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Revisiting menstrual bleeding patterns in adolescents using etonogestrel (ENG) implant

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Abstract

Etonogestrel (ENG) implant is an effective method of contraception. The implant is designed to provide contraceptive efficacy for three years with a relatively quick return of fertility upon its removal. Dysfunctional uterine bleeding (DUB) is a common side effect of long acting progestins and is often the reason patients state for removal or discontinuation. A retrospective chart analysis was completed on 292 patients who chose to be on the ENG implant. Age of patients ranged from 10-29 years of age with the average age at implant being 17 years +/- 3 years. Patients retained implant for 1-68 months with the average use being 21.0 months +/- 15.5 months. Over the 69 month period, 158 patients had the complaint of DUB (54.1%) and 46 patients with DUB had their implants removed because DUB was unresolved upon treatment and/or follow up (15.6%). Therefore, is it import for clinicians to be aware of the likelihood of DUB with implant usage and for them to be able to provide appropriate pre and post insertion counseling and treatment to all of their patients.

Keywords: Dysfunctional uterine bleeding, etonogestrel, adolescent contraception, abnormal uterine bleeding, subdermal contraceptive implant

Introduction

There are more than 20 million women worldwide who use long acting progesterone-only contraceptives (1, 2). Implanon™ and its radiopaque version, Nexplanon™, are Etonogestrel (ENG) implantable rods that are placed subdermally. These implants offer effective long term contraception for up to three years with a failure rate of only 0.3-1.0% annually. The implant is off-white, non-biodegradable rod of 4 cm in length with a diameter of 2 mm. Each implant contains 68 mg ENG and barium sulfate added to the Nexplanon™ version to allow for it to be radiopaque (3, 4). ENG prevents pregnancy by not just one but three mechanisms; (i) suppresses luteinizing hormone

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surge and partially suppresses follicle stimulating hormone (ii) increases viscosity of the cervical mucus that to impede penetration by sperm (iii) thins the endometrium to make implantation unlikely (3, 5, 6).

Studies show that ENG release from these implants is slow, steady, and gradually decreases over the 3 years of usage. One study showed that ENG releases 60 to 70 ug in the first day of implant, ensuring therapeutic levels are reached within the first few days after implant. After the initial surge of ENG release the rate decreases slightly to 40-45 µg/day with a gradual decline to 25-30 µg/day at the end of three years (5). This makes the 68 mg starting dosage more than adequate to prevent pregnancy over the three year duration of usage. Also of note is the quick return to fertility following implant removal. Unlike other long acting contraceptives, patients saw return of fertility 1-2 weeks post ENG implant removal (5). If used for the duration of the 3 years the ENG implant is also very cost effective, and cheaper than oral contraceptive pills as well as other hormonal methods.

Despite the many appeals of the ENG implants they are not without risks and unwanted side effects. The number one reason cited for removal of the implant is the troublesome side effect of dysfunctional uterine bleed (DUB). A review of data from the eleven clinical trials with Implanon™ found that 11.3% of users discontinued use due to bleeding irregularities, mainly frequent or prolonged irregular bleeding (3). Bleeding patterns vary from amenorrhea, to spotting, to prolonged heavy bleeding while on ENG implants (3, 4).

There are multiple causes of DUB. Causes include altered endometrial matrix metalloproteinase (MMP), irregular endometrial blood vessels, increased vascular fragility, decreased glandular and stromal support, and decreased epithelium integrity (5-7). A variety of treatments target these different mechanisms, with some treatments being more effective than others. Most common treatments include: Doxycycline, Mifepristone, Combination Oral Contraceptive, or NSAIDs. However, it should be noted that although these treatments may resolve a current episode of DUB, there has been no data to show long term improvement in subsequent bleeding patterns (1).

In Implanon™ users, the bleeding pattern is most likely to vary within the first three months post implant (5, 6). This can lead to frustration especially in an adolescent population which is so often more focused on the here and now than 3 months in the future. Since treatment is not always effective, it is important to discuss removal on a case by case basis. In supporting women's contraception needs it is important to remember and accept that all women have different levels of toleration for DUB and other side effects. Some women simply cannot tolerate the implant and encouraging retention without dealing with the distressing side effects may be counterproductive (8). This article focus is on DUB in adolescent ENG implant users, the treatment and counseling provided for DUB, and how treatment or lack of treatment contributed to the desire for implant removal in our patient population.

Methods

We conducted a chart review of the patients who received the ENG implant in our adolescent clinic. An analysis was completed based on symptoms experienced by patients who were on ENG implant and their management, which in some cases resulted in its removal. Patients who received implants on or after February of 2008 were included in this study (n=292). DUB was classified by amount of time and heaviness of flow and assigned a number 1-5 (see table 1). Any patient who was not amenorrheic was ultimately classified as a patient with DUB.

Table 1. Classifying Dysfunctional Uterine Bleed

1	Amenorrhea
2	Spotting for <7 days/month
3	Spotting for >7 days/ month
4	Heavy bleeding for <7 days per month
5	Heavy bleeding for >7 days per month

Results

From February 2008 to November 2013 a total of 292 patients had either Implanon™ or Nexplanon™ placed by a certified and trained clinician in the

Division of Adolescent Medicine, University of Kentucky, Lexington, KY, USA. The patient demographics of this clinic are summarized in table 2.

