Original Report

Assessing Weight Status in Adolescent and Young Adult Users of the Etonogestrel Contraceptive Implant

Mary E. Romano MD, MPH *, Debra K. Braun-Courville MD

Department of Pediatrics, Vanderbilt University Medical Center, Nashville, Tennessee

A B S T R A C T

Study Objective: There are inconsistent data regarding hormonal contraception and weight. Weight concerns might deter teens from using highly effective contraception such as the etonogestrel subdermal implant (ENG). There is little literature about weight gain and adolescent ENG use; most studies involve adult women. The purpose of this study was to evaluate weight/body mass index (BMI) change in adolescent and young adult ENG users compared with nonusers.
Design: Retrospective chart review of 197 ENG users and age, race, BMI, and follow-up time-matched controls.
Setting: Adolescent medicine clinic.
Participants: Individuals who had been using ENG for 6 months or more were eligible. A control group of non-ENG users who had been seen during the same period was identified to compare weight/BMI over time. Cases were matched to controls on age, BMI, and race.
Interventions and Main Outcome Measures: Electronic medical records were reviewed for weight/BMI change and ENG side effects. The study was designed to have 80% power to detect a 2-kg weight difference between cases and controls.
Results: Participant mean age was 17 (±2) years. Mean follow-up was 24.5 (±9.3) months. Forty-three of 197 ENG users removed the implant early; 3/43 (6.3%) patients cited weight gain as the primary reason for removal. Mean weight change for ENG users was +3.6 (±7.8) kg vs +3.1 (±5.9) kg for controls (P = .43); mean BMI change was +1.3 (±2.9) in cases vs +1.0 (±2.3) in controls (P = .204). Overall regression analyses showed no group differences among cases and controls.
Conclusion: Long-term ENG use did not lead to significant weight gain in this sample of adolescent and young adult women. This study supports the statement that ENGs are an effective and weight-neutral option.
Key Words: Contraceptive implant, Weight, Adolescents, Contraception, Etonogestrel

Introduction

Multiple national organizations including the American Academy of Pediatrics and the Society for Adolescent Health and Medicine recommend long-acting reversible contraception (LARC) as first-line contraception for adolescents.[1] When choosing among LARC methods, adolescents more often opt for the contraceptive implant vs an intrauterine device (IUD), compared with adults.[2] Etonogestrel subdermal implants (ENGs) are a form of LARC, a progestin-only birth control with a contraceptive efficacy of 99.9%, effective for at least 3 years.

There are many factors that affect contraceptive method decision-making, which have been well described in the literature (cost, reliability, side effects, patient adherence, provider recommendations, peer/family influence). Concern about weight gain can deter the initiation and/or continuation of contraceptive methods, particularly for adolescent and young adult women.[3,4] One of the possible side effects of depot medroxyprogesterone acetate (DMPA; an injectable progestin-only contraceptive method) is weight gain, with an average 8-pound weight increase over 2 years of use.[5] Previous studies have shown inconsistent data regarding other progestin-only birth control methods (including ENG) and weight gain.[3,6] In a 2006 retrospective study of ENG users, 5% of study participants discontinued the method with the complaint of weight gain, but most of those participants were adult users.[7] In a 2013 study of young adult LARC users (more than 50% were between 21 and 30 years of age), almost 20% of study participants discontinued ENG use with complaints of weight gain.[8] A substudy of the CHOICE project analyzed weight changes in young adult women using progestin-only contraceptive methods. The prospective cohort included 427 young adult women with a mean age of 24.4 years and ENG users experienced a 2.1 -kg weight gain compared with 0.2 kg for nonhormonal copper IUD users.[9] Adjusted analyses showed no difference in weight gain among all progestin contraceptive methods compared with the copper IUD. This study did show that black race was associated with significant weight gain (1.3 kg) among all users of progestin-only contraceptive methods (ENG, DMPA, and levonorgestrel IUD),[8] but there was no separate analysis of contraceptive method type. A more recent study (2018) showed a small but statistically significant weight increase in adult (18-44 years of age) ENG users compared with users of the copper IUD.[10] In nearly all of these studies, participants were adult women whose physical growth was complete. There is little information about weight gain and ENG use in adolescents; this is the reason for our study.

