Original Article

Inadvertent Extended use of Implanon[R] Contraceptive Implants by Clients in Jos, Nigeria: An Interesting Finding

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Abstract

Background: Contraceptive implants are popular methods among women accessing family planning in Jos. Women appear to be using these methods for longer periods despite adequate counselling including the use for a maximum period prescribed by the manufacturers.

Methodology: This was a retrospective, cross sectional study of all clients who had Implanon[R] classic removed between May 2006 and December 2019. The register of acceptors of the implant was retrieved and relevant variables collated and analyzed for age, duration of use of the implant and the indication for removal. The data was analyzed using the Stata statistical software version 14, College Station, Texas, USA.

Results: A total of 1,805 implants were inserted, when all of them would have been removed, only 596(33%) were documented to have been removed. The mean age of the clients was 31.031 ± 5.56 years, range 18-51 years. The mean duration of use of Implanon[R] was 29.370 ± 11.756 months, range 0.5-72months. About 83(13.9%) implants were used beyond the expected duration of use of 36 months. By the 3rd, 4th and 5th years, 86.1%, 97.5% and 99.2% had had the implants removed. Clients used the method beyond the stipulated expiration of the implants, up to twice the period expected. There was no failure or pregnancy recorded.

Conclusion: About one-sixth of women extended the use of Implanon[R] implants. This may be more as only 33.0% of them returned for removal at the facility where it was inserted. However, there was no pregnancy recorded in this group of women despite the extended duration of use.

Keywords: Contraceptive Implants; Implanon[R] Classic; Extended use; Jos; Nigeria.

Introduction

The contraceptive implants have been in use in Nigeria for over 3 decades, and well accepted by clients while it lasted.[1] They can therefore be said to be tested, long-acting and reversible methods of contraception. Implants provide effective, long-term and reversible contraception to desiring women. For the etonogestrel-based implant (Implanon[R]), duration of use is 36 months while the levonorgestrel based implant (formerly Norplant and now Jadelle[R]), it is 60 months.

The Implanon[R] implants prevent pregnancy for up to 3 years (36 months) and must be removed and replaced, if continuation is desired, at three-year point to continue to offer protection from unintended pregnancy. The use of the method beyond three years could therefore be considered as extended use. 'Extended use' is defined as 'the use of the implant beyond currently approved

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durations of use.[2] Extended use is unusual and therefore not anticipated to be done by clients. This is clearly stated during counselling session for the implant, and expected to be complied with. Implanon[R] classic was introduced in Jos in 2006, but discontinued in 2016 by its manufacturers; and replaced with a newer version called Implanon[R] NXT with the potential of location by x-ray, and useful for locating the implant when it becomes difficult to do so manually.

Most contraceptive methods can be placed, applied or discontinued without the involvement of the healthcare provider. However, to insert or stop using an implant, clients need to visit a health care facility. At clinic visits, adequate counselling is offered to all client, informed choice of the method is ensured and method provided. Documentation is done by the provider after basic minimum investigations are performed and the method given. The etonogestrel (ENG)-releasing subdermal contraceptive implant was developed in the 1980s and the first regulatory trials were conducted in the 1990s. Scientists involved in the early development of the product suspected that high contraceptive efficacy would extend beyond 3 years; however, the industry-sponsored trials were not designed to go past 3 years. Thus, the product was approved worldwide with a 3-year indication.

Regulated trials in the 1990s designed to measure cumulative 3-year efficacy established its safety and efficacy for up to 3 years and not beyond. However, pharmacokinetic data showed high levels of the hormone at 3 years, and some clinical research confirmed efficacy beyond the approved duration of 3 years.[3,4] To-date, women and the service providers abide by the labelled duration and counsel for the removal once this duration is reached. Extending the labelled duration of use of ENG-releasing contraceptive implants will have many benefits to the women and family planning programmes, especially with the increasing acceptability and use of contraceptive implants in Sub Saharan Africa[5].

The existing data suggested that an etonogestrel(ENG) concentration >90 pg/ml is necessary to effectively prevent ovulation[6]. In normal-weight women (i.e. BMI = 18.5–24.9 kg/m^2), the average ENG concentrations at 2 and 3years post-insertion are 194 and 156 pg/ml, respectively. The Implanon[R] subdermal contraceptive implant is a device which contains 68 mg of ENG as the active ingredient with an average release rate of 60–70 µg/day in weeks 5–6, decreasing to ~35–45 µg/day by the end of the first year, 30–40 µg/day by year 2, and then to 25–30 µg/day at the end of the third year.[7]The bioavailability remains constant and close to 100%, and the elimination half-life of the parent compound is around 25 hours.[3] Pharmacokinetic (PK) analysis showed that at the end of the life-span of the implant (i.e. 3 years), the serum levels are above the threshold for effective contraception.[3,8] This has prompted research into comparative studies to determine whether the duration of the use of Implanon[R] could be extended to 5 years to be at par with the Jadelle[R] contraceptive implant which contains levonorgestrel. Little has been done here in this direction and therefore no data to back up this suggestion. We therefore looked at our cohort of clients that used the method for various durations and the contraceptive outcomes.

