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Contraceptive Failure Rates of Etonogestrel Subdermal Implants in Overweight and Obese Women

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Abstract

Objective—To estimate the contraceptive failure rates of the etonogestrel subdermal contraceptive implant in overweight and obese women, and compare failure rates to women of normal weight and women using intrauterine devices (IUDs).

Methods—The Contraceptive CHOICE Project is a large prospective cohort study designed to promote the use of long-acting reversible contraceptive methods to reduce unintended pregnancies in the St. Louis region. Participants are provided reversible contraception of their choice at no cost. We collected baseline height and weight of each participant. During each survey, participants were asked about missed menses and possible pregnancies. Any participant who suspected a pregnancy was asked to come in for urine pregnancy testing. Analysis includes the first 8,445 participants enrolled in CHOICE of which 1,168 chose the implant and 4,200 chose the IUD. Student's t-test, χ^2 test, and Kaplan-Meier survival curves were used to perform statistical analyses to estimate failure rates in overweight and obese women using the implant and IUDs.

Results—Of the women choosing the implant, 28% were overweight and 35% were obese. Of the women who chose an IUD, 27% were overweight and 35% were obese. The 3-year cumulative failure rates for implant and IUD users were less than 1 per 100 women-years and did not vary by body mass index (BMI).

Conclusion—We found no decrease in the effectiveness of the implant in overweight or obese women. The implant may be offered as a first-line contraceptive method to any woman seeking a reversible, and reliable birth control method.

INTRODUCTION

There are few studies that examine the effectiveness of the etonogestrel (ENG) subdermal contraceptive implant in overweight and obese women. The ENG implant is the only contraceptive implant currently marketed in the United States and is FDA approved for 3 years of use. The implant is composed of a single rod that releases etonogestrel, a third-generation progestin (1), and is among the most effective contraceptive methods with

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efficacy that is indistinguishable from that of sterilization and intrauterine devices (IUDs) (2). Based on a systematic review of published trials, the failure rate for the ENG implant was found to be 0.00 per 100 women-years of use (3). However, the company-sponsored clinical trials excluded subjects who were >130% of their ideal body weight (4).

Half of the 6 million pregnancies that occur yearly in the United States are unintended (5). Of these unintended pregnancies, approximately 60% report using some form of contraception during the month the pregnancy occurred (6). Because most women use a contraceptive method that requires strict adherence and compliance, most pregnancies result from incorrect method use rather than method failure (7). To reduce the number of unintended pregnancies, clinicians should counsel women to use the most effective methods of contraception as first-line options. Long-acting reversible contraception (LARC), including IUDs and implants, has been proven to be safe, effective, cost-effective, “forgettable,” and not user-dependent (8). However, less than 6% of women between the ages of 15 and 44 years in the United States use one of these methods for birth control (9).

Given the fact that nearly two thirds of reproductive-aged women in the United States are overweight or obese (10), it is crucial to understand the effectiveness of the ENG implant in this population. Both the levonorgestrel intrauterine system (LNG-IUS) and the copper T380A IUD are ranked in the top tier of contraceptive effectiveness (11). While the scientific literature clearly suggests that body weight does not decrease the effectiveness of the IUD (12), there is little information regarding the effectiveness of the ENG implant in relation to body weight, leading to controversy and confusion when counseling overweight and obese patients. The purpose of this study is to provide an estimate of the contraceptive failure rates of the ENG implant among overweight and obese women. Our hypothesis was that there is no significant difference in failure rates by body mass index (BMI) status among implant users as compared to the reference group of IUD users.

MATERIALS AND METHODS

We analyzed data from the Contraceptive CHOICE Project (CHOICE) to estimate failure rates among overweight and obese women using the implant or IUD (LNG-IUS or copper T380A) for contraception. The CHOICE Project is a prospective cohort study of 9,256 women ages 14–45 in the St. Louis area designed to promote the use of long-acting reversible contraceptive (LARC) methods and reduce unintended pregnancies. The project has been fully described in a previous publication (13). The CHOICE protocol was approved by the Washington University in St. Louis School of Medicine Human Research Protection Office before the initiation of recruitment and participants provided informed written consent.

