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Dietary intake and weight gain among adolescents on depot medroxyprogesterone acetate

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Abstract

Study Objective—To examine the relationship between dietary intake and weight gain among adolescent females initiating depot medroxyprogesterone acetate (DMPA).

Design—Prospective observational study.

Setting—Two urban Adolescent Medicine clinics.

Participants—45 post-menarcheal females, age 12 to 21, enrolled after self-selecting to initiate DMPA.

Intervention—Participants received 150mg DMPA intramuscularly (IM) every 12 weeks. Height, weight, and 24-hour dietary recall were collected at baseline, 3, 6, and 12 months.

Main Outcome Measure—Body mass index (BMI) over time calculated as weight (kg)/height (m^2). Associations between dietary variables and BMI were evaluated with repeated measures analysis of variance (ANOVA) modeling.

Results—Mean chronological and gynecologic ages were 16.2 (±1.5) and 4.2 (±1.8) years, respectively. Mean BMI increased from 23.7 (±5.3) to 25.3 (±5.7) over 12 months. Average dietary intake included: 1781.4 (±554.1) total kilocalories, 228.5g (±69.8) carbohydrates, 71.0g (±27.3) fat, and 61.0g (±20.2) protein. These diet measures were not associated with BMI over time. Dietary fiber, magnesium, and linoleic acid were inversely associated with increased BMI over time ($p < 0.05$).

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Conclusion—We found no evidence that general measures of diet (energy, carbohydrates, fat, and protein), as assessed by 24-hour recall, were predictive of weight gain on DMPA. Several nutrients abundant in foods that benefit overall health were inversely associated with increased BMI over time, suggesting that diet quality, rather than quantity, is a more important predictor of DMPA-associated weight gain.

Keywords

contraception; nutrition; adolescent health; Depo Provera; BMI

INTRODUCTION

Depot medroxyprogesterone acetate (DMPA) is a highly reliable progestin-only contraceptive that is well-suited for use by adolescents.[1] However, previous research has shown that weight gain is a common side effect of DMPA and may be of special interest in this vulnerable population.[2,3] Approximately 25% of adolescents who initiate DMPA experience excessive weight gain, defined as 10% or more of baseline weight.[4] DMPA discontinuation due to weight gain is common among adolescents, and this side effect may dissuade wider uptake.[5–7]

Prior efforts to mitigate DMPA-associated weight gain have focused on the identification of clinical characteristics that place adolescents at increased risk. Race has been evaluated as a predictor of weight gain on DMPA, but results are inconclusive.[2,8–9] The effects of baseline obesity status on later weight gain have been explored, but consensus has not been reached.[10–13] Recent evidence is more robust with regards to the trajectory of weight gain. Adolescents who gain >5% of baseline body weight in the first 6 months on DMPA are at increased risk of continued excessive weight gain.[14–15]

To date, there has been little research on the role of dietary intake in DMPA-associated weight gain in adolescents, although some studies among adult populations have included older teens (≥16 years of age).[16] While it has traditionally been presumed that weight gain results from positive energy balance, prior research in adolescents has not established an association between weight gain on DMPA and changes in eating behavior[8] or energy consumption.[16] Previous analyses have reported intake of total calories and major macronutrients (carbohydrates, fat, and protein), but advances in dietary analysis software allow for a more detailed investigation.

Due to the lack of conclusive data on the role of nutrition in DMPA-associated weight gain, the objective of this study was to examine the relationship between dietary intake and weight gain among adolescent females initiating DMPA.

MATERIALS AND METHODS

The study cohort consisted of 45 healthy, post-menarcheal females, age 12 to 21, who self-selected to initiate DMPA. Participants were recruited from 2 urban, hospital-based, outpatient Adolescent Clinics between December 2007 and September 2011. 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 known to affect weight (e.g. diabetes); 5) use of medications known to affect weight (e.g. daily corticosteroids); and 6) need for confidential contraceptive care if under 18 years old.

Written informed consent was obtained from subjects who were 18 years of age or older. For those under 18, written informed consent was obtained from a parent/legal guardian and the subject provided written informed assent. Of 62 eligible patients approached, 45 enrolled in the study; 41 subjects were still participating at 3 months, 39 at 6 months, and 31 completed 12 months of data collection. IRB regulations precluded collection of data from nonparticipants; however, the primary reason for nonparticipation was discomfort with study procedures. No significant differences were evident between subjects who did and did not complete the study with regards to age, race, baseline body mass index (BMI), and reported physical activity. The study protocol was approved by the Institutional Review Boards of both institutions.

