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Weight and Body Composition Changes During Oral Contraceptive Use in Obese and Normal Weight Women

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Abstract

Background: Oral contraceptive (OC) use seems to have little effect on weight change in normal weight women. Most previous studies have excluded obese women, so the effect of OC use on weight change in obese women is unknown.
Methods: This analysis evaluates weight and body composition change with OC use among obese (body mass index [BMI] 30.0–39.9) and normal weight (BMI 19.0–24.9) women who were randomly assigned to two OC doses: 20 μg ethinyl estradiol (EE) and 100 μg levonorgestrel (LNG) OCs or 30 μg EE and 150 μg LNG OCs. Follow-up occurred after three to four OC cycles. Weight and body composition were measured at baseline and at follow-up using a bioelectrical impedance analyzer.
Results: Among 150 women (54 obese and 96 normal weight) who used OCs for 3 to 4 months, there were no clinically or statistically significant weight or body composition changes in the overall group or by BMI or OC formulation group.
Conclusions: These findings add to evidence that EE/LNG OCs are not associated with short term weight or body composition change for normal weight women and suggest that OCs are also are not associated with short term weight or body composition change in obese women.

Introduction

Many women and clinicians believe that weight gain is a common side effect of oral contraceptive (OC) use.[1,2,3] In a report from the 2006–2010 National Survey of Family Growth, 63% of women who had ever used OCs and discontinued use due to dissatisfaction cited side effects as a reason for discontinuation,[4] and weight gain is one of the most common side effects reported by OC users.[1,5,6,7] OC users who attribute weight gain to OCs are less likely to continue OC use.[8] This belief has the potential to have a significant public health impact, as unintended pregnancies among women who discontinue OCs significantly contributes to the number of unintended pregnancies in the United States.[9] In the 2006–2010 National Survey of Family Growth, concerns about side effects of birth control was cited as a reason for not using contraception at time of conception for 19% of unwanted births and 12% of mistimed births.[10]

Numerous studies have examined the effect of OCs on weight. In 2011, the Cochrane Collaboration conducted a meta-analysis of 49 trials,[2] and the authors concluded that the current literature is insufficient to draw a definite conclusion about the effect of OCs on weight gain, but that there is no evidence of a large effect.[2]

Although over 30% of women in the United States are obese,[11] most previous studies of the effect of OC use on weight gain have excluded obese women. It is possible that the effect of OCs on weight gain may differ among women with obesity compared to normal weight women. Most previous studies lack standardized measurement procedures, which could introduce random error and attenuate a small effect of OC use on weight change. Most previous studies have examined only the effect of OCs on weight, but if OC use is associated with weight gain, then body composition changes (changes in total body water, fat free mass, and fat mass) might indicate the causal pathway through which OC use leads to weight gain.

Hypothesized pathways through which OC use could cause weight gain include water retention[2,12]; an estrogen-mediated increase in subcutaneous fat[2,13]; an effect on satiety and appetite, leading to an increase in food intake[2,13]; and an androgen-mediated increase in muscle mass.[2,13] If OC use does have an effect on weight gain, then a higher dose OC

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might have a greater effect than a lower dose OC of the same estrogen and progestin types.[2]

The objective of this analysis was to examine weight and body composition change after three months of OC use in obese and normal weight women and to examine whether this relation differs between obese versus normal weight women, as well as between two widely marketed OC doses.

Materials and Methods

Study design and participants

This was a planned secondary analysis from a prospective randomized trial that evaluated whether obese women are at a higher risk of OC failure than normal weight women due to less contraceptive-mediated ovarian suppression.[14] The present analysis tested two hypotheses: (1) short term OC use is not associated with weight or body composition change among obese or normal weight women and (2) similarly, OC use is not associated with weight or body composition change for 20 μg ethinyl estradiol (EE) and 100 μg levonorgestrel (LNG) OCs or 30 μg EE and 150 μg LNG OCs. The primary outcome is weight change (kg) and the secondary outcomes are changes in (1) total body water (kg), (2) percent body fat, (3) fat mass (kg), and (4) fat free mass (kg). Change in body mass index (BMI) (kg/m^2) is captured by weight change, as BMI was calculated using the baseline height measurement for each study participant; thus, BMI change is not reported separately.