Participants selected their baseline contraceptive method after undergoing standardized contraceptive counseling that presented all reversible contraceptive methods during the in-person enrollment session. All method use was approved by a study clinician prior to initiation. Participants were provided no-cost contraception and could change methods at any time during study participation. We recorded height and weight of each participant at baseline enrollment and at any subsequent visits to the study clinic. Prior to contraceptive

method initiation, every participant completed a sensitive urine pregnancy test to rule-out preexisting pregnancy. Participants completed standardized surveys at enrollment and 3 months, 6 months, and every 6 months after enrollment for the duration of study participation. Recruitment began in August 2007; participants enrolled before January 1, 2010 were followed for 36 months and women enrolled after this date were followed for 24 months. This analysis includes the first 8,445 participants enrolled in the CHOICE Project between August 2007 and October 2010 of which 1,168 chose the implant and 4,200 chose an IUD. The full cohort of 9,256 participants was not analyzed because follow-up information is not yet available for all participants. Lost-to-follow-up among the cohort through 12, 24, and 36 months were low (6.9%, 12.8%, and 22.5%, respectively) and did not vary by contraceptive method.

At enrollment participants were instructed to call the project at any time during study participation if they suspected a pregnancy. During each follow-up survey, participants were asked about missed menses and possible pregnancies. When a woman reported a pregnancy during a regularly scheduled survey or at an interval time, we collected data regarding last menstrual period, contraceptive method used at time of conception, pregnancy intention at time of conception, and plans for pregnancy and contraception after pregnancy. Participants who suspected a pregnancy were asked to return to the study clinic for urine pregnancy testing. All pregnancies were recorded in a pregnancy log. Conception date was calculated from the last menstrual period, estimated gestational age, or estimated date of confinement.

We defined contraceptive method failure as conception that occurred during a period of method use. Survey data and research documentation recorded information about periods of contraceptive use, including method start and stop dates. For IUD and implant users we also recorded insertion and removal dates. If an IUD user experienced a known expulsion and became pregnant, the pregnancy was attributed to “no method use.” If the woman was not aware that the device had been expelled, the pregnancy was considered an IUD failure. Pregnancies that occurred during periods of “no method use” were not considered a method failure. Intended pregnancies, defined as a woman who stopped a method with the desire to conceive, were excluded from this analysis. All pregnancies were reviewed to rule out pre-insertion conception instead of a method failure.

Body mass index [BMI: (weight(kg)/height(m²))] was calculated using baseline measurements. We categorized participants as normal weight, overweight, or obese using NHANES criteria (14). Weight change during use was not considered in this analysis. The significance level alpha was set at 0.05. Means, standard deviations, frequencies and percentages were used to describe the baseline demographic characteristics of study participants. For the comparison between implant and IUD users, Student's t-test was used for continuous variables, and χ^2 test was performed for categorical data. Kaplan-Meier survival curves and logrank tests were constructed to compare implant and IUD contraceptive failure rates among normal weight, overweight, and obese women. We recorded segments of contraceptive method use for each participant. If a participant did not get pregnant, we censored her at the time when she stopped the use of her contraceptive method. In cases of lost-to-follow-up, we censored participants at the last survey date when they were reached by telephone. We completed a post-hoc sample size calculation. A sample

size of 1,168 participants of which 28% are classified as overweight and 35% as obese will have greater than 80% power to detect a difference in contraceptive failure rates of 0.5% in the normal weight group, to 0.8% of the overweight group, and 3% in the obese group (with type I error rate of 0.05) using chi-square test of equal proportions. We used STATA 11 (StataCorp LP, College Station, TX) to perform the statistical analyses.

RESULTS

Of the 8,445 women enrolled in CHOICE, 1,168 (14%) women chose the implant and 4,200 (50%) chose an IUD at enrollment. Continuation of implant and the IUD was 83.3% and 86.6% at one year, respectively. Table 1 presents the baseline demographic and reproductive characteristics of participants who chose the implant compared to participants who chose an IUD, separated into the three BMI categories. Compared to IUD users, implant users were younger, more likely to identify as black or Hispanic, be single and have lower educational level, lower income, and lower parity.

The BMI distribution among women using the implant and IUD were similar ($p=0.97$, results not shown). Among implant users, 37% were normal weight (BMI 18.5–24.9), 28% were overweight (BMI 25–29.9), and 35% were obese (BMI ≥ 30). Similarly, among IUD users, 38% were normal weight, 27% were overweight, and 35% were obese.

Table 1 also provides the baseline demographic and reproductive characteristics of participants by BMI distribution. Overweight and obese participants were significantly more likely to be older, black, married, less educated, uninsured, receiving public assistance, and report greater parity than participants who were normal weight.

