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A Longitudinal Comparison of Body Composition Changes in Adolescent Girls Receiving Hormonal Contraception

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Abstract

The objective of this study was to examine body composition changes in adolescent girls initiating depot medroxyprogesterone acetate (DMPA), oral contraceptives, or no hormonal contraceptive method. At 6 months, DMPA resulted in significant increases in adiposity with concomitant decreases in lean body mass. Supplemental estrogen may lessen these DMPA effects.

Adolescence is a period of rapid changes in total body fat and lean body mass. [1] Among adolescent girls, total body fat and lean body mass are expected to increase, with relative increase in adiposity.[2] Studies examining effects of hormonal contraception on body composition changes in adolescent girls are limited. One study found significant increases in adiposity among black, but not white, teens on the injectable contraceptive depot medroxyprogesterone acetate (DMPA).[3] However, a concurrent control group off hormonal contraception was not available for comparison. Two studies have found that among adult women, ages 18–35 and 16–33 respectively, body fat increases significantly with use of DMPA as compared to women on oral contraceptives (OC) or untreated controls.[4,5]

The objective of this study was to examine adiposity and lean body mass changes in adolescent girls initiating DMPA, OC, or no hormonal contraceptive (control).

The present study represents analysis of body composition data collected on all girls who enrolled in a larger 2-year study of hormonal contraception and bone mineral density (BMD) from April 2002 through September 2003. The study population consisted of post-menarcheal girls, age 12–18, attending one of four urban adolescent health clinics in a large metropolitan area. Adolescent girls requesting contraception, and selecting DMPA or OC, were eligible to participate. Adolescent girls who planned to receive no hormonal contraception were eligible for enrollment as control subjects.

Exclusion criteria for study participation included pregnancy or DMPA use within the preceding 6 months; OC use within the preceding 3 months; alcohol or drug dependence; medical condition (e.g. renal disease) or medication use (e.g. corticosteroids) known to be

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associated with the outcomes of interest; contraindication to estrogen use; weight exceeding 250 lbs (upper limit for DEXA scanner); and need for confidential contraceptive care. The study protocol was approved by the institutional review board of the participating institutions. Informed consent and assent were obtained from each guardian and adolescent recruited.

At baseline, a structured interview was conducted to elicit information on age; age at menarche; prior contraceptive use; pregnancy history; physical and mental health problems; and use of prescription, over-the-counter, and herbal medications. Total daily caloric intake was assessed by 24-hour recall. At baseline and 6 months, weight was measured with a calibrated digital scale, height was measured with a calibrated stadiometer, and body fat and lean body mass were measured by Hologic® dual energy x-ray absorptiometry (DEXA). Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. To reflect study participants' degree of pubertal maturation, gynecologic age was calculated by subtracting age at menarche from chronological age. OC compliance, assessed by monthly self-report and calculated as the number of pills taken divided by number prescribed (1 every day) × 100, was 86%. In order to remain in the study, subjects had to remain compliant with DMPA by clinic appointment.

A major aim of the parent study was to evaluate whether estrogen supplementation in subjects receiving DMPA resulted in decreased BMD losses. As such, DMPA subjects were randomized to receive either monthly injections of 5mg estradiol cypionate or placebo. For the present study, subjects receiving DMPA/placebo and DMPA/estradiol cypionate were analyzed separately.

The study purpose was to compare body composition changes in adolescents on different contraceptive methods. The main focus was mean group changes over time; therefore, all data points available at each study visit were eligible for analyses. Descriptive statistics were means and standard deviation for the continuous variables and counts and percentages for categorical variables. Univariate group comparisons were completed by using chi-square tests or analyses of variance (ANOVA), as appropriate. Multivariable models were built using standard ANOVA modeling techniques. Specifically, backward-elimination modeling methods were employed. $P \leq 0.05$ was considered statistically significant. Data analyses were conducted with SAS statistical software, version 9.1 (SAS Institute Inc., Cary, NC).

A total of 51 participants were recruited at baseline: 18 control, 18 OC, and 15 DMPA. Eight DMPA users were randomized to DMPA/placebo and 7 to DMPA/estradiol. At baseline, there was no statistically significant difference across groups in age, race, weight, total body fat, lean body mass and caloric intake (Table 1).

Percent changes in total body fat at 6 months by contraceptive group were 10.3% DMPA/placebo, 2.8% DMPA/estradiol, −0.1% OC, and −0.7% control ($p = 0.05$). Percent changes in lean body mass at 6 months were −3.4% DMPA/placebo, −1.2% DMPA/estradiol, 0.6% OC, and 0.6% control ($p = 0.07$).

