Original Article

Menstrual Bleeding Profile, Adverse Effects and Effectiveness of an Etonogestrel Subdermal Implant: A Prospective Study

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ABSTRACT

Objective: The aim of the study is to evaluate menstrual bleeding profile, adverse effects and effectiveness of an ENG implant (Nexplanon NXT) in healthy females during the first year of application.

Methods: This was a prospective observational study carried on Obstetrics& Gynecology department in Mansoura University Hospitals and Fertility Care Unit from April 2019 to April 2020. Including 95 healthy women of all ages who desired for long-term contraception by using ENG implant (Nexplanon NXT). Follow-up visits were every 90 days periods over 12 months after insertion of the implant, for bleeding pattern, BMI, and side effects.

Results: There was a statistically significant increase in BMI during follow up from 27.84±3.37 kg/m^2 at baseline that increased to 29.43±3.75 kg/m^2 at 4th visit. There was a statistically significant difference of bleeding abnormalities between first and fourth visit, between second and fourth visit. Insertion site pain was detected among 10.5% at 1st visit only. None of the studied cases have become pregnant during all visits.

Conclusion: We concluded that etonogestrel subdermal contraceptive implants are relatively safe with minimal side effects and high efficacy. However, the major side effects associated with implants use are weight gain and bleeding abnormalities.

Key Words: Etonogestrel subdermal implant. menstrual bleeding profile, nexplanon.

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INTRODUCTION

Steroid progestin is delivered by subcutaneous contraceptive implants using polymer capsules or rods inserted beneath the skin. For a period of one to five years, the hormone acts as a contraceptive, diffusing out gradually and steadily. Progestin implants have the following benefits: a low dose of extremely effective contraception without the use of estrogen, long-term contraceptive action without requiring the user's or provider's supervision, and easy reversibility of fertility upon implant removal[1,2]. The subdermal implant Nexplanon NXT releases etonogestrel (ENG), giving users three years of contraceptive protection. The implant has 68 mg of ENG, and during weeks 5–6, its average release rate is 60–70 µg/day, at the end of the first year, it is only 35–45 µg/day, it is 30–40 µg/day by the end of the second year, and by the end of the third year, it is 25–30 µg/day. When compared to Implanon, Nexplanon/ Implanon NXT features an applicator that is preloaded to minimize insertion errors, and the implant is visible through imaging methods since it includes barium sulphate. Most women, including those with a history of venous thromboembolism or congenital or acquired cardiovascular illness, can use these methods for contraception.[3,4] One of the most common reasons given for stopping Nexplanon NXT, particularly during the first year of treatment, was irregular bleeding. Headache, weight gain, acne, breast soreness, emotional instability, and stomach pain are some other side effects. Nonetheless, a lot of women have little to no trouble adjusting to the implant.[5, 6] As the Nexplanon NXT ENG implant is presently accessible in Egypt, the purpose of this study is to assess its efficacy, side effects, and related menstrual bleeding profile.

PATIENTS AND METHODS

A prospective observational study which was carried on Obstetrics& Gynecology department in Mansoura University Hospitals and Fertility Care Unit from April 2019 to April 2020. Including healthy, regular cycle women of all ages who desired for long-term contraception by using ENG implant (Nexplanon NXT) inserted, following the eligibility criteria for contraceptive use of the World Health Organization (WHO2010). We exclude, women with previous hormonal contraception in the last month, abnormal menstrual bleeding prior to the use of the contraceptive method, endocrine dysfunctions and concomitant treatment with other hormones uterine lesions; bleeding disorders; liver or renal disease and use

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of anticoagulant therapy and any contraindications to contraceptive steroids.

Sample Size Calculation

The sample size is calculated using the following formula (Dawson and Trapp, 2004):

$$n = \left[\frac{Z_{\alpha/2}}{E}\right]^2 * P(1-P)$$

Where: n = sample size. $Z_{\alpha/2}$ = 1.96 (The critical value that divides the central 95% of the Z distribution from the 5% in the tail). p = the prevalence of the outcome variable (proportion of reference periods "RPs" with favourable bleeding profile = 79% (Di Carlo et al. 2015). E = = the margin of error (=width of confidence interval) = = 0.08609

So, by calculation, the sample size will be equal to 86 subjects. Assuming a drop-out ratio of 10%, the total sample size will be 95 subjects.