We also looked at other high risk behaviors such as whether or not patients were sexually active at time of implant placement (see table 3). This data is relevant as prevention of unwanted pregnancy is especially important in patients with co morbid conditions such as substance abuse and sexually transmitted infections that could cause harm to an early developing fetus.

Table 2. Demographics of implant users at University of Kentucky Adolescent Clinic

Age at Placement		Race		Insurance		Occupation	
Mean	17 years old	White	52.7%	Private	70.9%	Student	83.9%
SD	3 years	Black	45.2%	Medicaid	29.1%	Employed	11.0%
Range	10-29 y/o	Hispanic	1.4%			Unemployed	4.8%
		Other	0.7%				

Table 3. High risk behaviors associated with implant users at University of Kentucky Adolescent Clinic at time of placement

Sexually Active		Smoking Status		Substance Abuse		Age of First Intercourse		Prior STDs	
Yes	67.8%	Current	22.6%	Current	22.6%	Average	14.5	Yes	28.1%
No	30.1%	Prior	9.6%	Prior	9.6%	SD	2.1	No	66.8%
Unknown	2.1%	Never	64.7%	Never	22.6%	Range	10-21 years	Unknown	5.1%
		Unknown	3.1%	Unknown	4.5%				

The age range of patients receiving implant was between 10 and 29 years. The number of months the patient retained their implant post insertion ranged from 0 month (26 days) to 69 months, average 21.0 months +/-15.5 months before they were electively removed.

DUB was classified on a scale from 1-5 (see table 1) and was managed in a variety of ways depending on patient and classification of DUB. Treatment was left up to the clinician's discretion. As seen in table 4, the most common treatment was combined oral contraceptive pills alone (31.5% of patients with DUB). Resolution of DUB was also variable, which helps to emphasize the importance of careful follow up and continued counseling post treatment of DUB.

Table 4. Treatment of patients with DUB

	% Treated	% Resolution with Treatment
OCPs and Follow Up	31.5%	66.3%
Naproxen Only	1.4%	75.0%
OCPs and Naproxen	2.4%	85.7%
Reassurance and Follow Up	13.0%	86.8%
No Treatment or Refused Treatment	6.5%	56.2%

In our experience 54.1% of patients experienced some level of DUB (158 out of 292). Also noteworthy is that 65.2% of patients inciting DUB were treated with some sort of pharmacological method (OCPS, Naproxen, or Both), while 13.0% seen in clinic received only reassurance and follow up. Over the 69 months of this study, 86 of 292 patients had their implants removed. Although DUB was the overwhelming reason for removal in our patient population, table 5 depicts other reasons why the device was removed. Of interest is that 5.8% of all patients, and 17.9% of all patients presenting for implant removal, chose to get a new ENG implant placed upon expiration of their old implant, suggesting these patients were pleased with this form of contraception.

Table 5. Reasons for implant removal

Dysfunctional Uterine Bleed	15.8%
Implant Expired, New Implant Placed	5.8%
Implant Expired, Patient Switched to Another Form of Birth Control	2.7%
Other* Reason Stated for Removal	5.1%
Implant Has Not Been Removed	70.5%

* "Other" reasons for removal included; cramping, weight gain, pain at implant site, mood disturbances, and patient desiring pregnancy.

In the end 46 of 158 patients citing DUB opted for removal of the implant (29.1% DUB patients and 15.8% of all patients receiving ENG implant). Of these 46 patients, the average time of implant usage was 16 months +/- 11 months. In comparison to a prior smaller scale study done at our institution looking at ENG implant and DUB, 15 of 58 patients (22.4%) opted for removal because of DUB, with a mean usage of 10.9 months. This would suggest that our clinicians are doing a better job of counseling and treating patients with DUB due to ENG implant use, and stresses the importance of clinicians being informed and competent at informing patients about side effects of ENG implant usage.

Discussion

Long acting progesterone contraceptive are extremely effective in preventing teen pregnancies, which is why it is often a contraceptive method of choice for patients in our Adolescent Medicine Clinic, especially those patients participating in high risk behaviors. However, DUB is one of the major reasons for the discontinuation and removal of the implant. There are patient specific recommendations to manage DUB which include: doxycycline, EE, mifepristone, combination oral contraceptives, and NSAIDs. Of these treatments none are guaranteed to resolve DUB or prevent future DUB. Therefore, it is crucial for clinicians to provide the patient with adequate pre and post insertion counseling, as well as adequate pre-removal counseling so that patients can have reasonable expectations of what side effects could occur with implant usage. Also due to the quick return to fertility upon implant removal, it is equally important to provide post removal recommendations for alternative contraceptive methods to prevent unintended pregnancy, especially in high risk adolescent populations. This study shows high prevalence of discontinuation of the method, because of bleeding. However, in adolescent population at high risk of unwanted pregnancy, it is still an effective, long acting method that should continue to be utilized with proper counseling and follow up.

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