Details of the study procedures have been described in detail elsewhere.[14] Briefly, between July 2006 and December 2008, 226 women (128 normal weight and 98 obese women) participated in this study. Participants were recruited in two groups: normal weight (BMI 19.0–24.9) and obese (BMI 30.0–39.9). Overweight women were not included to create a clear distinction between BMI groups. Participants were aged 18–35 and had no contraindications to OC use. Participants were stratified by BMI class and randomly assigned to one of the two 21-day monophasic OC formulations (1:1 allocation): 30 μg EE and 150 μg LNG, or 20 μg EE and 100 μg LNG (Portia and Lessina, respectively, Barr Laboratories, Inc.). Henceforth, we refer to these formulations as 30/150 and 20/100, respectively. Both OC formulations were FDA-approved and widely marketed. Follow-up occurred after three to four OC cycles. This length of follow up was selected based on the design of the parent trial, which specified biweekly blood draws and sonograms during the third or fourth cycle of OC use.

To evaluate weight and body composition change with OC use, the sample for the present analysis includes women who remained in the study for at least three OC cycles and were determined to be consistent OC users based on LNG assay, as previously described.[14]

All study visits took place at the Columbia University Medical Center in New York City. This trial was approved by the Columbia University Medical Center Institutional Review Board and was registered with ClinicalTrials.gov (NCT00827632).

Outcome measures

At baseline and follow-up, the research coordinator measured the height, weight, and body composition of each participant. For each participant, weight and body composition change was calculated as the difference between the measurements from baseline to follow-up. Standing height was measured to the nearest 1.0 cm using a stadiometer. Weight and body composition [total body water (kg), percent body fat, fat mass (kg), and fat free mass (kg)] were measured by bioelectrical impedance analysis (BIA) using the BC-418 (Tanita Corp., Tokyo, Japan), an eight-contact electrode single frequency 50-kHz body composition analyzer. To avoid inter-instrument variation, all BIA measurements were taken with the same machine.

BIA was chosen as the primary method of body composition assessment because it is easy to use, fast, safe, and relatively inexpensive.[15] Due to the large sample size and because body composition change was not the primary outcome of the parent trial, this method was chosen over more advanced techniques, such as dual-energy x-ray absorptiometry (DXA), which is less accessible and more costly. BIA measures the impedance of a small electrical current traveling through the body.[16] Based on impedance measurements, total body water is calculated, and subsequently, fat-free mass and fat mass are calculated.[15,16,17] BIA has been shown to provide reliable estimates of body composition in healthy adults.[16,18]

Statistical analysis

Characteristics of obese and normal weight participants were compared using *t*-tests for continuous variables and chi-square and Fisher's exact tests for categorical variables. We used *t*-tests to compare weight and body composition change from baseline to follow-up in the overall sample, within each BMI subgroup and each OC dose subgroup, as well as between BMI subgroups and OC dose subgroups. Multiple linear regression was used to examine BMI subgroup and OC dose subgroup together, and the following variables were considered as potential confounders: age, race/ethnicity, education, previous birth, smoking, OC use at baseline, and length of follow-up.

The sample size was selected based on power calculations for the primary objective of the parent study, which was to evaluate differences in follicular suppression during OC use in obese and normal weight women. Retrospective power analysis using observed sample size and variance for weight change showed that the present analysis had 90% power to detect a mean weight change of 1.05 kg in the obese group and 0.56 kg in the normal weight group as well as 90% power to detect a difference in weight change of 1.08 kg between BMI groups and 1.04 kg between OC randomization groups. Thus, the achieved sample size was sufficient to detect small changes in weight. Statistical analyses were performed using SAS statistical software, versions 9.1 and 9.2 (SAS Institute).

Results

A participant was included in the present analysis if she completed at least one follow-up visit and was a consistent OC user during the study, as defined by LNG assay.[14] Out of the 226 enrolled participants, 45 (19.9% overall, 17.2% in the normal weight group, 23.5% in the obese group) were lost to follow-up or withdrew from the study prior to the follow-up examinations. Of the 181 women who participated in follow-up examinations, 31 (17.1% overall, 9.4% in the normal weight group, 28.0% in the obese group) were not consistent OC users based on LNG assays. Thus, the present analysis includes 150 (66.4%) of the 226 enrolled participants: 96 (75.0%)

of the 128 normal weight and 54 (55.1%) of the 98 obese participants; 70 (61.4%) of the 114 participants assigned to 20/100 OCs, 80 (71.4%) of the 112 participants assigned to 30/150 OCs. Follow-up occurred during the third or fourth study cycle for 145 (96.7%) of the 150 participants and during the fifth to seventh study cycle for the five remaining participants due scheduling of the follow-up visits for the parent study, which required bi-weekly exams during the follow-up OC cycle.

Baseline characteristics of the analytic sample, stratified by BMI group, are presented in Table 1. Obese and normal weight participants differed with respect to race/ethnicity and reproductive history.