Patient evaluation

After selection, counseling, explaining the procedure to all participants, and obtaining a written consent to participate in the study; all participants were submitted to: History taking with special emphasis on; Personal history: age, duration and number of marriage, parity, and special habits especially smoking. Menstrual history: especially any abnormal bleeding or amenorrhea (exclude pregnancy). Obstetric history: stressing on gravidity and parity. Past history: of any gynecological operation as: hysterectomy, cauterization for cervical erosion. Family history: of any gynecologic malignancy, cancer breast or colorectal carcinoma. Complete clinical examination: Included general, abdominal and full gynecological examination. Body mass index (BMI) will be recorded for each patient at baseline and at each follow up visit.

$$\text{Body Mass Index} = \frac{\text{weight (kg)}}{\text{height (m)}^2}$$

Ultrasonographic assessment; A trans-vaginal ultrasound on one of the first 5 days of the menstrual cycle was done and Nexplanon was inserted between days 1 and 5 of the menstrual cycle.

Follow up and outcomes: Follow-up visits were every 90 days periods over 12 months after insertion of the implant.

Follow up of bleeding; The Patients record the occurrence of any bleeding or spotting. The following definitions were used; Bleeding-day is any day with vaginal discharge containing blood that required more than one sanitary pad per day. Spotting-day is any day with vaginal discharge containing blood that required at most one sanitary pad per day. Bleeding-free day is a day during which neither bleeding nor spotting were reported. Bleeding–spotting episode – one or more consecutive days during which bleeding or spotting are reported, bounded by bleeding-free days. Bleeding patterns were assessed and evaluated based on the original World Health Organization (WHO)-recommended definition: Amenorrhoea: no bleeding or spotting days throughout the 90-d reference period.

Infrequent bleeding

less than three bleeding–spotting episodes in a 90-d reference period. Normal frequency: 3–5 bleeding–spotting episodes in a 90-d reference period. Frequent bleeding: more than five bleeding–spotting episodes in a 90-d reference period. Prolonged bleeding: any bleeding-spotting episode (uninterrupted) lasting more than 14 d in the 90-d reference period (10-12).

Follow up of anthropometric measures

Weight, height, and BMI were recorded for each patient at baseline and at each follow-up visit. An increase or reduction of 1000 g in body weight was considered a significant weight change. Recording of other side effects: Other side effects as headache, acne, breast pain, and abdominal pain were recorded. In case of implant removal, the time and the reason for discontinuation were recorded. The occurrence of pregnancy after insertion the implant were reported.

Ethical considerations

The study takes into account the following ethical research considerations: Before beginning the study, the IRB of the Mansoura University Faculty of Medicine granted research approval. Prior to participation, every patient provided written, informed consent. The study's purpose and objectives were made clear to the study's subjects by the researcher. The researcher promised to protect the subjects' data's confidentiality and anonymity. The subjects were made aware of their freedom to decide whether or not to engage in the study and their right to leave the study at any moment, for any reason. Subjects' ethics, values, cultures, and beliefs were all honored.

Statistical analysis

SPSS software, version 25 (SPSS Inc., PASW statistics for Windows version 25), was used to analyze the data. The SPSS Inc., Chicago. Numbers and percentages were used to describe the qualitative data. Mean± was used

to describe quantitative data. standard deviation for data that is regularly distributed following the Kolmogrov-Smirnov test for normalcy. The results were evaluated for significance at the (≤0.05) level. The qualitative data was compared before and after therapy using the McNemar test. Two paired readings of scattered data were compared using the Paired T test.

