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Association of Progestin Contraceptive Implant and Weight Gain

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Abstract

OBJECTIVE: To evaluate initiation of a two-rod, 150-mg levonorgestrel contraceptive implant on women's perceived and observed body weight.

METHODS: We conducted a secondary analysis of data from an open, randomized controlled trial of adult, nonpregnant, human immunodeficiency virus-negative women attending a public clinic in Kingston, Jamaica, who were assigned to initiate implant use either immediately or after a 3-month delay. The primary objective of the parent study was to assess the effect of initiation of the implant on the frequency of condom use. We compared study arms during follow-up using one-sided χ^2 tests for differences in perceived weight gain and loss, one-sided Wilcoxon-Mann-Whitney tests for median gain in measured weight, and logistic regression with generalized estimating equations for risk of gaining greater than 2 kg.

RESULTS: From 2012 to 2014, women were assigned to the implant (n = 208) or delay arm (n = 206). At 3 months, more women in the implant arm (15.3%) reported perceived weight gain than in the control arm (4.3%) (P=.01). Despite differences in perception, the implant and control arms did not differ significantly in median weight gain at 1-month (0.0 kg and 0.0 kg, respectively; P=.44) and 3-month visits (0.5 kg and 0.0 kg, respectively; P=.27). Study arms did not differ in risk of gaining greater than 2 kg (odds ratio 0.9, 95% confidence interval 0.6–1.3).

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CONCLUSION: We found no evidence of weight gain from short-term implant use. Through the power of the nocebo effect, the practice of counseling women to expect possible weight gain from initiating implant use could lead them to perceive weight gain even in its absence and contribute to the early discontinuation of this highly effective contraceptive method.

Many clinicians and patients believe that hormonal contraception, including progestin-only implants, causes weight gain. Product labeling for implants lists weight gain as a commonly reported side effect and as a leading cause of method discontinuation.[1,2] This labeling, which was based on noncomparative clinical trials or those comparing two implant types,[3] could simply reflect background noise because adult women tend to gain weight over time.[4–8] Given the lack of randomized trials with a nonhormonal control arm,[9] the causal effect of implants on weight gain is unknown.

The U.S. Centers for Disease Control and Prevention recommends that clinicians counsel implant users on possible side effects and consider measuring patient weight at baseline to monitor changes.[10] However, attempts to manage patient expectations by counseling new users on potential side effects could have the opposite effect than that intended. Counseling women on possible weight gain could lead to the perception of weight gain, even in the absence of a true effect, through the power of negative suggestion, that is, the nocebo effect.[11]

The perception of negative side effects is an important cause of method discontinuation or imperfect adherence to contraception. Discontinuation of implants is common with large studies in the United States and the United Kingdom reporting discontinuation rates of 12–17% at 1 year[12,13] and 31% at 2 years.[14] This discontinuation is a critical public health issue because implants are a highly effective method[15] and discontinuers often switch to a less effective method or use no method.[16] Establishing the true effect of implants on weight is needed to be able to provide evidence-based counseling to women. Our objective was to compare changes in weight (perceived and measured) between women randomized to either start the implant or to delay its initiation.

MATERIALS AND METHODS

We conducted a secondary analysis of data from an open randomized controlled trial on the effects of contraceptive implant on condom use conducted in 2012–2014 at a public clinic in Kingston, Jamaica (www.clinicaltrials.gov, NCT01684358).[17] Women seeking to use the Sino-implant (II) (150-mg levonorgestrel implant) were randomized to either receive it at enrollment (“implant” arm) or after 3 months of follow-up (“control” arm). The two-rod subdermal contraceptive implant contains the same amount of active ingredient as in the implant Jadelle.[18] Participants were nonpregnant, human immunodeficiency virus-negative women 18–44 years of age who met the following requirements: without contraindications to the implant, were not already using a long-acting contraceptive method or planning to start one in the next 3 months, and provided written consent to enroll. During the study consenting process, women were informed about the implant’s potential side effects, including weight gain. At the time of implant initiation, participants received a brochure listing these side effects. At 1 and 3 months, participants were weighed and completed

a face-to-face questionnaire, which included a question about perceived changes in health since their last visit: “Have you noticed any changes in your health since your last visit?” “Weight gain” or “weight loss” were two possible responses listed. Sample size calculations were based on the primary study objective.[17] Ethical review boards at the Jamaica Ministry of Health, the Centers for Disease Control and Prevention, and the University of West Indies approved the study. The trial was registered at ClinicalTrials.gov, number NCT01684358.