We observed one unintended pregnancy among 1,377 women-years of implant use. The pregnancy occurred in an obese participant who had a BMI of 30.7 at enrollment. The cumulative implant failure rates among both normal and overweight participants was 0.00 per 100 woman-years; whereas the cumulative implant failure rate among obese participants was 0.23 per 100 woman-years.

In our analysis of 5,985 women-years of IUD use, we observed 5 unintended pregnancies in normal weight, zero in overweight, and 7 in obese participants during the first year of use. In the second year of use, there was 1 pregnancy in normal weight, 4 in overweight, and zero in obese participants. Finally, in the third year of use, there were zero in normal weight, 2 in overweight, and zero pregnancies in obese participants. Twelve pregnancies occurred in women who were unaware that their IUD had expelled, 4 women who had partial IUD expulsions and 3 during method use. The overall failure rates were less than 1 per 100 women-years and did not vary by BMI status.

We performed Kaplan-Meier survival curves estimating unintended pregnancies for the implant compared with IUD in normal weight, overweight, and obese women (figure not shown). We found no differences in the contraceptive failure rates by method type (implant versus IUD) in normal weight, overweight, and obese women (respective p -values are 0.24, 0.28, and 0.62).

DISCUSSION

In this analysis, we examined whether overweight or obese women using the implant experienced higher contraceptive failure rates than normal weight women. Of the 1,377 women-years of implant use, we observed only one pregnancy in an obese participant. This participant reported oral contraceptive pill (OCP) use prior to the implant insertion. The implant instructions specify insertion may occur anytime within 7 days of the last active pill (15). We cannot be certain that this participant was taking her OCPs as instructed; incorrect use may have resulted in ovulation prior to the implant insertion at our clinic. We found no other device failures in the 1,168 women who chose the implant. We also compared the failure rate of implant users to IUD users in the survival analyses and found contraceptive failure rates did not vary by weight in women using implants or IUDs. There were no failures even among women who had BMI greater than 40.

There is limited information regarding typical-use failure rates in overweight and obese women who use the ENG implant. The findings from this analysis add to the limited literature on the relationship between efficacy of the ENG implant and body weight. Our findings are particularly salient given the current epidemic of obesity in the U.S. population where 30% of adults are obese (16). Given the dual epidemic of unintended pregnancy and obesity, preventing unintended pregnancy in the obese population is an important public health concern (17). Because obesity complicates pregnancy, it is imperative that clinicians recognize the risk of unintended pregnancy for obese women outweighs the risk of contraceptive use. LARC methods, including the implant and IUD, have very few contraindications and are appropriate for almost all women. Our study findings can help clinicians provide more appropriate counseling and support to patients considering the implant regardless of BMI status.

A number of studies have investigated the relationship the effect of weight on oral contraceptive effectiveness. However, the results are not consistent. Some studies have suggested that obese and overweight adult women have a greater risk of unintended pregnancies while using oral hormonal contraceptives (18, 19), but other studies have failed to demonstrate this association (20). Obese women may be more likely to be noncompliant which could lead to contraceptive failure and unintended pregnancies (20). In a randomized double-blind trial of two 21-day monophasic OCP formulations in normal weight and obese women, it was determined that higher OCP failure rates in obese women was attributed to OCP noncompliance, not decreased ovarian suppression (21).

Our study has a number of strengths. The CHOICE Project is a large prospective cohort study of women who initiated a new contraceptive method, including 14% who chose the implant. Our low rate of loss of follow-up through 36 months (81%) does not vary by contraceptive method. The participants represent a diverse group of women in terms of race, ethnicity, marital status, and socioeconomic status that strengthens the generalizability of our findings. We also realize that BMI reflects overall amount of fat in an individual, whereas body weight indicates total body mass (22); thus, we performed multivariate analyses comparing pregnancy rates of all LARC users who are >70 kg to those who are 70 kg. We found that women who are >70 kg were no more likely to experience a failure with

the implant compared to those who are ≥ 70 kg (adjusted relative risk= 1.34, 95% CI 0.53, 3.43), but the precision of this estimate is limited by rare outcomes and the number of women in this weight group.

