Original Article

Three-Year Continuation Rate of Etonogestrel Subdermal Implant and Associated Factors

Assavapokee N, MD[1], Wattanayingcharoenchai R, MD[1], Aimjirakul K, MD[1]

[1] Department of Obstetrics and Gynecology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Objective: To determine continuation rate of etonogestrel subdermal implant (ESI) and to investigate the factors associated with continuation and reasons for early discontinuation.

Materials and Methods: Medical records of women who had ESI insertion at family planning clinic between January 1, 2014 and April 30, 2015 were reviewed. All implant clients who had a minimum follow-up period of three years or had implant removal at any time before three years of use were included in the study. Demographic data, information about contraceptive use, adverse hormonal effects including menstrual changes and weight changes were collected. Date of implant insertion and removal, and reasons for early implant removal were recorded.

Results: Of the 598 ESI clients, follow-up data was available for 431 cases (72.1%). Mean age of the ESI users was 25.1±8.9 years. About 43% of ESI users were teenagers. The continuation rates were 95.4%, 88.4%, and 83.1% in 1, 2, and 3 years, respectively. Women with age group less than 20 years and more than 40 years showed significant higher continuation rate than women in age group of 20 to 40 years ($p<0.001$). There was no association between BMI, education, obstetric history, previous contraceptive use, weight changes, menstrual changes, and ESI continuation. Unscheduled bleeding was the main reason for early implant removal. However, only 16.9% of ESI users having unscheduled bleeding discontinued implant use because of their bleeding problem.

Conclusion: Etonogestrel subdermal implant is highly effective and a cost-effective method of contraception. A high continuation rate of ESI through three years indicates the high acceptability of this methods in all age groups.

Keywords: Etonogestrel, Subdermal contraceptive implant, Long-acting reversible contraception, LARC, Continuation rate

J Med Assoc Thai 2019;102(6):657-62
Website: http://www.jmatonline.com
Received 17 Dec 2018 | Revised 30 Apr 2019 | Accepted 2 May 2019

Despite the high contraceptive prevalence rate in Thailand, the number of unintended pregnancy that leads to abortion remain high[1]. Most unintended pregnancies result from inconsistent use of contraceptive methods or no contraceptive use[2]. Therefore, non-user dependent contraceptive methods including contraceptive implant and intrauterine device may be the appropriate choice for women who would like to defer their pregnancies.

The long acting reversible contraception (LARC), a contraceptive implant, has several advantages over the other reversible contraceptive methods including highest efficacy in pregnancy prevention, low possibility of user error, no need for pelvic examination, and less frequent follow-up visits need[3-5]. The first implant, 6-rod system containing levonorgestrel (Norplant®) was introduced into the market in 1983 in Finland[5]. Due to the difficulty in implants removal, one rod system containing etonogestrel (Implanon®) and etonogestrel plus barium sulphate (Implanon-NXT® or Nexplanon®) had been developed in 1998 and 2011, respectively[6,7]. At present, etonogestrel subdermal implant (ESI) has been approved for contraception in more than 90 countries.

Although ESI offers proven effectiveness and safety, low use of this method may contribute to high unintended pregnancy rate. The reported 3-year continuation rate varied from 25% to 65%[8-16]. Main reason for early implant removal was irregular

Correspondence to:

Wattanayingcharoenchai R.

Department of Obstetrics and Gynecology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand.

Phone: +66-2-2012167, **Fax**: +66-2-2011416

Email: littleru@hotmail.com

How to cite this article: Assavapokee N, Wattanayingcharoenchai R, Aimjirakul K. Three-Year Continuation Rate of Etonogestrel Subdermal Implant and Associated Factors. J Med Assoc Thai 2019;102:657-62.

bleeding, accounting for up to 45% of discontinued users[14].

ESI had been available in Thailand since 2000, but its utilization rate remains low. Contraceptive prevalence rate of implant, surveyed by the Thai Ministry of Public Health in 2014, was only 0.22% of all methods used in reproductive age women[17]. Several factors that may contribute to low use of contraceptive implant in Thai women include lack of provider's knowledge and skill, fear of hormonal adverse effects, inaccessibility of family planning service, and high contraceptive cost[18]. To increase implant utilization, the National Health Security Office announced the policy to provide LARC (i.e., implant and intrauterine device) without charge for all women aged under 20 years old in May 2014. From the Thailand Multiple Indicator Cluster Survey in 2015 to 2016, contraceptive prevalence of implant was increased five times from that reported in 2014[19].