RESULTS

Demographic data of the studied group (Table 1), main age of the studied cases is 31.02 ±5.61 years ranging from 20 to 43 years ,median duration of marriage is 10 years ranging from 1 to 26 years , median gravidity is 3 ranging from 1 to 7 ,median parity is 3 ranging from 1 to 5 , mean menses duration is 4.78±0.97 ranging from 3 to 7 days , mean TVUS is 4.42±0.63 mm ranging from 3 to 6 mm. (Table 2) illustrates that all implants were insitu during 1st visit then at 2nd visit 2 implants were removed (one due to bleeding irregularities & weight increase and one removed due to planning pregnancy), during third visit one case lost follow up and at fourth visit ; 3 cases have removed implants due to Bleeding irregularities & weight increase .None of the studied cases have become pregnant during all visits. (Table 3) demonstrates a statistically significant increase in body weight during follow up from 74.63±12.34 kg at baseline to 76.94±12.91 kg at first visit to 77.93±13.30 kg at 2nd visit, 77.99±13.09 kg at 3rd visits and increased to 78.65±13.15 kg at 4th visit. Mean body mass index is 27.84±3.37 kg/m2 at baseline that increased to 28.71±3.58 kg/m2 at first visit then 29.04±3.75 kg/m2 at second visit to 29.18±3.72 kg/m2 at 3rd visit and 29.43±3.75 kg/m2 at 4th visit with statistically significant change during follow up. (Table 4): illustrates statistically significant difference of bleeding abnormalities between first and third visit (p=0.009), between second and third visit (p=0.017), between first and fourth visit (p<0.001), between second and fourth visit (p=0.035). Amenorrhea is detected more among 3rd& 4th visits (41.3% & 46.7%, respectively). (Table 5) : shows non statistically significant difference of headache incidence during different follow up (p>0.05).Headache was detected among 16.8% at 1st visit that remains 16.8% at 2nd visit that decreased to 14.1% at 3rd visit and 13% at 4th visit. (Table 5) : shows non statistically significant difference of acne incidence during different follow up (p>0.05).Acne was detected among 6.3% at 1st visit that remains 6.3% at 2nd visit that decreased to 5.4% at 3rd visit and 4.3% at 4th visit. Table (5): illustrates non statistically significant difference of breast pain incidence during different follow up (p>0.05). Breast pain was detected among 9.5% at 1st visit that remains 9.5% at 2nd visit that decreased to 7.6% at 3rd visit and 6.5% at 4th visit. (Table 5): demonstrates a non-statistically significant difference of abdominal pain incidence during follow up. Abdominal pain was detected among 12.6% at 1st visit decreases to 11.6% at 2nd visit that decreased to 7.6% at 3rd visit and 6.5% at 4th visit. (Table 5): demonstrates a statistically significant difference of insertion site pain between first and second visit (p= 0.002), between first and 3rd visits (p= 0.002) , between 1st and 4th visit (p=0.002). Insertion site pain was detected among 10.5% at 1st visit only.

Table 1: Personal and obstetric history of the studied cases

	Total number=95
Age / years mean±SD (Min-Max)	31.02 ± 5.61 (20 - 43.0)
Duration of marriage(years) Median (Min-Max)	10 (1 - 26)
Gravidity Median (Min-Max)	3 (1 - 7)
Parity Median (Min-Max)	3 (1 - 5)
menses duration(days) mean±SD (Min-Max)	4.78 ± 0.97 (3 - 7)
TVUS(ET)/mm mean±SD(Min-Max)	4.42 ± 0.63 (3 - 6)

Table 2: Implant position among studied cases during different visits

Implant position	1st Visit N=95(%)	2nd N=95(%)	3rd N=92(%)	4th N=92(%)
Removed	0	2(2.1)	0	3(3.3)
Insitu	95(100)	93(97.9)	92(100)	89(96.7)
Comparison between different follow up		p1=0.157	p1=1.0 p2=1.0	p1=0.250 p2=0.250 p3=0.250
Reasons for discontinuation				
Bleeding irregularities & weight increase	0	1	0	3
Planning pregnancy	0	1	0	0
Lost to follow up	0	0	1	0
pregnancy (failure)	0	0	0	0

p1: difference from first visit, p2: difference from second visit, p3: difference from third visit, *statistically significant used test :MC-Nemar test

Table 3: weight, height and body mass index during follow up of the studied cases from baseline to 4th visit.

