum adiponectin concentration; baseline serum leptin concentration; and baseline serum leptin:adiponectin concentration ratio. Potential confounders considered in analyses included: race/ethnicity; chronological age (age since birth); gynecologic age (age since menarche); baseline BMI; baseline percent body fat; total daily caloric intake (kcal); total daily exercise (hours); and total daily sedentary time (hours).

Crude associations between absolute change in percent body fat at 6 months with each main predictor and potential confounder were assessed through linear regression models, adjusted only for baseline percent body fat. Predictors of interest and potential confounders which were significantly ($p < 0.05$) associated with the primary outcome variable in crude analyses were eligible for the final multivariable linear regression model (adjusted for baseline percent body fat). All analyses were repeated using 6-month change in BMI as the outcome variable and very similar associations were observed (data not shown). Model assumptions and diagnostics were evaluated graphically and no major violations were noted. Calculations were performed using SAS (version 9.2, SAS Institute, Cary, NC). All reported p-values and confidence intervals are two-sided and unadjusted for multiple comparisons.

Results

Of 45 subjects who enrolled, 41 and 39 returned at 3 and 6 months, respectively. Thirty-eight participants had full data for the current analysis. Baseline characteristics were similar between subjects who did and did not complete data collection. Mean chronological and gynecologic age were 16.2 (± 1.5) and 4.1 (± 1.8) years, respectively (Table 1). Thirteen (34.2%) subjects self-identified as white non-Hispanic, 15 (39.5%) as black non-Hispanic, and 10 (26.3%) as Hispanic. The majority reported regular menstrual cycles and no prior pregnancy. Mean BMI at baseline was 24.4 (± 5.3). Mean percent body fat was 31.6% (± 7.6) at baseline. The mean absolute change in percent body fat at 6 months was 1.9 (± 2.8).

In crude linear regression models (adjusted only for baseline percent body fat), ethnicity, total daily sedentary time, and serum adiponectin concentration were significantly ($p < 0.05$) associated with absolute change in percent body fat at 6 months (Table 2). Sedentary time was positively associated with change in percent body fat, whereas Hispanic ethnicity and baseline serum adiponectin concentration were inversely associated. In multivariable linear regression modeling (adjusted for baseline percent body fat), Hispanic ethnicity and baseline serum adiponectin concentration remained significantly associated with absolute change in percent body fat at 6 months (Table 2). Daily sedentary time was eligible for multivariable modeling; however, with the inclusion of Hispanic ethnicity, it no longer contributed significantly to explaining change in percent body fat and was not included in the final model.

Discussion

We identified serum adiponectin concentration as a potentially useful biological marker for establishing risk of DMPA-associated weight gain in adolescents. This biological marker was independently predictive after adjustment for baseline percent body fat. Of note, we found that Hispanic ethnicity appeared to confer protection against weight gain in this sample of adolescent subjects on DMPA.

To our knowledge, no prior research has explored biological predictors of DMPA-associated weight gain. The current study is limited by small sample size and lack of control group, yet it provides a new direction for evaluating DMPA's effect on weight. Although mechanisms are unclear, our findings suggest that decreased serum adiponectin places an individual at

greater risk of weight gain on DMPA. This may be of particular concern in adolescents who are already obese at time of method initiation. Serum adiponectin concentration can be readily measured and may prove helpful in assessing risk. Prior to changes in clinical practice, studies in larger and more diverse cohorts should evaluate whether specific adiponectin concentration cut points can be established to better predict risk of DMPA-associated weight gain.

Acknowledgments

The authors would like to thank Mary Jo Day, LPN, for her help with study recruitment, Joan Lippus for her help processing serum and fat biopsy specimens, and all the adolescent girls who participated in the study.

Funding Acknowledgement: Funded by the National Institutes of Health (NIH) Award Number Grant K23RR024029. This project was made possible by the National Center for Research Resources Grant UL1RR024989, which is now the Clinical and Translational Science Collaborative of Cleveland, Award Number Grant UL1TR000439 from the National Center for Advancing Translational Sciences (NCATS). Additional support was received from The Ohio State University Center for Clinical and Translational Science, NCATS Award Number Grant UL1TR000090. The content of this manuscript is solely the responsibility of the authors and does not necessarily represent the official views of the NCATS or the NIH.

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Table 1

Characteristics of analysis cohort (n=38).

Characteristic	Summary statistics
Age (years), n(%)	
12– <15	9 (23.7%)
15– <17	17 (44.7%)
17–19	12 (31.6%)
Race/Ethnicity, n(%)	
White non-Hispanic	13 (34.2%)
Black non-Hispanic	15 (39.5%)
Hispanic	10 (26.3%)
Gynecologic age (years), n(%)	
0– <2	5 (13.2%)
2– <4	13 (34.2%)
4+	20 (52.6%)
Regular menstrual cycles, n(%)	
Yes	35 (92.1)
No	3 (7.9)
Previous pregnancy, n(%)	
Yes	3 (7.9%)
No	35 (92.1)
Number of births if previously pregnant, n(%)	
0	1 (33.3%)
1	2 (66.7%)
Daily caloric intake (kcal)	
Mean (SD)	1684.8 (462.2)
Daily exercise time (hours) ^a	
Mean (SD)	2.2 (1.9)
Daily sedentary time (hours) ^a	
Mean (SD)	2.5 (1.4)
Percent total body fat	
Baseline	
Mean (SD)	31.6 (7.6)
6 months	
Mean (SD)	33.5 (7.6)
Absolute change at 6 months	
Mean (SD)	1.9 (2.8)

Characteristic	Summary statistics
Baseline serum adiponectin concentration (ng/ml) ^b	
Mean (SD)	23.4 (10.4)
Baseline serum leptin concentration (ng/ml) ^b	
Mean (SD)	20.4 (11.4)
Baseline serum leptin:adiponectin ratio ^b	
Mean (SD)	1.14 (0.9)

^a Available for 34 participants.

^b Available for 31 participants.

Table 2

Linear regression associations between subject characteristics and absolute change in percent body fat at 6 months.

Characteristic	Crude Model Estimate (95% CI) ^a	Multivariable Model Estimate (95% CI) ^{a,b}
Age (years)	−0.08 (−0.73, 0.57)	
Gynecologic age (years)	−0.19 (−0.74, 0.35)	
Hispanic ethnicity	−2.22 (−4.23, −0.21) ^c	−2.94 (−5.04, −0.84) ^c
Daily caloric intake (100 kcal)	−0.04 (−0.25, 0.16)	
Daily exercise time (hours)	−0.36 (−0.92, 0.20)	
Daily sedentary time (hours)	0.71 (0.00, 1.42) ^c	
Serum adiponectin concentration (ng/ml)	−0.11 (−0.22, 0.00) ^c	−0.12 (−0.22, −0.02) ^c
Serum leptin concentration (ng/ml)	0.03 (−0.18, 0.23)	
Serum leptin:adiponectin ratio	0.59 (−1.17, 2.34)	

^a Adjusted for baseline percent body fat.

^b Variables significant in crude analyses (ethnicity, sedentary time, adiponectin concentration) were eligible for multivariable model.

^c p 0.05.