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ORIGINAL ARTICLE

Implanon: Subdermal Single Rod Contraceptive Implant

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Abstract
Objectives Study was conducted to determine acceptability, efficacy, safety, return of fertility with Implanon.
Methods Volunteers having regular menstruation, requiring spacing formed study population. Implanon was inserted within 5 days of LMP or concurrent with MTP. Woman was asked to record bleeding pattern, side effects. Implanon duration was 3 years but Implanon was removed before, if patient wanted pregnancy/for side effects. Subjects who did not adopt family planning method after removal were followed up for return of ovulation and pregnancy.
Results 200 subjects were enrolled (160 within 5 days of LMP, 40 concurrent with MTP). 74 implanon removals were done. (16 after tenure completion, 58 for other reasons.) 16% cases discontinued implanon for polymenorrhagia, 10% for irregular bleeding, 4.5% for amenorrhea. There was no failure of implanon. 40% had return of ovulation within one month, 95.8% conceived within 12 months.
Conclusions Implanon is safe, effective, well accepted method of contraception.

Keywords Implanon · Contraceptive · Etonogestrel

Introduction

There are currently several innovative contraceptive implant systems under development. Initially Norplant implant consisting of 6 levonorgestrel containing capsules for subdermal insertion was developed. It lost popularity when reports appeared about the difficulty in removal of implant. Hence newer implants, Jadelle (2 LNG rod) and Implanon were developed.

Implanon is a single rod contraceptive implant and it provides contraceptive protection for 3 years. It is a silicon free implant in a pre loaded sterile disposable applicator. It is a non biodegradable implant which contains 68 mg of etonogestrel (progestogen) in ethylene vinylacetate (EVA) copolymer core, surrounded by EVA membrane. Each rod has a length of 4.0 cm and a diameter of 2.0 mm. Each rod consists of inner core containing 60% etonogestrel and 40% ethylene vinyl acetate (EVA) and an outer membrane containing 100% ethylene vinyl acetate (EVA). Half life of etonogestrel (ENG) is 25 h and its bioavailability is 94–99%. There is no accumulation of ENG. It is excreted 60% in urine and 40% in faeces.

Mechanism of action of Implanon is by ovulation inhibition and increase in viscosity of cervical mucus. The most common

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side effects associated with Implanon are irregular periods, weight gain, acne, headache and breast tenderness. The present study was conducted on Indian women to determine the acceptability, efficacy, bleeding pattern and safety with Implanon and return of fertility after its discontinuation.

Methodology

Healthy female volunteers having regular menstruation, at least one living child and requiring spacing methods formed the study population. Implanon was inserted within 5 days of LMP or concurrent with MTP.

Systemic and Pelvic examination was done prior to insertion. After screening and counseling the women were offered the contraceptive device of their choice. All women accepting Implanon signed an informed consent in their own regional language. Implanon was inserted in the inner side of left upper arm using a pre-loaded applicator.

All subjects enrolled were rigorously followed up for their general health and well being. First follow up visit was at 7 days of insertion to check the condition of site of insertion and displacement/expulsion of implant. Subsequent follow up visits were at 1, 3, 6 and 12 months and at 6 monthly intervals thereafter for a period of 3 years. Each woman was provided with a menstrual diary card wherein she recorded the bleeding pattern and any untoward complaints or side effects and treatment taken. Cases with prolonged bleeding and spotting were treated with best medicines available. When poor response to treatment was observed and bleeding persisted or patient requested for removal of Implanon, removal was done. If patient had amenorrhea beyond 45 days, pregnancy was excluded by pregcolor card test and/or clinical examination.

The duration of Implanon use was for a period of 3 years but Implanon could be removed before the prescribed duration if the patient wanted pregnancy or wanted removal due to side effects. Removal was done under all aseptic precautions in OT under local anesthesia.

All the subjects who did not adopt any family planning method after the implant was removed and were exposed to the risk of pregnancy were followed up at 3–4 weeks after discontinuation for return of ovulation which was estimated by serum progesterone level as a surrogate marker of return of fertility (Serum Progesterone as surrogate marker was not done in cases who adopted hormonal contraception after removal of Implanon). Further follow up was done at 3 monthly intervals till 1 year for return of fertility in terms of pregnancy. Those women who did become pregnant during the follow up period were followed until delivery to note the pregnancy outcome.