The aim of our study wasto determine the proportion of clients that used Implanon[R]contraceptive implants beyond the recommended duration by the manufacturers and to identify any failure of the method during the period of the extended use.

Study Questions

Did clients / women extend the use of the 3-year contraceptive implant Implanon[R] classic beyond the 3 years recommended by the manufacturers? Were there any failures of the method among the women extending its use?

Study Design

This was a cross sectional,retrospective review of all women who had Implanon[R] Classic removed in the Family Planning clinic in Jos University Teaching Hospital, Jos, Nigeria from November 2006 to December, 2019. The Implanon[R] was in use from May 2006 to October 2016 when it was withdrawn and later replaced by Implanon[R] NXT.

Setting

he hospital has a family planning unit that provides all forms of family planning methods (Type - A Facility). The facility provides the services to all

clients from 9:00am to 3:00pm, Monday to Friday. Adequate counseling is offered to all clients after which informed choice is made by the client.

The register of acceptors of the Implanon[R] classic was retrieved and those who had the implants removed were all collated and analyzed for total number of insertions and removals, age of client, duration of use of the implant (calculated from date of insertion to the date of removal),the indication for removal and contraceptive failure if any. These variables / parameters were collated and analyzed. These variables were usually taken and recorded in a dedicated register for Implanon[R] at the family planning clinic at insertion and at removal of the implants. The data was analyzed using the Stata statistical software version 14, College Station, Texas, USA.

Results

A total of 1,805 Implanon[R] classic implants were inserted from its introduction in October 2006 to its withdrawal in November 2016 by the manufacturers. Figure 1 shows the package containing a single Implanon classic implant.

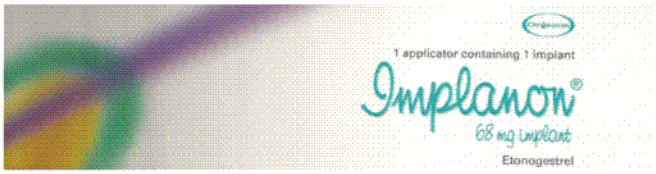

Figure 1: Package of Implanon Classic
Contains one rod for single use, has 68mg of Etonogestrel, meant for 3 years; developed by Organon

Three years later, November 2019, at a time when all the Implanon classic would have been removed, only 595(33%) were documented to have been removed. Out of all the removals, 83(13.9%) extended the use of the implants. The age range of the clients was 18-51 years, with a mean of 31.03 ± 5.56 years. The average age of those who extended the use of the implant was 33.0 years, and apparently older than the general users by 2 years. Duration of months of use of the implants showed a range of 0.5-72 months with a mean of 29.37 ± 11.76 months, Table 1.

Table 1: Average duration of use of the Implanon[R] Classic

Months of Use	Number (%)
1-6	22 (3.7)
7-12	45 (7.6)
13-18	64 (10.8)
19-24	72 (12.1)
25-30	39 (6.6)
31-36	270 (45.4)
37-42	52 (8.7)
43-48	16 (2.7)
49-54	3 (0.5)
55-60	7 (1.2)
≥ 61	5 (0.8)
Total	**595 (100.0)**

(Range of Months of use 1-72 months, mean = 29.37 months)

The average duration of extended use was 43.8months, with a range of 37-72months, Table 2; while it was 27.0 months for those who used it within 36 months.

Table 2: Clients using the Implanon[R] Implants beyond the stipulated 36 months

Extended use (in Months)	Number (%)
37 - 38	26 (31.3)
39 - 40	16 (19.3)
41 - 42	10 (12.0)
43 – 44	5 (6.0)
45 – 46	5 (6.0)
47 - 48	6 (7.2)
49 - 50	2 (2.4)
≥ 51	13 (15.7)
Total	**83 (100.0)**

(Average duration of use: 43.8 months)

Table 3 shows the distribution of the clients by year of use of the implants. By the 3rd year, 86.1% of them had had it removed, and majority (51.9%) being in the 3rd year. By the 4th year, 97.5% had had them removed while by the 5th year, almost all of them (99.8%) had been removed.

Table 3: Distribution of clients using Implanon[R] Classic by year

Year	Number (%)
1	67 (11.3)
2	136 (22.9)
3	309 (51.9)
4	68 (11.4)
5	10 (1.7)
6	5 (0.8)
Total	**595 (100.0)**

There was no pregnancy recorded among the extended users of the method.