	Baseline N=95	1st Visit N=95	2nd N=95	3rd N=92	4th N=92
Weight (kg)	74.63±12.34 (47-112)	76.94±12.91 (47-114) p1<0.001*	77.93±13.30 (47-117) p1<0.001* p2<0.001*	77.99±13.09 (46-116) p1<0.001* p2<0.001* p3<0.001*	78.65±13.15 (47.0-114.0) p1<0.001* p2<0.001* p3<0.001* p4<0.001*
Comparison between different follow up					
Height (cm)	163.31±5.78 (150-172)	163.31±5.78 (150-172) p1=1.0	163.31±5.78 (150-172) p1=1.0 p2=1.0	163.11±5.76 (150-172) p1=1.0 p2=1.0 p3=1.0	163.11±5.76 (150-172) p1=1.0 p2=1.0 p3=1.0 p4==1.0
Comparison between different follow up					
Body mass index (kg/m2)	27.84±3.37 (20.89-38.97)	28.71±3.58 (20.89-40.39) p1<0.001*	29.04±3.75 (20.89-41.45) p1<0.001* p2<0.001*	29.18±3.72 (20.44-41.1) p1<0.001* p2<0.001* p3<0.001*	29.43±3.75 (20.89-40.04) p1<0.001* p2<0.001* p3<0.001* p4<0.001*
Comparison between different follow up					

Parameters described as mean ±SD (Min-Max), p1: difference from baseline, p2: difference from first visit, p3: difference from second visit, p4: difference from third visit.

Table 4: incidence of bleeding abnormalities among studied cases during different visits

Bleeding abnormality	1st Visit N=95(%)	2nd N=95(%)	3rd N=92(%)	4th N=92(%)
Normal	4(4.2)	5(5.3)	2(2.2)	3(3.3)
Prolonged	22(23.2)	11(11.6)	10(10.9)	11(12.0)
Infrequent	40(42.1)	48(50.5)	41(44.6)	35(38.0)
Frequent	6(6.3)	4(4.2)	1(1.1)	0
Amenorrhea	23(24.2)	27(28.4)	38(41.3)	43(46.7)
Comparison between different follow up		p1=0.224	p1=0.009* p2=0.017*	p1<0.001* p2=0.035* p3=0.726

p1: difference from first visit, p2: difference from second visit, p3: difference from third visit, *statistically significant used test: MC-Nemar test

Table 5: incidence of other side effects among studied cases during different visits

Headache	1st Visit N=95(%)	2nd N=95(%)	3rd N=92(%)	4th N=92(%)
Absent	79(83.2)	79(83.2)	79(85.9)	80(87.0)
Present	16(16.8)	16(16.8)	13(14.1)	12(13.0)
Comparison between different follow up		p1=1.0	p1=1.0 p2=0.317	p1=1.0 p2=0.317 p3=0.317
ACNE	1st Visit N=95(%)	2nd N=95(%)	3rd N=92(%)	4th N=92(%)
Absent	89(93.7)	89(93.7)	87(94.6)	88(95.7)
Present	6(6.3)	6(6.3)	5(5.4)	4(4.3)
Comparison between different follow up		p1=1.0	p1=1.0 p2=1.0	p1=0.500 p2=0.50 p3=1.0
Breast pain	1st Visit N=95(%)	2nd N=95(%)	3rd N=92(%)	4th N=92(%)
Absent	86(90.5)	86(90.5)	85(92.4)	86(93.5)
Present	9(9.5)	9(9.5)	7(7.6)	6(6.5)
Comparison between different follow up		p1=1.0	p1=1.0 p2=1.0	p1=0.791 p2=0.500 p3=1.0
Abdominal pain	1st Visit N=95(%)	2nd N=95(%)	3rd N=92(%)	4th N=92(%)
Absent-	83(87.4)	84(88.4)	85(92.4)	86(93.5)
Present	12(12.6)	11(11.6)	7(7.6)	6(6.5)
Comparison between different follow up		p1=1.0	p1=0.125 p2=0.062	p1=0.250 p2=0.125 p3=1.0
insertion site pain	1st Visit N=95(%)	2nd N=95(%)	3rd N=92(%)	4th N=92(%)
Absent	85(89.5)	95(100)	92(100)	92(100)
Present	10(10.5)	0	0	0
Comparison between different follow up		p1=0.002*	p1=0.002* p2=1.0	p1=0.002* p2=1.0 p3=1.0

p1: difference from first visit, p2: difference from second visit, p3: difference from third visit, *statistically significant used test: MC-Nemar test