In multivariable modeling (Table 2), contraceptive group was the only candidate variable predictive of total body fat changes. DMPA use alone resulted in larger increases in adiposity than use of no hormonal contraception, OC, or DMPA with supplemental estrogen. In multivariable modeling predicting lean body mass changes, contraceptive group approached, but did not reach, significance. Sample size may have limited our ability to see a contraceptive effect; there was only 40% statistical power to detect the observed changed as statistically significant.

Contraceptive group was predictive of changes in adiposity with girls on DMPA gaining more body fat than untreated controls. Supplemental estrogen may lessen this DMPA effect. The

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mechanisms by which DMPA could exert such effects on body composition are not clear. DMPA is known to induce a hypoestrogenic state.[6] Hypoestrogenism has been associated with central obesity and weight gain in animal and human models.[7] Certainly the lessening of the adipose accruing effect of DMPA by supplemental estrogen in the current study points towards a role for hypoestrogenism. However, estrogen supplementation in adolescents on DMPA did not fully normalize body composition changes to match those seen in untreated adolescents. Either the estrogen dose was insufficient or additional effects of MPA are at play. Progesterone receptors have been identified in human adipose tissue suggesting that the mechanism of action of DMPA on fat could be direct. [7] In addition, MPA can bind to the glucocorticoid receptor [7] and in high doses result in glucocorticoid-like changes in fat mass. [9]

The current study is limited by small sample size and short period of follow-up. Multiple factor analyses were explored with these limitations in mind. Having found statistical significance, study findings suggest a negative effect of DMPA on adiposity in adolescents. The clinical significance of such increases in adiposity must be weighed against the negative social and health effects of adolescent pregnancy. The decrease of adolescent pregnancy over the past decade has been attributed, in part, to the increased use of DMPA. [10] Future studies are needed to better define the role MPA may play in the development of obesity.

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Table 1

Characteristic Summary of Subjects by Contraceptive Method

Characteristic	Statistic	Control (n=18)	OC (n=18)	DMPA[1] (n=8)	DMPA/E[2] (n=7)	P-Value[3]
Age (years)	Mean±SD	15.7 ± 1.75	15.6 ± 1.61	16.0 ± 1.59	15.1 ± 0.90	0.72
Gynecologic Age (years)	Mean±SD	3.3 ± 2.32	4.1 ± 2.11	5.7 ± 1.76	3.7 ± 2.50	0.09
Race (N, %)	Black	11 (61.1 %)	8 (44.4 %)	4 (50.0 %)	6 (85.7 %)	0.28
	White	7 (38.9 %)	10 (55.6 %)	4 (50.0 %)	1 (14.3 %)	
Weight (kg)	Mean±SD	63.8 ± 15.39	69.8 ± 15.41	60.8 ± 12.70	60.6 ± 13.10	0.36
Body Mass Index (kg/m^2)	Mean±SD	24.4 ± 5.13	26.5 ± 4.80	22.7 ± 5.04	23.5 ± 3.92	0.23
Daily caloric intake (kcal)	Mean±SD	1583.3 ± 338.91	1565.4 ± 336.95	1865.3 ± 169.24	1636.1 ± 287.01	0.14
Baseline Total Body Fat (%)	Mean±SD	29.4 ± 8.01	31.7 ± 7.57	26.8 ± 8.94	29.2 ± 5.38	0.51
Baseline Lean Body Mass (%)	Mean±SD	70.6 ± 8.01	68.3 ± 7.57	73.2 ± 8.94	70.8 ± 5.38	0.51
Δ Total Body Fat (%)[4]	Mean±SD	−0.7 ± 8.94	−0.1 ± 10.52	10.3 ± 10.49	2.8 ± 4.40	0.05
Δ Lean Body Mass (%)[4]	Mean±SD	0.6 ± 3.39	0.6 ± 4.67	−3.4 ± 3.57	−1.2 ± 1.77	0.07

[1] Subjects self-selecting DMPA for contraception and randomized to receive monthly placebo injections.

[2] Subjects self-selecting DMPA for contraception and randomized to receive monthly estradiol injections.

[3] P-value from analysis of variance or chi-square test, as appropriate.

[4] Change from Baseline to 6 Months.

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Table 2

Multivariable Models Predicting Change in Percent Total Body Fat and Lean Body Mass at 6 Month

Endpoint	Significant Factors[1]	F-Value	P-Value	Significantly Different Groups
Δ Total Body Fat (%)	Contraceptive Group	2.90	0.045	Control-1% vs. DMPA 10% (p=0.04)
Δ Lean Body Mass (%)	Contraceptive Group	2.52	0.07	N/A
	Height	4.79	0.03	
	Race	6.11	0.02	
	BMI	74.15	<0.001	

[1]Candidate variables included contraceptive group, age, gynecologic age, race, weight, height, BMI, caloric intake, baseline total body fat and baseline lean body mass.