Conflict of Interest Statement: Nothing to disclose.

* *Address correspondence to:* Mary E. Romano, MD, MPH, Division of Adolescent/Young Adult Health, Department of Pediatrics, Children's Hospital at Vanderbilt, Vanderbilt University Medical Center, 719 Thompson Lane, Suite 36200, Nashville, TN 37204

E-mail address: mary.romano@vumc.org (M.E. Romano).

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Thus the purpose of this study was to evaluate weight and body mass index (BMI) changes in adolescent and young adult users of ENG compared with nonusers. We hypothesized that adolescent and young adult women who use the contraceptive implant for more than 6 months will have a measurable change in weight and/or BMI compared with controls. Because one of the reported side effects of DMPA is weight gain, we hypothesized that adolescents who had used this contraceptive method before ENG insertion would be at increased risk for weight/BMI change.

Materials and Methods

Participants

This was a retrospective chart review of 197 adolescent and young adult women who chose ENG insertion at an adolescent medicine clinic in Nashville, Tennessee. This is a primary care and subspecialty clinic that routinely provides contraceptive counseling and management options. Nursing and clinical staff enter adolescents who chose LARC methods in a database panel, which is housed within the institutional electronic medical record system. This database includes patient name, medical record number, and ENG insertion date and removal (if applicable). On the basis of this database, we reviewed medical chart data for all female adolescents ages 12-22 years who received the ENG implant between August 2011 and August 2016 in this clinic. All adolescents who had the ENG implant in place for 6 months or longer were eligible and selected as cases, and then followed for the duration of ENG use. ENG users with previous pregnancy were not excluded but these data were abstracted from their chart and used in analysis.

A normal, natural part of adolescent pubertal development involves linear and weight growth. Therefore, distinguishing between normal and abnormal weight gain can be difficult. To aid in analysis, a group of control patients who had been seen at the same clinical site for a well visit during the same time frame (2011-2016) was identified to compare weight change/trajectory over time.

Case-Control Matching

The following objective weight variables were collected for cases: weight at insertion (time 0), weight at last documented follow-up clinic visit (or removal, time 1), BMI at insertion (time 0), BMI at last documented follow-up clinic visit (or removal, time 1), and BMI percentile at insertion (time 0) and at last documented follow-up clinic visit (or removal, time 1). As per office triage procedures at this clinical site, weight and height were measured at each visit and entered into the electronic medical record by a licensed medical assistant. BMI is calculated in the electronic medical record on the basis of height and weight at the time of visit. BMI percentile (for those younger than 20 years of age) was also abstracted from electronic medical record chart review. Postinsertion office visit notes and phone call records were reviewed to obtain objective weight and BMI values, patient-reported side effects, and reasons for early ENG discontinuation (if applicable).

All female adolescents who had been seen at the same clinic site for an annual well physical examination visit during the study period (2011-2016) were eligible to be controls. Cases were matched to controls with respect to age, BMI ($\pm$1) and race (on the basis of demographic data at the time of ENG insertion). Because of the potential weight gain association with DMPA, controls with current or previous DMPA use were excluded. Controls with a recent (defined as $<$1 year ago) or current pregnancy were also excluded. Controls were ineligible if they had a previous or current ENG use. Those using oral contraceptive pills, transdermal patch, or vaginal ring were not excluded because these contraceptive methods are thought to be weight-neutral. Because this study was on the basis of chart review data, we were unable to screen for other medical conditions at the time of inclusion. On the basis of electronic medical record review, we identified 1999 possible control subjects. From this sample, a single control was matched to a single case using the following criteria: case age at the time of ENG insertion (within 6 months), race, and follow-up. Follow-up was defined according to case duration of ENG use. For cases, months since ENG insertion was obtained from the electronic database and we identified controls who had been seen in the clinical setting and had a weight documented on a similar time frame ($\pm$1 month). As an example, if a 16-year-old African American, non-Hispanic female case with a BMI of 17 had ENG in place for 20 months, we identified a 16-year-old African American non-Hispanic control with a similar BMI of 17 ($\pm$1) who had been seen in the clinic for an annual well visit within the study period (time 0), and then had a follow-up visit 20 months later (time 1). Both authors were responsible for matching controls and followed the same procedure.