Although implant utilization tend to increase, but there are limited data regarding continuation rate of implant in Thailand. Chaovisitsaree et al (2005) found 7.6% of implant users discontinued using ESI during the one-year period of study[20]. In 2008, Thamkhantho et al[21] reported one-year continuation rate of 54% in women receiving single rod subdermal implant at Siriraj Hospital. Suntipap (2018) found the discontinuation rate of 1.7% in teenage mothers receiving single rod subdermal implant during postpartum periods. However, the follow-up rate in the present study was only 24.7% of total contraceptive clients[22]. At present, only one study reported the 3-year continuation rate of single rod implant in Thailand, which was 74.7%[23]. However, that pilot study aimed to evaluate the efficacy of single rod implant over a period of four years and recruited only 100 women, therefore, it might not represent implant continuation rate under the real circumstance. The objectives of the present study were to assess 3-year continuation rate of ESI and to identify factors associated with continuation and reasons for early discontinuation.

Materials and Methods

The medical chart review was conducted after approval by the Ethical Clearance Committee on Human Rights related to Researches involving Human Subjects, Faculty of Medicine Ramathibodi Hospital, Mahidol University. Medical records of women aged 10 to 49 years old who had ESI insertion for contraceptive purpose at the family planning clinic between January 1, 2014 and April 30, 2015 were accessed to obtain implant-related information. Eligible participants were ESI users who had completed a 3-year follow-up period after implant insertion, or had implant removal at any time before three years of use. The present study protocol was registered with the Thai Clinical Trial Registry (TCTR20180405003).

Demographic data including age, level of education, body mass index, and number of living children were collected. Information about contraceptive use including time of implant insertion (i.e., interval, post-abortion, or postpartum), prior contraceptive method use, date of implant insertion and removal, and common adverse hormonal effects (i.e., weight changes and pattern of bleeding events) were also collected. Weight changes were defined as weight loss or weight gain of 1 kg or more per year of implant use[24]. Pattern of bleeding events were categorized into three groups, regular or normal menstruation, amenorrhea, and unscheduled bleeding.

Participants were categorized into "implant continuation" group or "implant discontinuation" group. Implant continuation was defined as participant continued the etonogestrel implant for at least 36 months, whereas implant discontinuation was defined as implant removal occurred before 36 months after insertion. For implant discontinuation group, reasons for early removal and contraceptive choice after implant removal were recorded.

Sample size calculation

The sample size was calculated from the formula for estimating single proportion where Z_α was set as 1.96 with a type I error of 5%, confidence interval width was set as 0.05. Given an estimate 56.4% of three-year continuation rate of etonogestrel implant from the study of Diedrich et al[14], the calculated sample size was 378 participants. The calculated number was increased by 10% of the calculated number of participants for data loss. Therefore, 420 participants would be required in the study.

Statistical analysis

Statistical analyses were performed using IBM SPSS statistical software version 22 for Windows (IBM Corp., Armond, NY, USA). Continuous data were reported as the mean and standard deviation. Categorical data were shown as the frequency and percentage. Pearson chi-square or Fisher's exact test were used to compare categorical characteristics between implant continuation and implant discontinuation groups. All variables

Table 1. Characteristics of etonogestrel subdermal implant participants (n=431)

Characteristics	Implant continuation (n=358) n (%)	Implant discontinuation (n=73) n (%)	OR (95% CI)
Age group at insertion (years)			
<20	165 (46.1)	19 (26.0)	2.74 (1.55 to 4.83)
20 to 40	165 (46.1)	52 (71.2)	1
>40	28 (7.8)	2 (2.7)	4.41 (1.01 to 19.15)
BMI, (kg/m^2)			
Underweight (<18.5)	61 (17.0)	8 (11.0)	1.39 (0.61 to 3.23)
Normal (18.5 to 22.9)	158 (44.1)	29 (39.7)	1
Overweight and obese (≥23.0)	139 (38.8)	36 (49.3)	0.71 (0.41 to 1.22)
Education			
Primary school	27 (7.5)	9 (12.3)	1
High school	223 (62.3)	40 (54.8)	1.86 (0.81 to 4.24)
College or higher	108 (30.2)	24 (32.9)	1.50 (0.63 to 3.60)
Living children			
No	86 (24.0)	15 (20.5)	1
Yes	272 (76.0)	58 (79.5)	0.82 (0.44 to 1.52)
Timing of insertion			
Interval	115 (32.1)	26 (35.6)	1
Post-abortion	69 (19.3)	14 (19.2)	0.89 (0.44 to 1.83)
Postpartum	174 (48.6)	33 (45.2)	1.07 (0.54 to 2.12)
Prior contraceptive method use			
None	152 (42.5)	33 (45.2)	1
Non-LARCs	141 (39.4)	28 (38.4)	1.09 (0.63 to 1.90)
LARCs	65 (18.2)	12 (16.4)	1.18 (0.57 to 2.42)
Weight change			
No change	42 (11.7)	8 (11.0)	1
Decrease	108 (30.2)	30 (41.1)	0.69 (0.29 to 1.62)
Increase	208 (58.1)	35 (47.9)	1.13 (0.49 to 2.61)
Pattern of bleeding events			
Regular	57 (15.9)	7 (9.6)	1
Unscheduled bleeding	148 (41.3)	41 (56.2)	0.44 (0.19 to 1.05)
Amenorrhea	153 (42.7)	25 (34.2)	0.75 (0.31 to 1.83)