Subjects received 150mg of DMPA intramuscularly (IM) every 12 weeks and completed data collection at baseline, 3, 6, and 12 months. Height, weight, body composition, and physical activity were assessed at baseline, 3, 6, and 12 months. Height was measured on a calibrated stadiometer and weight was measured on a calibrated digital scale with the subject gowned and in stocking feet. BMI was calculated as weight (kg)/height (m^2). Percent body fat and lean body mass were assessed with total body dual-energy X-ray absorptiometry (DXA) Hologic® QDR 4500W fan beam densitometer. Participants completed the Child and Adolescent Trial for Cardiovascular Health Self-Administered Physical Activity Checklist (CATCH - SAPAC), a self-reported measure of exercise habits and sedentary time which has been validated in a pediatric population.[17] Daily exercise time was defined as the total number of minutes spent doing physical activity of any intensity. Similarly, daily sedentary time was the total number of minutes spent using the computer or watching television.

At baseline, 3, 6, and 12 months, a trained research nurse administered a 24-hour dietary recall using the United States Department of Agriculture (USDA) Automated Multiple Pass Method. The USDA Automated Multiple Pass Method includes five steps in which the subject: 1) reports an uninterrupted list of all foods and beverages consumed; 2) responds to a series of questions regarding foods that are frequently forgotten; 3) gives the time and occasion that each item was consumed; 4) provides detail about the quantity of each food or beverage; and 5) responds to a final probe from the researcher regarding anything else that may have been consumed but not reported.[18] An observational validation study of this methodology in women found that reported consumption of calories, carbohydrate, fat, and protein was within 10% of actual intake, regardless of BMI.[19] Since 2002, the USDA Automated Multiple Pass Method has been used in the National Health and Nutrition Examination Survey (NHANES) which includes adolescents age 12–19.[20]

Dietary recalls were analyzed using the Nutrition Data System for Research (NDSR) software program which utilizes the multiple-pass system interview methodology. To reflect the marketplace throughout the study, dietary intake data were collected using NDSR software versions 2009, 2010, and 2011, developed by the Nutrition Coordinating Center

(NCC), University of Minnesota, Minneapolis.[a] The NDSR time-related database updates analytical data while maintaining nutrient profiles true to the version used for data collection. Final calculations were completed using NDSR version 2011.

A dietary recall was missing for two subjects at baseline. At all other time points, dietary data were available for each subject who was still participating (41 at 3 months, 39 at 6 months, 31 at 12 months). Dietary recalls were averaged to provide an estimate of each subject's usual diet over the study period as a single 24-hour recall does not reflect variability in day-to-day eating.[21,22] Averages were calculated for each subject for total energy in kilocalories (kcal); total carbohydrate, fat, and protein (in grams); and over 30 selected nutrients[b] including vitamins D and E, calcium, magnesium, phosphorous, dietary fiber, and omega-3 fatty acids.

The primary outcome measure was BMI over time. Patient demographics, weight measures, and dietary intake were described for the overall subject cohort. To account for variation in pubertal development, gynecologic age was calculated as the difference between

a) http://www.ncc.umn.edu/products/ndsr.html

b) Full list of nutrients examined

Energy (kcal)
Total Fat (g)
Total Carbohydrate (g)
Total Dietary Fiber (g)
Total Protein (g)
Total Saturated Fatty Acids (SFA) (g)
Total Monounsaturated Fatty Acids (MUFA) (g)
Total Polyunsaturated Fatty Acids (PUFA) (g)
Vitamin D (calciferol) (mcg)
Vitamin E (Total Alpha-Tocopherol) (mg)
Vitamin E (International Units)
Beta-Tocopherol (mg)
Gamma-Tocopherol (mg)
Calcium (mg)
Phosphorus (mg)
Magnesium (mg)
SFA 12:0 (lauric acid) (g)
SFA 14:0 (myristic acid) (g)
SFA 16:0 (palmitic acid) (g)
SFA 17:0 (margaric acid) (g)
SFA 18:0 (stearic acid) (g)
MUFA 14:1 (myristoleic acid) (g)
MUFA 16:1 (palmitoleic acid) (g)
MUFA 18:1 (oleic acid) (g)
MUFA 20:1 (gadoleic acid) (g)
MUFA 22:1 (erucic acid) (g)
PUFA 18:2 (linoleic acid) (g)
PUFA 18:3 (linolenic acid) (g)
PUFA 18:4 (parinaric acid) (g)
PUFA 20:4 (arachidonic acid) (g)
PUFA 20:5 (eicosapentaenoic acid [EPA]) (g)
PUFA 22:5 (docosapentaenoic acid [DPA]) (g)
PUFA 22:6 (docosahexaenoic acid [DHA]) (g)
Total Trans-Fatty Acids (g)
Omega-3 Fatty Acids (g)
Natural Alpha-Tocopherol (RRR) (mg)
Synthetic Alpha-Tocopherol (mg)
Total Conjugated Linoleic Acid (g)
Cis-9, Trans-11 Conjugated Linoleic Acid (g)
Trans-10, Cis-12 Conjugated Linoleic Acid (g)

chronological age at enrollment and age at menarche. Paired t-tests were used to compare baseline and 12-month BMI and body composition measures.