All 150 participants are included in analysis of weight change, but 5 participants were excluded from analyses of BIA measurements. Baseline BIA measurements were not taken for one normal weight participant (30/150 group). Four [$n=3$ normal weight (all 20/100) and $n=1$ obese (30/150)] BIA change observations were extreme outliers. For all four of these participants, measured fat mass change was disproportionate to or in the opposite direction of weight change. Due to conditions known to affect BIA values (hydration, consumption of food and beverages, and changes in the menstrual cycle)[16,18] that were not standardized for this study, it was concluded that these extreme outliers were due to measurement error, and not due to true changes in body composition. The resulting sample size for BIA analyses was 145 participants ($n=92$ *n*ormal weight, $n=53$ obese; $n=67$ 20/100, $n=78$ 30/150).

Table 1. Baseline Characteristics of Consistent Oral Contraceptive Users by Body Mass Index Group

Variable	*Normal weight* (n = *96*)	*Obese* (n = *54*)	p[1]
Height (cm)	164.1 ± 6.4	163.8 ± 6.6	0.83
Weight (kg)	59.6 ± 6.7	91.9 ± 9.3	< 0.01
BMI (kg/m^2)	22.1 ± 1.5	34.2 ± 2.6	< 0.01
Percent body fat (%)[2]	29.2 ± 3.7	47.4 ± 3.5	< 0.01
Fat mass (kg)[2]	17.6 ± 3.7	43.8 ± 6.9	< 0.01
Fat free mass (kg)[2]	42.1 ± 3.9	48.2 ± 4.0	< 0.01
Total body water (kg)[2]	29.4 ± 2.9	36.8 ± 3.6	< 0.01
Age	24.7 ± 4.5	25.7 ± 4.0	0.17
Race/ethnicity			
Hispanic	19 (19.8)	19 (35.2)	< 0.01
Non-Hispanic black	30 (31.3)	23 (42.6)	
Non-Hispanic white	33 (34.4)	11 (20.4)	
Non-Hispanic Asian	14 (14.6)	1 (1.9)	
Education			
Less than a bachelor's degree	43 (44.8)	31 (57.4)	0.14
Bachelor's degree or more	53 (55.2)	23 (42.6)	
Previous pregnancy			
Yes	29 (30.2)	28 (51.9)	< 0.01
No	67 (69.8)	26 (48.2)	
Previous birth			
Yes	9 (9.4)	20 (37.0)	< 0.01
No	87 (90.6)	34 (63.0)	
Using OC at enrollment			
Yes	22 (22.9)	12 (22.2)	0.92
No	74 (77.1)	42 (77.8)	
Smokes cigarettes			
Yes	11 (11.5)	10 (18.5)	0.23
No	85 (88.5)	44 (81.5)	
OC dose			
20 μg EE/100 μg LNG	47 (49.0)	23 (42.6)	0.45
30 μg EE/150 μg LNG	49 (51.0)	31 (57.4)	

Values are shown as mean ± standard deviation or *n* (%).
[1]*t*-test for continuous variables and chi-square test or Fisher's exact test for categorical variables.
[2]Baseline measurements for these variables were unavailable for one normal weight participant due to machine malfunction.
EE, ethinyl estradiol; LNG, levonorgestrel; OC, oral contraceptive.

Table 2. Weight and Body Composition Change After Three Months Among All Consistent Oral Contraceptive Users

Variable	*Difference (follow-up − baseline)*	p
Weight (kg) ($n=150$)	0.016 ± 1.95	0.92
Total body water (kg) ($n=145$)	0.080 ± 1.15	0.40
Fat free mass (kg) ($n=145$)	0.035 ± 0.84	0.61
Fat mass (kg) ($n=145$)	0.008 ± 1.60	0.95
Percent body fat ($n=145$)	0.018 ± 1.35	0.87

Values are shown as mean ± standard deviation.

The results support our hypotheses that on average, short term OC use has little effect on weight and body composition for both normal weight and obese women and for both 20/100 and 30/150 OC formulations. No significant changes in weight or body composition were observed in the overall sample (Table 2), in either BMI group (Fig. 1), or in either OC group (Fig. 2). Additionally, no significant differences in weight or body composition change were observed between BMI groups (Table 3) or between OC formulation groups (Table 4). Multiple linear regression analyses adjusted for potential confounders showed that BMI group (obese vs. normal weight $b=-0.63$ kg, $p=0.08$), OC formulation (30/150 vs. 20/100, $b=-0.036$ kg, $p=0.92$), and their interaction ($p=0.76$) were not significantly associated with weight change.