Results

200 subjects were enrolled over a period of 1 year i.e., July 04–June 05. 160 patients had Implanon insertion within 5 days of LMP and 40 patients had Implanon insertion concurrent with MTP. During the same period, 1044 women accepted copper T. When offered through cafeteria approach, relative acceptability of Implanon was 1:5.22 as compared to Copper T.

There was no difficulty/complication during insertion or removal in any patient. There was expulsion in one subject on 3rd day of insertion.

74 cases of Removal of Implanon were carried out (16 cases after completion of tenure and 58 cases for other reasons). There was no difficulty during removal in any case.

92% cases continued Implanon for 6 months, 81.5% continued for 12 months and 71% continued for 24 months (Table 1).

16% cases discontinued implanon due to polymenorrhagia, 10% due to irregular bleeding P/v and 4.5% due to amenorrhea. 1.5% cases got removal done due to Koch's intestine (Table 2).

Commonest side effect was irregular bleeding per vaginum in 27% cases, however only 5% cases got implanon removed due to this disorder. Prolonged spotting was reported in 23% cases but only 1% cases had implanon removal due to this. 24% cases complained of amenorrhea but only 4.5% cases got removal done due to amenorrhea. Polymenorrhagia was observed in 22.5% cases and 16% cases got removal done due to polymenorrhagia (Table 3).

Weight gain >5 kg was observed in 7.5% cases, but none had removal due to this reason.

Table 1 Continuation rates in months

Months	No. of cases	%
6	184	92
12	163	81.5
18	151	75.5
24	142	71
30	126	63

Table 2 Reasons for discontinuation before tenure completion

Reasons for discontinuation	No.	%
Polymenorrhagia	32	16
Irregular bleeding pv	10	10
Prolonged spotting	2	2
Amenorrhea	9	4.5
Medical reasons (Koch's Intestine)	3	1.5
Wanted to conceive	2	1

Table 3 Side effects—menstrual disorders

Menstrual disorder	No. (%)	Discontinuation due to disorder
Polymenorrhagia	45 (22.5%)	32 (16%)
Irregular bleeding pv	54 (27%)	10 (5%)
Prolonged spotting	46 (23%)	2 (1%)
Amenorrhoea	48 (24%)	9 (4.5%)

Table 4 Return of ovulation

Return of ovulation within 1 month	No.
Total cases of Implanon removal	74
Accepted OC	34
Tested for ovulation by progesterone estimation	40
Return of ovulation +ve	16 (40%)

Table 5 Return of fertility—number of pregnancies

Pregnancies in cases not accepting contraception	
Total cases of implanon removal	74
Alternative contraceptive accepted	50
Alternative contraceptive not accepted	24
Pregnancy within 3 months	7 (29.16%)
Pregnancy within 6 months	15 (62.50%)
Pregnancy within 9 months	16 (66.66%)
Pregnancy within 12 months	23[a] (95.80%)

[a] One patient who did not conceive within 1 year had hypothyroidism

There was no failure of Implanon in the present study.

The cases who did not adopt alternative methods of contraception after removal of Implanon were studied for return of ovulation at 3–4 weeks by progesterone estimation (cases who adopted hormonal contraception were excluded). 40% cases had return of ovulation within one month (Table 4).

Implanon removal was done in 74 cases. 50 cases out of these accepted alternative methods of contraception. Out of 24 cases who did not adopt alternative methods of contraception, 29.16% conceived within 3 months, 62.50% within 6 months, 66.66% within 9 months and 95.8% within 12 months (Table 5). One patient who did not conceive within 12 months was suffering from hypothyroidism. Out of 23 cases who conceived, 10 got MTP done, 13 delivered normal babies.

Discussion

In recent years, the most important trend in contraceptive research has been the development of a range of contraceptive methods designed to meet the needs of individual users. With the development of synthetic polymers, it has become possible to develop delivery systems with a long duration of action, which continuously release low amounts of hormones. The development of such a system, in the form of a subdermal implant called Implanon, based on the selective progestogen etonogestrel, illustrates the ongoing search for innovative contraceptive methods. Contraceptive implants are a proven method for long-term prevention of pregnancy. Advantages of this contraceptive method include unsurpassed efficacy, independence from user compliance and prompt return of fertility after removal.

Implanon is a progestogen-only method, so it is suitable for a wide range of women. Implanon makes family planning possible throughout reproductive life; it may be used to postpone a first pregnancy, to 'space' pregnancies or to provide reversible, long-term contraception when the desired family size is reached. Since Implanon does not contain an estrogen, it can also be used in women who do not want to or cannot use combined oral contraceptives (COCs). Implanon does not exert a negative effect on cardiovascular risk factors such as CRP and cholestrol/HDL ratio as reported by Merk feld et al. [1].