The following objective weight variables were collected for controls: weight and BMI at time 0 (including BMI percentile if 20 years of age or younger), weight and BMI/BMI percentile at time 1 (which was on the basis of months since ENG insertion for the age-matched case). As was done with case subjects, weight and height were measured at each clinical visit and entered into the electronic medical record by a licensed medical assistant. BMI percentile was abstracted from electronic medical record during chart review. Additional demographic and patient characteristics obtained in data abstraction for cases and controls included: race, insurance status, sexual history, current and previous contraceptive use (when applicable), and current or previous pregnancy.

Statistical Analysis

On the basis of previously reported literature, a BMI change of 1 and a weight change of 2 kg over time is considered clinically significant.[11] Therefore, this study was sufficiently powered to provide 80% power to detect a change of: (1) 1 in BMI between the 2 groups (assuming a common SD of 5); and (2) 2 kg in weight (assuming an SD of 10). We calculated the mean and median weight and BMI change over time in our sample. Continuous variables were compared between matched cases and controls using Wilcoxon signed rank test. Binary variables were compared

between groups using McNemar χ^2 test (of note, race was treated as a binary variable: black vs other). The primary outcomes were weight at time 1, weight change, BMI at time 1, and BMI change. We fit separate linear mixed effects models to assess the differences between cases and controls. Other covariates in the model included weight at time of insertion, height, duration of use, race, and previous pregnancy. We also fit multiple linear model for weight and BMI among cases including weight or BMI at time of insertion, height (for weight model), age, duration of use, race, use of DMPA, and previous pregnancy as the independent variables. Data analysis was conducted using statistical software R version 3.3.0.[12] This project met criteria for expedited review by the institutional review board.

Results

The mean age of participants in cases and controls was 17 (±2) years and almost 70% identified as non-Hispanic black (Table 1). The median BMI at study onset for both cases and controls was in the 86th percentile, which is considered overweight. We found significant differences between the cases and controls at baseline (time 0) for insurance status, with cases being more likely to have public insurance ($P < .001$). There was also a significant difference in sexual activity and use of hormonal contraceptive pills. Cases were more likely to be sexually active ($P < .001$), and more likely to have previously used oral contraceptive pills ($P = .04$). In addition, cases were significantly more likely than controls to have previously used DMPA and ENG. Because DMPA users were excluded from the control group and some cases were repeat ENG users, these differences were expected.

The mean duration of ENG use was 24.5 (±9.3) months with 21.8% of users (43/197) discontinuing the method early (before 3 years). Among those with early removal, 6.3% (n = 3) cited weight gain as the primary reason for removal. Overall mean (±SD) weight gain for ENG users, 3.6 (±7.8) kg, was not statistically different than that for controls, 3.1 (±5.9) kg ($P = .43$). The mean BMI increase for ENG users was 1.3 (±2.9) compared with 1.0 (±2.3) for controls ($P = .204$).

On the basis of linear models, cases had an increase in weight that was 0.55 kg more than controls (95% confidence interval, −0.84 to 1.95; $P = .4286$) with the same baseline weight, height, race, and previous pregnancy status. We used the same linear mixed effects model to compare BMI between cases and controls. Cases had a 0.26 higher change in BMI compared with controls (95% confidence interval, −0.27 to 0.79; $P = .3254$) with the same baseline BMI, current height, race, and previous pregnancy status. These findings are summarized graphically in Figure 1. Additional subanalyses of cases did not show any statistically significant change in weight or BMI, controlling for DMPA use. Overall regression analyses showed no group differences between cases and controls, when adjusted for age, length of ENG use, race, previous DMPA use, or previous pregnancy.