Discussion

About one-sixth of Implanon[R] classic users extended the use before presentation to the clinic for removal. This percentage could be much higher than this as only 33% of all clients who had the implant inserted returned for removal. It is unlikely that more than two-thirds of them would have gone elsewhere for removal. In addition, no client presented with method failure resulting in pregnancy and thus requesting for removal. We are of the view that most of these defaulters are still using the implant, and therefore extending the duration of use. Whatever the reason for extended use, the patients may be relying on its efficacy while extending its use. Results from other studies corroborate previous evidence showing high contraceptive efficacy of Implanon[R] classic through 4 to 5 years.[9,10] This is suggestive of the product's capability to provide safe and effective contraception beyond the prescribed maximum period of use of 36 months by the manufacturers. Implanon[R] was introduced for use in the facility in May 2006 and withdrawn in October 2016, thus it was in use for the period of 11 years and 5 months. By November 2019, all the implants should have been removed from clients using them. Our findings further provide valuable information for the manufacturers, policy makers, family planning programmers and clinicians that the etonogestrel releasing contraceptive implant (Implanon[R]) may still be highly effective beyond the 36 months and probably up to 60 months after insertion.

Although the Implanon[R] implant is approved for use up to 3 years, some reports demonstrate effectiveness beyond that. Two studies did not report any pregnancies through the fourth year of use.[4,11] The extended use of the ENG-implant could reduce the frequency of removal/insertion procedures, and consequently improve implant cost-effectiveness, while improving convenience for women. Extending the duration beyond the currently approved length of use, if shown to be efficacious, could also offer another means of enhancing accessibility by maximizing the lifetime of the implant. Furthermore, knowledge about the extended effectiveness beyond the labelled duration would allow women to confidently continue to use their current method in the event that they could not access or afford a new device.

Extending use of the ENG-implant will save resources, including the time of health personnel, and for the users, save additional cost and will require fewer removal and insertion procedures.

Our study corroborate the findings of other studies, although of different designs, but all on extended use of ENG-releasing subdermal implants.[9,12] In a study on extended use up to 5 years of the ENG-releasing subdermal contraceptive implant compared to levonorgestrel-releasing subdermal implant, in a geographically diverse population, the WHO study group showed that the ENG- and LNG-subdermal implants have the same contraceptive effectiveness beyond 3 years up to 5 years with no major differences in occurrence of side effects.[9] A study on the use of ENG implant and levonorgestrel intrauterine device, 2 years beyond the Food and Drug Administration approved duration of use, no documented pregnancies were noted in implant users during the 2 years of post-expiration follow-up in the fourth and fifth-year of use.[12] Additionally, that study indicated that the contraceptive implant, and the 52-mg hormonal intrauterine device continue to be highly effective for at least 2 additional years of use. In our setting, the ENG-releasing contraceptive implants are much more accessible and affordable than the levonorgestrel-releasing intrauterine device. Serum etonogestrel evaluation demonstrates median levels remain above the ovulation threshold of 90 pg/ml for women in all body mass index classes.[12]

Extended duration of the ENG-subdermal implant would have many policy and programmatic benefits. First, it is safer for users; less frequent removal and fewer insertion cycles reduce trauma to the skin and reduce the chances of surgical errors. Furthermore, it would also save time and resources for the health system and opens new hours of consultation at services habitually full of women seeking attention. Second, extended use saves resources. For example, if international donor agencies pay US$ 9 per unit, and if the product has two additional years, then the cost per couple-year of protection drops from US$ 3 to US$ 1.80. Third, voluntary continued use of a long-acting contraceptive method reduces the chances of unintended pregnancy when users transition to other products. However, a systematic review of efficacy with extending contraceptive implant found that at this time, there appears to be insufficient evidence to recommend extended duration of the LNG implant.[2]To the best of our knowledge, this is the first report on extended ENG-subdermal implant use up to 5 years in our country. Without securing a change in the product label, the logical next step is that WHO evaluate the available evidence on ENG-subdermal implant safety and efficacy as for DMPA, and make similar recommendations for extended use.

Conclusion

About one-sixth of women extended the use of Implanon[R] implants. This may be higher as only 33.0% of them returned for removal at the facility where is it was inserted. However, there was no pregnancy recorded in this group of women despite the extended duration of use.

Recommendations

There is need for further research into why some women extend the use of implanon implants. Prospective studies are also needed to evaluate the efficacy of the product over the extended period by assaying the serum levels of the active hormone. If extended efficacy is proven; it will reduce cost, inconvenience and risks to these women.

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