Limitations of this study include non-randomization of study participants, a convenience sample, and inclusion criteria that participants must initiate a new contraceptive method. Despite a sample size of over 1,000 implant users, we recognize that our study is underpowered to detect smaller differences than those listed in our sample size calculation. However, our study is one of the largest prospective contraceptive implant studies in the literature, and one of the few to include overweight and obese women. Because the outcome of unintended pregnancy is so rare in implant users, future research with a larger sample size could help determine whether a more modest difference exists.

In conclusion, our results suggest that the effectiveness of the implant does not vary by BMI. Both the implant and IUD have very low failure rates in normal-weight women and in overweight and obese women. Clinicians should counsel women to use highly-effective contraceptive methods, such as the implant and IUD, regardless of the patient's weight.

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Table 1
 Characteristics of Participants by Body Mass Index, Stratified by Baseline Chosen Method

	IUDs (n=4200)				Implant (n=1168)			
	Normal Weight (n=1584)	Overweight (n=1149)	Obese (n=1467)	P*	Normal Weight (n=439)	Overweight (n=324)	Obese (n=405)	P*
								P†
Age (mean, SD)	25.3(5.6)	26.5(6)	27.5(6.1)	<0.01	21.5(5.1)	23.1(5.9)	24.2(5.9)	<0.01
Race				<0.01				<0.01
Black	471(29.9)	549(47.9)	965(65.9)		218(50.5)	199(62.2)	263(65.4)	
White	980(62.2)	513(44.8)	418(28.5)		174(40.3)	93(29.1)	106(26.4)	
Others	125(7.9)	83(7.2)	82(5.6)		40(9.3)	28(8.8)	33(8.2)	
Hispanic				0.13				<0.01
Yes	81(5.1)	61(5.3)	56(3.8)		23(5.3)	33(10.2)	30(7.4)	
No	1499(94.9)	1086(94.7)	1410(96.2)		415(94.7)	290(89.8)	375(92.6)	
Marital status				0.01				<0.01
Never married	918(58)	616(53.7)	756(51.6)		322(73.7)	204(63)	247(61)	
Not married but living with partner	345(21.8)	252(22)	336(22.9)		78(17.8)	68(21)	95(23.5)	
Married	219(13.8)	179(15.6)	248(16.9)		23(5.3)	36(11.1)	37(9.1)	
Divorced, separated, or widowed	101(6.4)	101(8.8)	126(8.6)		14(3.2)	16(4.9)	26(6.4)	
Education				<0.01				0.79
High school or less	432(27.3)	376(32.8)	479(32.7)		232(53)	179(55.2)	215(53.1)	
Some college or more	1152(72.7)	771(67.2)	988(67.3)		206(47)	145(44.8)	190(46.9)	
Insurance				0.05				0.01
No	590(37.3)	458(40.1)	609(41.6)		154(35.9)	135(41.9)	184(45.9)	
Yes	990(62.7)	684(59.9)	855(58.4)		275(64.1)	187(58.1)	217(54.1)	
Income per month				<0.01				0.21
None	309(19.9)	197(17.4)	233(16.1)		138(31.9)	94(29)	104(25.8)	
\$1-800	477(30.7)	309(27.2)	388(26.8)		170(39.3)	115(35.5)	151(37.5)	
\$801-1600	420(27)	357(31.5)	505(34.9)		83(19.2)	74(22.8)	102(25.3)	

	IUDs (n=4200)		<i>P</i> [*]	Implant (n=1168)		<i>P</i> [†]
	Normal Weight (n=1584)	Obese (n=1149)		Overweight (n=439)	Obese (n=405)	
\$1601 and higher	348(22.4)	272(24)		42(9.7)	46(11.4)	
Receives any form of public assistance [‡]			<0.01			<0.01
No	1156(73)	686(59.7)		303(69)	167(43.7)	
Yes	428(27)	463(40.3)		136(31)	228(56.3)	
Parity			<0.01			<0.01
0	838(52.9)	402(35)		279(63.6)	148(36.5)	
1	381(24.1)	312(27.2)		91(20.7)	128(31.6)	
2	241(15.2)	267(23.2)		47(10.7)	78(19.3)	
3 or more	124(7.8)	168(14.6)		22 (5)	51(12.6)	

IUD, intrauterine device; SD, standard deviation.

Data are mean(SD) or n(%) unless otherwise specified.

^{*} *P*-value for the comparison among body mass index groups

[†] *P*-value for the comparison between intrauterine devices and implant.

[‡] Currently receives food stamps, Women, Infant, and Children (WIC), welfare, or unemployment.