Because the weight data were not normally distributed, we used one-sided Wilcoxon-Mann-Whitney tests[19] to evaluate whether the implant arm had greater median gain in weight between enrollment and the two follow-up visits. As a secondary evaluation, we compared the risk of gaining greater than 2 kg (a common weight outcome in contraceptive research[20]) at either follow-up visit by study arm using logistic regression with generalized estimating equations to account for multiple visits from individual women. We also calculated one-sided χ^2 tests to test whether the implant arm was more likely than the control arm to perceive weight gain, and less likely to perceive weight loss, at the two follow-up visits. All analyses used an intent-to-treat approach.

RESULTS

Although 555 women were recruited, 133 did not meet the screening criteria and eight declined to consent (Fig. 1). Thus, 414 women were enrolled and randomized to the implant (n = 208) or control arm (n = 206). The 1-month and 3-month visits were completed by 203 women in the implant arm and by 198 and 186 women, respectively, in the control arm. As previously reported, participants had a median age of 25 years and most had completed high school (69%) and had never been married (71%).[17] History of contraceptive implant use was rare (3%). During follow-up, women in the implant arm had the device removed because of a preclinical pregnancy at the time of implant insertion (n = 3) or because of change in pregnancy intentions (n = 1). No other implant removals were known to have occurred.

Overall, the median weight at enrollment was 70.6 kg (range 36.0–128.0 kg) with no difference by arm (P= .93). Women in the implant arm gained a median of 0.0 kg and 0.5 kg by the 1-month and 3-month visits, respectively (Table 1). Women in the control arm gained a median of 0.0 kg by both follow-up visits. These median changes in weight were not statistically significantly different between arms at the 1-month (P= .44) or 3-month visit (P= .27). Similarly, women in the implant arm were not at higher risk of gaining greater than 2 kg than those in the control arm (odds ratio [OR] 0.9, 95% confidence interval [CI] 0.6–1.3). We also evaluated differences between arms in the percentage change in body mass index (calculated as weight (kg)/[height (m)]^2) and found no difference in interpretation (data not reported).

Few participants reported having gained or lost weight since their last visit (Table 1). Perceived weight gain did not differ between arms at the 1-month visit (P=.10) but at the 3-month visit, more women in the implant arm (15.3%) reported gaining weight than in the control arm (4.3%) (P= .01). Perceived weight loss did not differ by arm at either follow-up visit. Most of the visits (63% [38/60]) in which the woman perceived weight gain were not accompanied by a measured gain of greater than 2 kg. Perceived weight gain was associated

with having a measured gain of 2 kg among women in the implant arm (OR 3.5, 95% CI 1.8–6.9) but not among women in the control arm (OR 2.1, 95% CI 0.7–6.3). There was no relationship between women's overall weight and their perception of weight gain (OR 1.01, 95% CI 1.00–1.02).

DISCUSSION

We found no evidence that women initiating a levonorgestrel subdermal implant gained significantly more weight compared with control women over 3 months from insertion. Median changes in weight, overall, were negligible. A previous analysis of 11 trials of the single-rod etonogestrel implant that studied 942 women for 2 years or more found that most women gained weight: 0.1–2.5 kg (25%), 2.6–5.0 kg (24%), 5.1–7.5 kg (9%), and greater than 7.5 kg (11%).[21] However, these gains could reflect background noise; the annual weight increase in adult women has been estimated at 0.4–0.6 kg,[4,5] 0.1–0.2 kg/m^2 (body mass index),[6,7] and 0.5% change in weight.[8] Despite a lack of observed difference in weight between study arms in the present study, women using the implant were more likely to perceive weight gain than those in the control arm. This finding underscores the power of expectations on patient experiences.

The main limitation of the present trial is its short follow-up, which could have been inadequate for detecting gains. For ethical reasons, the control arm was offered the implant after 3 months of follow-up, an interval similar to the delay that the target population typically experienced in accessing contraceptive methods. Another limitation is that weight was not a primary trial outcome, and methods were not implemented to standardize its measurement such as weighing patients at the same time of the day or adhering to standard procedures regarding the amount of clothing worn. Although variations were unlikely to systematically differ between study arms or visits, they could be expected to bias the results toward the null of finding no difference between arms. Given the site's tropical climate, substantial differences in clothing weight, however, were unlikely. Also, because weight was not a focus of the trial, participants would have had no reason to attempt to manipulate their weight (eg, by skipping meals) before study visits. The retention rate of the cohort was excellent with 94% of enrolled women completing both follow-up visits. Furthermore, the randomized controlled design provides the strongest type of evidence for evaluating the method's effects.