DISCUSSION

The aim of the current study was to evaluate menstrual bleeding profile, adverse effects and effectiveness of an ENG implant (Nexplanon NXT) in healthy females during the first year of application. In the current study, the mean age of the studied cases is 31.02 ±5.61 years ranging from 20 to 43 years. The median gravidity is 3 ranging from 1 to 7, median parity is 3 ranging from 1 to 5. According to the researcher's point of view, the prevalence of use of implants in this age group with these number of gravidities could be explained due to the need to provide more prolonged spacing between pregnancies to keep their beauty or due to economic reason as there is higher prevalence of working females in this age group within the Egyptian society. Similarly, women between the ages of 25 and 29 made up the plurality (23%) of those surveyed in a study conducted at the Atrium Medical Center in the Netherlands, which involved 214 women. It was discovered that ninety percent of the women who selected the implant had previously given birth to three or less children.[7] In the current study, all implants were placed during the first visit. Two implants were removed during the second visit (one because of weight gain and bleeding irregularities, and the other because the patient was planning a pregnancy). One case lost follow-up during the third visit, and three cases had implants removed because of weight gain and bleeding irregularities during the fourth visit. Not even one of the cases under study has become pregnant at every visit. Obijuru et al. examined the charts of 116 teenagers after the installation of contraceptive implants and reported on 94 individuals, finding a higher incidence of removal. She provides rates of both "irregular bleeding" and nuisance bleeding eradication. Overall, 18% (17/94) underwent a removal because of bleeding, and 48% (45/94) reported bothersome bleeding[8].

In a systematic review by Moray et al., the one-year continuation rates ranged from 57–97%; 44–95% at the end of second year and 25–78% by 3 years of use. Abnormal menstruation was the most reported side effect[9].

A study involving 304 women in Upper Egypt, with a median age of 32, was carried out. According to the study, the most common reason for selecting an etonogestrel implant was to use extended contraception (39.5%), but the most common reason for stopping the implant was to experience side effects, mostly monthly irregularities[10]. According to Berlan et al. (2016), 61% of teenagers asked to be removed before the age of 12 months because they were bleeding[11]. Additionally, 47% of patients stated that AUB was the reason for removal, whereas 68% of patients who requested removal earlier than 12 months did so, according to the Fei et al. study. Adolescents who experienced frequent or protracted bleeding episodes were more likely to undergo early removal[12].

In addition to bleeding abnormalities, Funk et al.'s multicenter clinical trial including 330 women demonstrated that emotional lability (6.1%), weight gain (3.3%), depression (2.4%), and acne (1.5%) were prevalent adverse events that resulted in cessation[13]. According to research by Blumenthal et al., the overall discontinuation rate in a sample of 942 women was 32.7%. The most reported reasons for stopping the medication were adverse events (AEs) (13.9%), bleeding irregularities (10.4%), and planning a pregnancy (4.1%). The most commonly reported drug-related complication was headache 15.3%[14]. The current results coincide with the results in a report by Maddox et al.2008, which stated that the most common side effect and reason for removal was infrequent bleeding[15].

In the current study, there is statistically significant increase of weight and body mass index between baseline and during follow up visits from 74.63±12.34 kg to 78.65±13.15 kg for body weight and from 27.84±3.37 to 29.43±3.75 kg/m^2 (at baseline and at the fourth visit respectively). Weight gain was detected among 66.3% at 1st visit increases to 70.5% at 2nd visit that decreased to 54.3% at 3rd visit and 50.0% at 4th visit. This agreed with Wali et al. who showed that 46 (54.76%) women reported weight gain[16].