Discussion

This study is one of the first to examine weight and BMI changes in a large sample of exclusively adolescent and

Table 1
Demographic and Clinical Characteristics According to Group

	ENG Users (n = 197)	Control (n = 197)	*P*
Mean age ± SD, years	17 ± 2	17 ± 2	–
Mean weight at time 0 ± SD, kg	69 ± 19	69 ± 19	.265
Mean BMI at time 0 ± SD	26.3 ± 6.8	26.3 ± 6.8	–
Mean BMI percentile at time 0 ± SD	73 ± 29 (n = 180)	73 ± 29 (n = 183)	.41
Mean weight at time 1 ± SD, kg	72 ± 21	72 ± 20	.764
Mean BMI at time 1 ± SD	27.6 ± 7.6	27.3 ± 7.3	.207
Mean BMI percentile at time 1 ± SD	75 ± 28 (n = 138)	72 ± 31 (n = 138)	.104
Race, n (%)			–
Non-Hispanic white	51 (26%)	52 (26%)	
Non-Hispanic black	136 (69%)	137 (70%)	
White Hispanic	8 (4%)	6 (3%)	
Asian	1 (1%)	1 (1%)	
Black Hispanic	1 (1%)	1 (1%)	
Previous DMPA usage (yes), n (%)	51 (26%)	0 (0%)	<.001
Insurance status, n (%)			
Private	37 (19%)	78 (40%)	<.001
Public	160 (81%)	119 (60%)	<.001
Previous pregnancy (yes), n (%)	19 (10%)	12 (6%)	.265
Previous birth (yes), n (%)	12 (55%)	4 (33%)	1
Sexually active (yes), n (%)	153 (78%)	73 (37%)	< .001
Previous oral contraceptive pill use (yes), n (%)	99 (50%)	80 (41%)	.04
Previous transdermal contraceptive use (yes), n (%)	6 (3%)	4 (2%)	.752
Previous NuvaRing (Merck) use (yes), n (%)	8 (4%)	5 (3%)	.579
Previous progestin-only pill use (yes), n (%)	3 (2%)	2 (1%)	1
Previous ENG use (yes), n (%)	7 (4%)	0 (0%)	.023
Previous IUD use (yes), n (%)	4 (2%)	4 (2%)	1
Mean Duration of ENG use ± SD, months	24.5 ± 9.3		
Mean weight change time 0 to time 1 ± SD, kg	+3.6 ± 7.8	+3.1 ± 5.9	.43
Mean BMI change time 0 to time 1 ± SD	+1.3 ± 2.9	+1.0 ± 2.3	.204

P values not provided for matching variables (age, race, BMI).
BMI, body mass index; DMPA, depot medroxyprogesterone acetate; ENG, etonogestrel subdermal implant; ESI, etonogestrel subdermal implant; time 0, date of ESI insertion for cases and date matched within 1 month of insertion for controls; time 1, last documented clinic visit or date of ESI removal for cases and date matched within 1 month of last documented clinic visit for controls.