Given health concerns[22] and strong social norms about weight, it is not surprising that women would factor in weight when making contraceptive decisions. The belief that contraceptive implants cause weight gain likely derives from two sources: data from studies with an inadequate design for answering this question and the phenomenon of women's perceptions conforming to their expectations. Study findings do not appear to support substantial gains in weight gain during the short-term interval after implant insertion and do not support counseling women that weight gain is an expected potential consequence of implant use.

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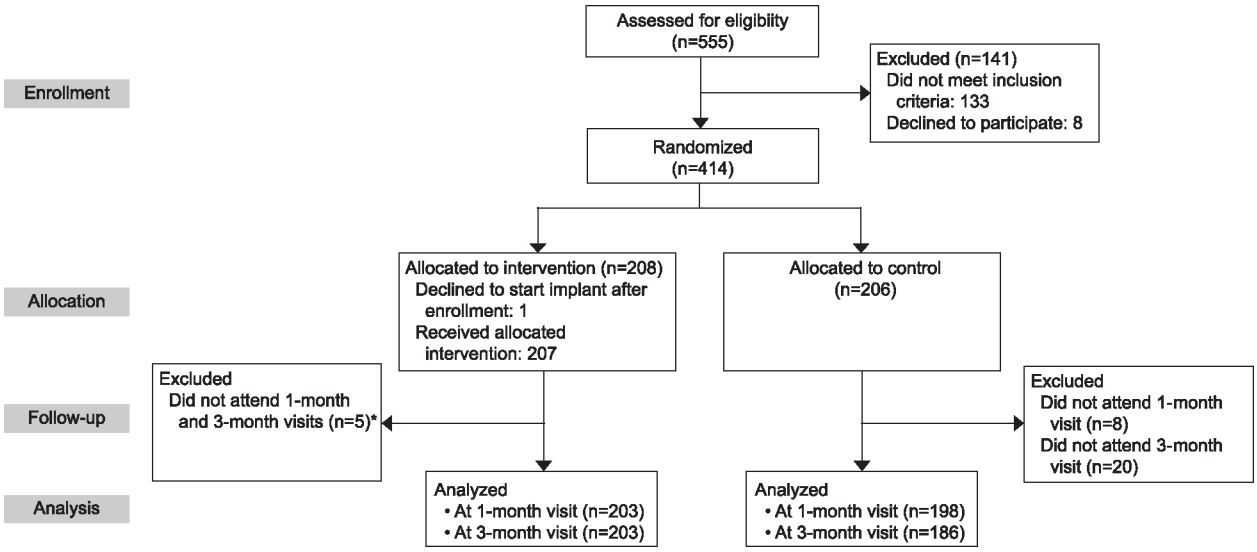

Fig. 1.

Screening, enrollment, and follow-up. *Includes woman who declined to continue in study after declining to start implant.

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Table 1.

Measured Weight Gain and Perceived Weight Gain and Loss by Study Visit and Arm

	1-Month Visit			3-Month Visit		
Weight Outcome	**Implant (n=203)**	**Control (n=198)**	***P*** *	**Implant (n=203)**	**Control (n=186)**	***P*** *
Change from enrollment (kg)	0.0 (−18.8 to 19.5)	0.0 (−13.0 to 3.3)	.44	0.5 (−16.5 to 19.0)	0.0 (−20.3 to 13.1)	.27
Gained more than 2 kg	24 (11.8)	34 (17.2)	.95	46 (22.7)	41 (22.0)	.61
Perceived weight gain	14 (6.9)	7 (3.5)	.10	31 (15.3)	8 (4.3)	<.001
Perceived weight loss	12 (5.9)	6 (3.0)	.95	15 (7.4)	13 (7.0)	.64

Data are median (range) or n (%) unless otherwise specified.

* *P* values from one-sided test of more (measured or perceived) weight gain, or less perceived weight loss, in the implant arm compared with the control arm.

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