Potential associations of dietary intake variables with BMI over time were examined with repeated measures analysis of variance (ANOVA) modeling. Age, race, average daily exercise, and average daily sedentary time were considered as potential confounders. Gynecologic age was more strongly correlated with BMI over time than chronological age and was therefore used in multivariate modeling. All data were analyzed with SAS® software, Version 9.3 of the SAS System for Windows 7, copyright © 2011 SAS Institute Inc[c].

RESULTS

The study cohort was 35.6% black, 35.6% white, and 28.9% Hispanic (Table 1). Mean chronological and gynecologic age were 16.2 (±1.5) and 4.2 (±1.8) years, respectively. The majority of participants had never been pregnant.

Neither race ($p = 0.47$) nor previous pregnancy ($p = 0.86$) was associated with BMI over time in repeated measures modeling. Age was significantly ($p < 0.01$) directly associated with BMI over time whether measured as chronological age or gynecologic age. Daily exercise ($p = 0.13$) and sedentary time ($p = 0.78$) were not associated with BMI over the study period.

Mean BMI increased significantly ($p < 0.001$) from baseline to 12 months, and a wide BMI range was noted at each time point (Table 2). Mean percentage body fat also increased significantly ($p < 0.001$) over the study follow-up period, while lean mass decreased ($p < 0.001$).

Reported energy intake decreased over the course of the study (Table 3). We found no association between general measures of dietary intake (kilocalories, carbohydrate, fat, and protein) and BMI over time. This remained the case when race and gynecologic age were added to the model. Of over 30 selected nutrients[b] examined, we found that dietary fiber, magnesium, and linoleic acid were significantly inversely associated ($p < 0.05$) with BMI over time in repeated measures modeling. These nutrients remained inversely correlated with BMI over time even when controlling for race and gynecologic age. Specific nutrients which demonstrated no association with BMI over time included vitamins D and E, calcium, phosphorus, and omega-3 fatty acids.

DISCUSSION

The body composition changes that we observed (increased percent body fat and decreased lean mass) are consistent with prior reports of DMPA-associated weight gain in adolescents.[23] Contrary to the traditional clinical hypothesis, however, our findings suggest that DMPA-associated weight gain cannot be explained by a simple, direct relationship to

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increased food consumption. We found no evidence that intake of calories or major macronutrients (carbohydrate, fat, and protein) affected BMI while on DMPA. While the study cohort's overall diet quality was poor and intake of some nutrients was too low to be meaningful, overall means for calories, carbohydrate, fat, and protein were roughly in line with Dietary Reference Intake (DRI) values for a 16-year-old girl of similar BMI.[24,25] Of note, a large study conducted by Berenson and Rahman found that protein was protective against weight gain on DMPA.[16] However, this study included a predominantly adult population and the amount of protein consumed was not reported.

Total dietary fiber, magnesium, and linoleic acid were found to be inversely associated with BMI over time. All three of these nutrients are abundant in foods that benefit overall health. The role of fiber in a healthy diet has been well-documented.[26] Magnesium is essential for hundreds of biochemical reactions and physiological functions.[27] Sources of magnesium include: leafy green vegetables, whole grains, nuts, legumes, soy and some fruits.[28]

Linoleic acid is an essential omega-6 fatty acid found in most vegetable oils, but is especially abundant in safflower, sunflower, and corn oils. Diets rich in linoleic acid are generally considered to be heart healthy.[29,30] Additionally, linoleic acid has been shown to decrease trunk adiposity and increase lean mass in obese post-menopausal women.[30] Menopause is characterized by an estradiol-deficient state similar to that which is induced by DMPA.

Specific nutrients of interest that were found to have no association with BMI over time included vitamins D and E, calcium, phosphorus, and omega-3 fatty acids. Studies of calcium intake and dairy consumption in pediatric populations have found conflicting results; some point to an inverse association between calcium intake and adiposity[31] while others conclude that dairy consumption promotes weight gain.[32] Although no association was found in our study cohort between calcium intake and weight change, mean reported calcium intake (633mg) was only 51% of DRI (1300mg).[25] Similarly, intake of magnesium and fiber, which were found to be protective in our cohort, was well below recommendations. Reported intake was 46% and 38% of DRI for magnesium and fiber, respectively. In a population with adequate nutrient intake, associations between dietary variables and DMPA-associated weight gain may be absent or entirely different.