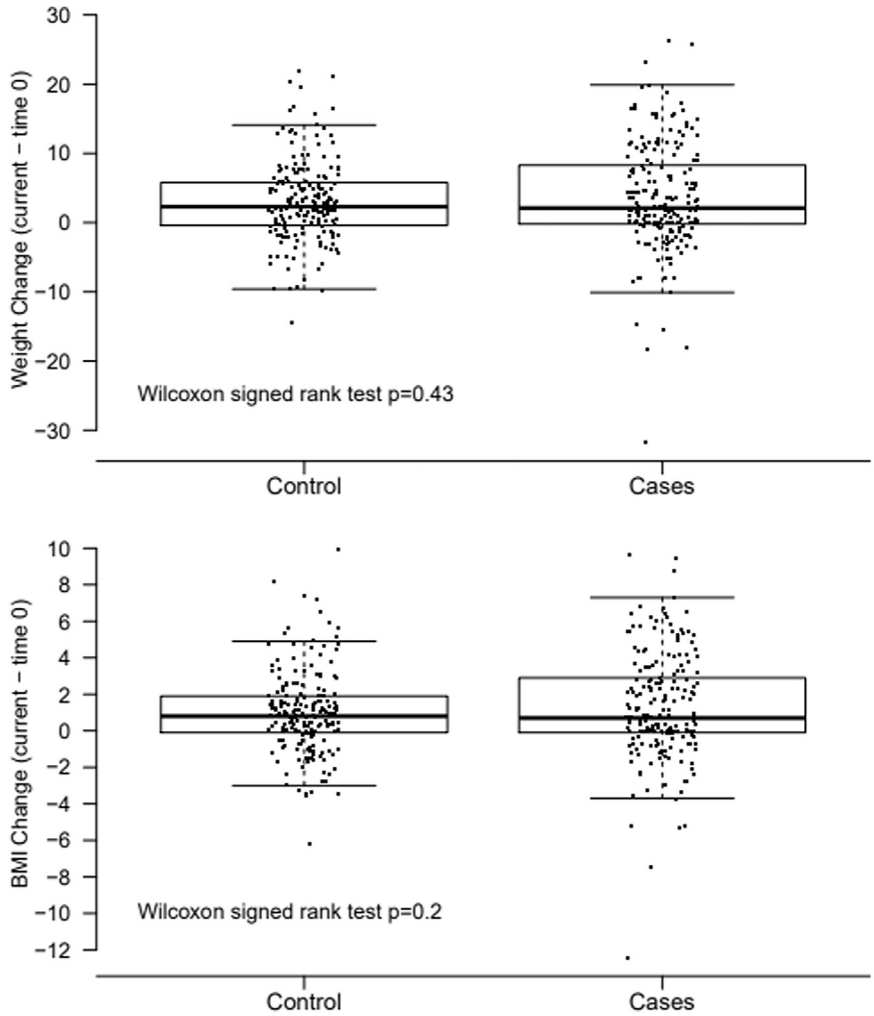

Fig. 1. Box and whisker plots of weight (in kilograms) and body mass index (BMI) change according to group. The bold solid line represents median value, and the upper and lower box margins represent the 75th and 25th quartiles, respectively. "Current" indicates time 1 as referenced in the text.

young adult women with long-term use of the etonogestrel contraceptive implant. It is also to our knowledge, the first study to investigate weight and BMI changes in a younger patient population who can be expected to have some developmentally normal changes in weight and BMI. This study showed that long-term ENG use does not lead to significant weight change. This lack of effect persisted even when adjusted for multiple potentially confounding factors, such as previous DMPA use, pregnancy, baseline weight/BMI, and race.

Weight gain is a reported side effect in 5%-22% of ENG users and perceived weight gain has been cited as a reason for hormonal method discontinuation.[9,13] However only a small percentage of patients actually discontinue ENG use because of weight changes.[9,14] Although in this study we did not investigate subjective patient assessment of weight gain, we did objectively collect information about weight and BMI in adolescent and young adult ENG users. The international multisite randomized trial by Bahamondes et al in 2018 showed that adult ENG users gained a mean of 3.0 kg over 36 months of use, compared with 1.1 kg in nonhormonal IUD users.[10] We showed a similar weight increase over time in our adolescent ENG users, with a mean increase of 3.6 (±7.8) kg (over a mean of 24.5 ± 9.3 months). This weight change was in an adolescent and young adult sample that is expected to gain weight as part of normal adolescent growth and development. Because we do not have a large number of nonhormonal copper IUD users in our clinic, we used BMI and age-matched population controls for study comparisons. Thus, our case-control study revealed that weight gain in ENG users was not statistically different compared with weight gain in nonusers. The previously referenced study by Bahamondes et al showed a 1.1 kg annual increase in weight per year over the duration of ENG device use, but this was thought to have little clinical significance and similar to normal annual adult weight trends.[10] Although 3.6 kg in our adolescent and young adult sample might seem clinically significant, it was not statistically significant compared with the 3.1 kg weight gain in non-ENG users. Our study results are also consistent with the 2017 CHOICE project prospective data, which showed no differences in BMI, body weight, or composition among 149 young adult LARC users (levonorgestrel IUD, nonhormonal copper IUD, or ENG) over 12 months of continuous use.[14] Modesto et al recently reported a 4.1-kg increase in weight in adult ENG users (mean age, 30.4 years) after