Discussion

In this planned secondary analysis from a prospective study of obese and normal weight women randomly assigned to use either 20/100 or 30/150 OC, no clinically or statistically significant changes in weight or body composition were observed in the overall group, in either BMI subgroup, or in either OC formulation subgroup, despite adequate power to identify small changes. No differences in weight or body composition change were observed in obese women compared to normal weight women or in women taking 30/150 OCs compared to those taking 20/100 OCs.

We observed only minor changes in weight and body composition in the overall sample and in the BMI and OC dose subgroups; these changes were not clinically or statistically significant. The standard deviations of these estimates

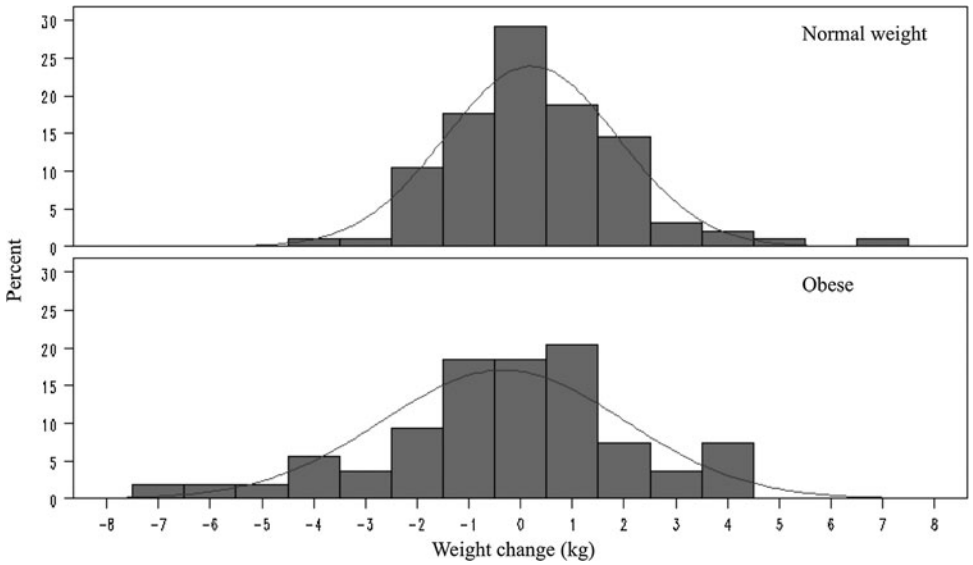

FIG. 1. Weight change (kg) after 3 months of oral contraceptive use by body mass index group.

were also relatively small, which indicates that it is unlikely that these null results are due to random error. While most women experienced no significant weight change, a few women gained or lost significant weight; among those women, weight loss was as common as weight gain.

Although average weight change was small in the overall group and in each subgroup, obese participants and participants assigned to the lower dose OCs lost a small amount of weight on average, while normal weight participants and participants assigned to the higher dose OCs gained a small amount of weight on average. The slight weight loss in the obese group and weight gain in the normal weight group is likely due to regression to the mean. It is possible that over a longer follow-up period these differences between groups could become clinically meaningful.

The present study compared two distinct BMI groups. To our knowledge, there are no published trials that compare weight and body composition change with OC use in obese and normal weight women, and only two published studies that compare weight change in obese (BMI ≥ 30) and nonobese (BMI < 30) OC users. The first study included adolescent girls who initiated OC use at a health clinic visit.[19] Over 18 months of OC use, the nonobese participants gained significantly more weight than obese participants. The second study is a cohort study of women using EE/desogestrel OCs and nonhormonal methods over 36 months.[20] Body composition change was measured with DXA. The authors found that women using OCs experienced a small increase in body fat compared to the control group, but that weight change did not differ between obese and nonobese women.

The findings of this study are limited by the duration of follow-up and the lack of a placebo group. It is possible that changes in weight or body composition could have been observed over a longer period of follow-up. Approximately 33% of participants either dropped out of the study prior to follow up examinations or were not consistent OC users and were excluded from this analysis. While BIA is not the gold standard measure of body composition, the present study was concerned with change rather than absolute values of body composition, and BIA has been shown to be a reliable measure