Limitations on the measurement of “typical” dietary intake are inherent to any nutritional research. However, 24-hour dietary recalls are generally considered among the more reliable and valid methods of nutrient intake assessment in pediatric populations.[33] In addition, national reports, such as NHANES, frequently rely on one to two 24-hour dietary recalls to assess nutrient intake in the adolescent population.[20] Findings of the current study are also limited by small sample size and lack of control group.

Despite the limitations of our study, we found no association between total caloric intake and weight gain on DMPA. Our evidence at this time does not support the recommendation of a specific diet or supplement to mitigate weight gain, but factors reflective of a nutrient-rich diet were inversely associated with increased BMI. These results suggest that counseling on diet quality rather than quantity may be more useful for adolescents initiating

DMPA. Future research with larger sample sizes and comprehensive dietary intake assessment should further explore specific nutrients and potential mechanisms of protection.

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Table 1

Baseline subject characteristics (N = 45)

Characteristic	n (%)
Race/Ethnicity	
Black Non-Hispanic	16 (35.6)
White Non-Hispanic	16 (35.6)
Hispanic	13 (28.9)
Previous Pregnancies	
0	41 (91.1)
1	4 (8.9)
	Mean (SD)
Chronological Age (years)	16.2 (1.54)
Age at Menarche (years)	12.0 (1.29)
Gynecologic Age (years)	4.2 (1.82)
Total Daily Exercise (minutes) [a]	127.9 (112.11)
Total Daily Computer/TV (minutes) [a]	144.6 (109.68)

[a] n = 41

Table 2

Body mass index (BMI) and body composition measurements over time

Measurement	Baseline (n = 45)	3 Months (n = 41)	6 Months (n = 39)	12 Months (n = 31)	%Δ over 12 months	p-value[b]
BMI (kg/m^2)						<0.001
Mean (SD)	23.7 (5.31)	24.3 (5.18)	25.2 (5.53)	25.3 (5.71)	6.2 (9.29)	
Range	16.6 – 37.6	16.7 – 36.6	16.4 – 37.5	16.4 – 36.6	−10.5 – 31.2	
% Body Fat [a]						<0.001
Mean (SD)	30.9 (7.39)	32.8 (8.00)	33.5 (7.61)	35.2 (7.89)	13.9 (12.97)	
Range	18.0 – 49.7	17.9 – 53.1	20.7 – 52.0	20.4 – 51.0	−6.6 – 50.4	
% Lean Mass [a]						<0.001
Mean (SD)	69.1 (7.40)	67.2 (8.00)	66.5 (7.61)	64.7 (7.77)	−6.1 (5.56)	
Range	50.3 – 82.0	46.9 – 82.1	48.0 – 79.3	49.0 – 79.6	−22.4 – 3.4	

[a] Measured with total body dual-energy X-ray absorptiometry scan

[b] Paired t-tests comparing baseline and 12-month measures

Table 3

Dietary intake and association with BMI over time[a]

	Baseline Mean (SD) n = 43	3 Month Mean (SD) n = 41	6 Month Mean (SD) n = 39	12 Month Mean (SD) n = 31	Overall Mean (SD)	P-value[b]	P-Value[c]
Total Energy (kcal)	1928.1 (796.88)	1743.5 (799.06)	1741.1 (669.31)	1522.2 (748.59)	1781.4 (554.13)	0.09	
Total Carbohydrate (g)	246.0 (112.28)	227.4 (93.92)	215.9 (89.60)	196.0 (87.48)	228.5 (69.83)	0.15	-
Total Fat (g)	78.1 (39.30)	69.5 (45.11)	70.4 (37.46)	59.3 (36.42)	71.0 (27.29)	0.08	-
Total Protein (g)	64.5 (31.42)	56.9 (31.85)	64.5 (31.17)	53.8 (29.25)	61.0 (20.22)	0.23	-
Total Dietary Fiber (g)	10.5 (5.92)	10.6 (6.53)	8.3 (4.78)	9.8 (6.07)	9.8 (3.36)	<0.001	0.005
Magnesium (mg)	174.9 (76.94)	163.6 (70.14)	165.9 (81.94)	151.5 (81.98)	166.3 (51.81)	0.04	0.02
Linoleic Acid (g)	17.3 (18.62)	14.9 (11.52)	14.5 (10.21)	12.6 (9.66)	15.1 (7.76)	0.03	.006

[a] Unadjusted and adjusted repeated measures analysis of variance

[b] Unadjusted p-value

[c] Adjusted for gynecologic age and race