Implanon is based on an ethylene vinyl acetate (EVA) carrier and consists of a single rod, 4 cm long and 2 mm in diameter. The core of the implant contains 68 mg of crystalline etonogestrel, dispersed in a matrix of ethylene vinyl acetate copolymer surrounded by a 0.06 mm EVA membrane.

The early phase of clinical development of Implanon had two main objectives (1) to establish the minimum daily dose of etonogestrel for complete ovulation inhibition (2) to find a long-term release system to enable maintenance of this level.

Earlier subdermal implants suppressed ovulation only during the first year. After this time, contraceptive protection was mainly provided by increasing the viscosity of cervical mucus.

The single-rod implant with etonogestrel was developed in order to achieve complete inhibition of ovulation during the total duration of use. Based on the combined results of dose finding studies, it was concluded that a daily release rate of approximately 30 μg etonogestrel inhibited ovulation in the majority of women. In order to maintain the required release rate of 30 μg etonogestrel/day for a projected duration of use of 3 years, it was found that an initial release rate of about 60 μg/day was necessary. Within 8 h after subdermal insertion, etonogestrel levels are sufficient to provide contraceptive protection. A continuous release of etonogestrel is maintained for 3 years. Within 1 week after removal etonogestrel is no longer detectable in human serum.

The present study was conducted to evaluate subdermal single rod contraceptive implant-Implanon for its acceptability, efficacy and safety in Indian population. 200 subjects were enrolled over a period of one year. During the same period, 1044 women accepted copper T and 115 women accepted oral pills. When offered through cafeteria approach, relative acceptability of Implanon was 14.75% which was more than oral pills (8.48%) but less than copper T (76.77%).

There was no difficulty/complication during insertion/removal in any subject. Injury to antebrachial cutaneous nerve during insertion/removal has been reported by Wechselberger et al. [2]. Injury to ulnar nerve during insertion has been reported by Osman et al. [3]. There was expulsion of Implanon in one subject on 3rd day of insertion. Expulsion has also been reported by Harrison-Woolrych and Hill [4]. Spontaneous snapping of Implanon in two halves in situ at 33 months has been reported by Agrawal and Robinson [5], but it was not observed in any case in the present study.

92% cases continued Implanon for 6 months, 81.5% cases continued for 12 months and 71% cases continued for 24 months. Lower continuation rates have been reported by Lakha and Glasier [6] which were 89% at 6 months, 75% at 1 year and 59% at 2 years.

Commonest side effect was irregular bleeding pv in 27% cases, however, only 5% cases got implanon removed due to this disorder. Prolonged spotting was reported in 23% cases but only 1% cases had implanon removal due to this disorder. 24% cases complained of amenorrhea but only 4.5% cases got removal done due to amenorrhea. Polymenorrhagia was observed in 22.5 and 16% cases got removal done due to polymenorrhagia. Gezginck et al. [7] reported less incidence of irregular bleeding P/v (17.5%), but they reported a much higher incidence of amenorrhea (41.25%).

Weight gain >5 kg was observed in 7.5% cases, but no subject got removal done due to this reason. Side effects such as breast tenderness, acne, headache and dizziness, depressive mood disorders, pelvic pain and loss of libido have also been reported by Gezginck et al. [7], but they were not observed in the present study.

Hiddalgo et al. [8] reported ovarian cysts in 5.2% cases of Implanon at 3 months, 7.2% at 6 months and 26.7% at 12 months, but they concluded that these ovarian cysts were transient and should not be interpreted as pathological. No case of ovarian cysts was observed in the present study.

There was no failure of contraception in the present study. Harrison-Woolrych and Hill [4] have reported approximate failure rate of 1 per 1000 insertions (218 out of 204486). Pregnancy due to implanon failure has also been reported by Hamontri and Weerkul [9]. One case of ectopic pregnancy following Implanon failure has been reported by Mansour et al. [10]

Implanon has to be used as a spacing method hence return of ovulation and fertility is an important parameter to be studied. 40% cases had return of ovulation within 1 month which was confirmed by progesterone estimation. Among the cases who did not adopt any alternative contraception methods, 95.8% conceived within 12 months. There was only one case who did not conceive within 1 year and she was suffering from hypothyroidism.

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