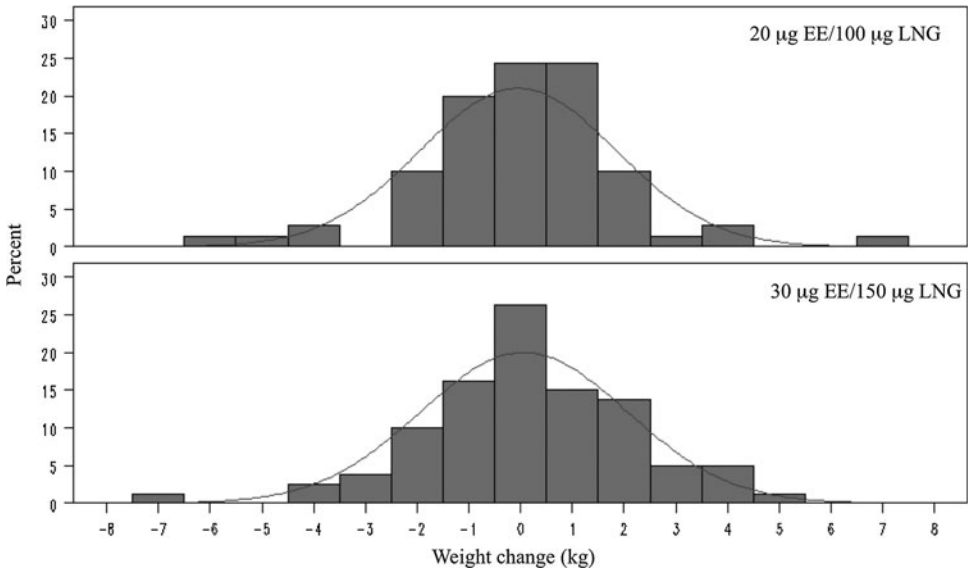

FIG. 2. Weight change (kg) after 3 months of oral contraceptive use by oral contraceptive group.

Table 3. Weight and Body Composition Change After Three Months Among Consistent Oral Contraceptive Users by Body Mass Index Group

Variable	*Normal weight Difference (follow-up – baseline)*	*Obese Difference (follow-up – baseline)*	p
Weight (kg) ($n=150$)	0.21 ± 1.67	−0.33 ± 2.34	0.11
Total body water (kg) ($n=145$)	0.16 ± 1.18	−0.051 ± 1.11	0.30
Fat free mass (kg) ($n=145$)	0.11 ± 0.98	−0.096 ± 0.48	0.15
Fat mass (kg) ($n=145$)	0.12 ± 1.32	−0.19 ± 1.98	0.25
Percent body fat ($n=145$)	0.10 ± 1.53	−0.13 ± 0.95	0.33

Values are shown as mean ± standard deviation.

of body composition.[16,18] There are some limitations of using BIA to measure body composition. First, fat free mass and fat mass estimates are based on the estimate for total body water, so if total body water changes, fat free mass and fat mass estimates will also change. Since no changes in weight, total body water, fat free mass, or fat mass were observed, this did not limit our conclusions. Second, we did not standardize several factors known to affect BIA estimates: hydration status, time since last meal, time of day, recent physical activity, and phase of the menstrual cycle.[16] This probably accounts for the four extreme outliers that were excluded from BIA analyses. Given the large number of participant study visits required for the parent study, it was not feasible to standardize time of day that BIA measurements were taken.

This study is innovative in that it included obese women, an understudied group that makes up over 30% of the population.[11] Another strength is that participants were randomized to use one of two widely marketed OC formulations of the same estrogen and progestin types. Another strength of this study is that measurement procedures were standardized to minimize random variation and the study had sufficient statistical power to detect small changes in weight and body composition.

Table 4. Weight and Body Composition Change After Three Months Among Consistent Oral Contraceptive Users by Oral Contraceptive Pill Dose

Variable	*20 μg EE/100 μg LNG* *Difference (follow-up – baseline)*	*30 μg EE/150 μg LNG* *Difference (follow-up – baseline)*	p
Weight (kg) ($n=150$)	−0.044 ± 1.90	0.069 ± 2.00	0.72
Total body water (kg) ($n=145$)	0.128 ± 1.13	0.038 ± 1.18	0.64
Fat free mass (kg) ($n=145$)	0.013 ± 0.82	0.054 ± 0.85	0.77
Fat mass (kg) ($n=145$)	−0.046 ± 1.61	0.054 ± 1.60	0.71
Percent body fat ($n=145$)	−0.007 ± 1.50	0.040 ± 1.21	0.83

Values are shown as mean ± standard deviation.

In conclusion, our findings support previous evidence that on average, OC use is not associated with weight change. Among the minority of women who did experience weight change, weight loss was as common as weight gain. Furthermore, our findings suggest that this association does not differ in obese women compared to normal weight women.

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Disclosure Statement

C.L.W. is an advisory board member of Agile and a consultant for Merck and Bayer.

The other authors have no potential conflicts of interest to report.

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