This was also consistent with findings from Fei et al., which demonstrated that among the people included in the study, the average BMI upon implant placement was 25.6 kg/m^2, and the average percentage rise in BMI throughout the first year was 3.2% (0.87 kg/m2). During the study period, 63.5% of women saw a rise in their BMI overall[12].

This was in line with the findings of Romano and Braun-Courville (2019), who revealed that 43 out of 197 ENG users in their study had their implants removed early; of those patients, 3/43 (6.3%) had weight increase as their main cause for removal. For ENG users, the mean change in weight was +3.6 (±7.8) kg, and the mean change in BMI was +1.3 (±2.9)[17].

Also, the current study agreed with a study of 75 ENG implant users by Modesto and colleagues found that women using the ENG implant had a 2% increase in body fat and a 2.4 kg increase in fat mass[18].

In the current study, there was a statistically significant difference of bleeding abnormalities between first and third visit (p=0.009), between second and third visit (p=0.017), between first and fourth visit (p<0.001), between second and fourth visit (p=0.035). The incidence of bleeding abnormalities was 95.8%, 94.7%, 97.8% and 96.7% at the 1st visit, 2nd visit, 3rd visit and 4th visit respectively. Amenorrhea is detected more among 3rd & 4th visits (41.3% & 46.7%, respectively).

Similar findings were seen by Yildizbas et al., who found that 92% of participants reported changes in the length or frequency of their menstrual cycle during the study's first year, and that 9% of participants removed their etonogestrel implant for this reason[19].

Comparing the incidence of abnormal bleeding to Hines et al.'s study from 2015–2017, which involved 216 women, the incidence was greater. They revealed that 53% of individuals (n=115) experienced irregular uterine hemorrhage as the most frequent side event[20]. Moreover, different women had different bleeding patterns in a recent study by Wali et al. Twenty (23.81%) of the ladies said they bled in spots, and 24 (28.57%) said their bleeding was irregular[21]. Of the women who used etonogestrel implants, only 10 (11.90%) reported regular bleeding patterns, while 30 (35.71%) indicated there was no bleeding at all. Of the women who reported bleeding of any kind, 27 (50.00%) had bleeding that persisted for a long time. Of the ladies, fifty-three (63.10%) had an unusual bleeding pattern[16].

In a retrospective 12-center trial carried out in Switzerland, 991 women utilizing etonogestrel implants who were enrolled in at least one follow-up visit to evaluate satisfaction, side effects, bleeding patterns, and duration of treatment also demonstrated a decreased incidence of bleeding. Only 11% of the 991 women reported normal bleeding, compared to 28% who reported irregular bleeding and 33% who reported amenorrhea[22]. According to research by Mansour et al., implant users who experienced good bleeding during the first reference period that is, amenorrhea, rare bleeding, and normal frequency bleeding without protracted bleeding are likely to continue experiencing favorable bleeding throughout the subsequent two years[23].

According to Croxatto et al., bleeding abnormalities were the primary cause of cessation[24,25]. In 2010, a prospective longitudinal trial involving 32 women of reproductive age demonstrated a 100% efficacy rate and a 93.8% continuation rate; at the six-month follow-up, 56.3% of patients showed a reduction in their pattern of bleeding, whereas 40.6% of patients had irregular bleeding[26]. Furthermore, Modesto et al. showed that the percentage of ENG implant withdrawal because to irregular menstrual bleeding was 17% at one year and 62% at two years[19].

According to the CADTH review, between 3.8% and 46.2% of patients treated with the radiopaque etonogestrel implant experienced specific bleeding-related adverse events (AEs), such as dysmenorrhea, menorrhagia, metrorrhagia, vaginal hemorrhage, and genital hemorrhage[27].

In the current study, none of the studied cases have become pregnant during all visits. This indicated the high efficacy of the ENG implants. This was in line with findings from a recent systematic review by Moray et al., which covered 51 studies and 23,078 cases. The clinical effectiveness was reported to be 100%, and the pearl index ranged from 0 to 1.49 overall. To assess Nexplanon's contraceptive effectiveness in healthy users, the Canadian Agency for Drugs and Technologies in Health released a Clinical Review Report in December 2020. Based on a review analysis, there were zero contraceptive failures per 100 woman-years in the entire Pearl Index[27].