12 months of continuous ENG use.[15] Comparatively, we report a 3.6-kg increase in weight over a longer duration (mean, 24.5 months) and in a younger population (mean age, 17 years). We were unable to stratify according to baseline status (underweight, normal weight, overweight, obese), which might have been helpful because Bahamondes et al reported that heavier adult women tended to gain more weight compared with their thinner counterparts.[10] This might have been particularly relevant for our study because the median BMI percentile for ENG users and controls at time 0 was at the 86th percentile, which meets the criteria for overweight. Therefore, stratifying according to baseline BMI and BMI percentile might be a suggested area for further study. In our study we did, however, investigate baseline weight as a confounding variable in weight/BMI change. No association was found in our study participants.

In general, adolescent and young adult users of ENGs are satisfied with their contraceptive method.[8,16,17] Despite the anecdotal reports of weight gain in progestin-only methods, only 6.3% of our study patients cited weight gain as the primary reason for removal.

This study has several strengths including a large, racially diverse study population and the inclusion of age- and BMI-matched controls in data analysis. We also controlled for a number of variables that might affect weight and BMI change in an adolescent and young adult population (pregnancy and previous injectable contraceptive use). We also used objective measurement of body weight at 2 distinct time points, not subjective reports of weight gain. However, there are also some study limitations. This retrospective study was conducted via chart review and retrospective data might be inaccurate or incomplete. There was also no standard follow-up or scheduled postinsertion appointments and therefore data points used in analysis were on the basis of the available chart review data. Matched controls were selected at time of data collection, not at time of ENG insertion because study design did not allow for control matching at the study onset. We also did not control for diet, exercise, or metabolic conditions that might affect weight. However, this is true for ENG users and controls. There were also certain characteristics for which there was a significant difference between cases and controls. Cases were more likely to be sexually active, to have used oral contraceptive pills, and to have public insurance. We cannot accurately assess or predict what role sexual activity or insurance played in weight changes or behaviors that might contribute to changes in weight. Oral contraceptive pills are thought to be weight-neutral, so should not have altered the weight/BMI findings. Because weight gain is a known side effect of DMPA, controls with a previous use of this contraceptive method were excluded. Despite that that only cases had been previously exposed to DMPA, there was still no difference in weight gain between cases and controls. We originally hypothesized that adolescents who had used DMPA at a time before ENG insertion would be at increased risk for weight/BMI change. However, we did not find this to be true. This further supports the conclusion that ENG is a weight-neutral contraceptive option. Although our study does not suggest that ENG use contributes to weight gain, some of the cases were repeat ENG users; we treated each ENG insertion as a separate case. If longer duration of ENG use is a contributor to weight or BMI change (ie, patients who underwent replacement/reinsertion of a second ENG), a separate study on only repeat ENG users (or duration of continuous ENG use) might be helpful.

Future studies should consider identifying risk factors that might predispose adolescent and young adult women to gain more weight, particularly in participants who have gained more than 2 kg (which is commonly cited as a meaningful weight change in contraceptive research).[11] Dickerson et al showed that weight gain with LARC methods was more commonly reported by overweight and obese women, as opposed to their normal-weight counterparts.[8] As such, another area of future study would be to prospectively study weight change over time in those who are overweight or obese at baseline.

As the population of adolescent and young adult users of LARC increases, we have the ability and opportunity to investigate long-term side effects such as weight change. Weight gain is often a major concern and deterrent for adolescent patients when choosing a hormonal contraceptive method. Although the safety, efficacy, and acceptability of LARCs are well established, there has not been significant data reported on weight effects in this dynamic population, until now. This study supports the current recommendation of the etonogestrel implant as a weight-neutral, first-line hormonal contraceptive option for adolescents. We believe that this study adds to the contraceptive literature by providing evidence-based counseling recommendations that the etonogestrel implant does not carry a risk of weight gain in adolescent and young adult users. Because of the highly effective contraceptive efficacy of ENGs, adolescent and young adult women should be discouraged from changing to a less effective contraceptive option because of perceived weight gain. Adolescents and young adult women should continue to be counseled and reassured that ENGs are a safe and weight-neutral contraceptive method.

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