This was similarly supported by Xu et al. (2012), who included 1,377 female ENG implant users. Among the 1,377 women who used implants for a year, they reported one unplanned pregnancy[28]. Mommers et al. conducted a three-year, multicenter, no-comparative research on 301 implant users who were of reproductive age. They did not find any evidence of pregnancy[29]. Fischer conducted a study in which the failure rate of etonogestrel implants at three years' follow-up was assessed. Remarkably, over 1200 woman-years of exposure, no pregnancy (Pearl Index, 0; 95% CI 0.0–0.2) was observed[30].

The effectiveness of etonogestrel subdermal implant (ESI) was compared with other LARC, including implants, in a Cochrane systematic review conducted in 2007. Nine trials were reviewed for this study; eight of them compared Norplant, a Levonorgestrel-six-capsule implant, with ESI, and one of them compared Jadelle, a Levonorgestrel-1-capsule implant, with Norplant. Review results indicated that ESI was very successful; no reported pregnancies occurred[5].

In a research by Croxatto et al., there was a quick restoration of ovulation following its removal, with no pregnancy reported throughout 53,530 cycles (4103 women-years) [Pearl Index = 0.0 (95% CI, 0.00–0.09)][31].

While ENG is thought to be a safe alternative, using it can have certain negative effects, such as headache, weight gain, acne, and breast soreness. 13.6% of women stop using the etonogestrel implant due to all-cause adverse effects[32]. There is a correlation between these adverse effects and a general decline in satisfaction[33].

In the current study, Headache was detected among 16.8% at 1st visit that remains 16.8% at 2nd visit that decreased to 14.1% at 3rd visit and 13% at 4th visit. Acne was detected among 6.3% at 1st visit that remains 6.3% at 2nd visit that decreased to 5.4% at 3rd visit and 4.3% at 4th visit. Breast pain was detected among 9.5% at 1st visit that remains 9.5% at 2nd visit that decreased to 7.6% at 3rd visit and 6.5% at 4th visit.

In addition to bleeding abnormalities, Funk et al.'s multicenter clinical trial including 330 women demonstrated that emotional lability (6.1%), weight gain (3.3%), depression (2.4%), and acne (1.5%) were prevalent adverse events that resulted in cessation[13]. According to research conducted by Blumenthal et al., the overall cessation rate in a sample of 942 women was 32.7%. The most common reasons given for stopping the medication were adverse events (AEs) (13.9%) and pregnancy planning (4.1%); on the other hand, the most common drug-related problem reported was headache (15.3%)[34].

A cross-sectional community-based study of 430 women revealed that 34% of them had stopped using their etonogestrel implant altogether. Women who never used a method of contraception other than an etonogestrel implant (OR 2.96, 95% CI 1.53–5.74), women who did not discuss the procedure with a partner (OR 3.32, 95% CI 1.57–7.04), poor counseling and follow-up (OR 9.23, 95% CI 4.7–18.13), fear of side effects (OR 0.12, 95% CI 0.058–0.24), and low service satisfaction (OR 5.2, 95% CI 2.77–9.76) were among the cases of women who discontinued their etonogestrel implant[35].

In the current study, there was a statistically significant difference of insertion site pain between first and second visit (p= 0.002), between first and 3rd visits (p= 0.002), between 1st and 4th visit (p=0.002). Insertion site pain was detected among 10.5% at 1st visit only.

Poor surgical technique (placing the capsules too deeply or superficially) was typically the cause of pain during insertion; ulnar nerve neuropathy following insertion or removal was also noted[36]. The results of this study indicate that with time, discomfort decreases until it eventually vanishes completely.

CONCLUSIONS

Etonogestrel subdermal contraceptive implants are

relatively safe with minimal side effects and high efficacy. However, the major side effects associated with implants use are weight gain and bleeding abnormalities.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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