OR=odds ratio; CI=confidence interval; BMI=body mass index; LARCs=long-acting reversible contraceptives

significantly associated with implant continuation use in univariate logistic regression analysis were entered in multivariate logistic regression analysis. All reported probability values are two-tailed, and a p-value of less than 0.05 was considered to be statistically significant.

Results

Between January 1, 2014 and April 30, 2015, 598 women who selected ESI as their contraceptive method were included in this study. Follow-up data of 431 participants could be retrieved from medical record, resulting in a 72.1% completed follow-up

Table 2. Reasons for ESI early discontinuation and duration of implant use (n=73)

Reasons	n (%)	Duration of implant use (months) Mean±SD
Unscheduled bleeding	32 (43.8)	21.5±8.2
Weight gain	11 (15.1)	14.4±5.6
Acne	2 (2.7)	16.2±11.9
Not related to ESI*	28 (38.4)	16.2±9.0

SD=standard deviation; ESI=etonogestrel subdermal implant

* No contraceptive need, permanent contraception

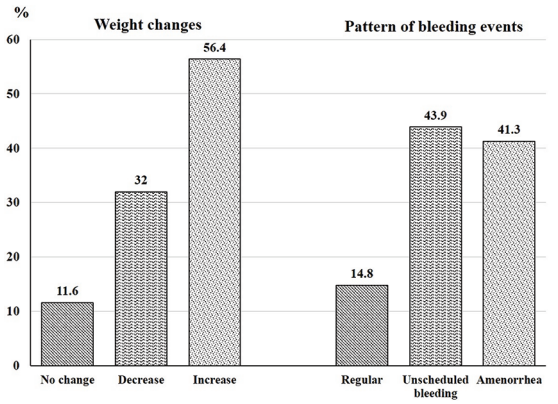

Figure 1. Weight changes and pattern of bleeding events after ESI uses.

rate. Mean age of the participants was 25.1±8.9 years. About 43% of the subjects were teenagers. Nearly half (48.1%) of implant users had implant insertion during the postpartum period. Only 17.8% had ever used LARCs prior to the present study. Table 1 shows the baseline characteristics of the continued users and the early-discontinued users.

Continuation rates at 1, 2, and 3 year(s) were 95.4%, 88.4%, and 83.1%, respectively. Mean duration of implant use in continued users and early-discontinued users was 36.8±0.5 and 18.3±8.6 months, respectively. Women in age group of 20 to 40 years had significant higher early discontinuation than that in the other two age groups. There was no association between levels of education, body mass index (BMI), living children, time of ESI insertion, prior contraceptive use, and early discontinuation rate (Table 1).

Regarding common adverse hormonal effect of ESI, 56.4% of ESI users had weight gain and over 80% of users reported either menstrual irregularity or amenorrhea (Figure 1). However, changes in weight did not affect implant continuation. Early discontinued users tended to have more unscheduled bleeding. Reasons for early discontinuation and duration of implant use are shown in Table 2. The reasons for early implant discontinuation were unscheduled bleeding, weight gain, and acne, accounting for 43.8%, 15.1%, and 2.7%, respectively. However, there was reason for early discontinuation that was not related to ESI such as changes to permanent contraception and no contraceptive need, accounting for 38.4% of discontinued users.

Discussion

Contraceptive implant is the most effective long-term reversible contraception. ESI utilization in Thailand tend to increase since the government provided free implant to all teenagers requiring contraception. However, continuation of implant use is an important factor contributing to its contraceptive efficacy in the real-life situation. In the present study, in the family planning clinic, all women had chosen contraceptive choice based on their own preference after attending group counseling. All clients who selected contraceptive implants were individually informed about the insertion procedure and possible adverse effects including unpredictable bleeding and weight change.

In the present study, 3-year continuation rate was 83.1%, which was higher as compared to Teunissen et al's (25%), Diedrich et al's (56.2%), Obijaru et al's (40%), and Asaye et al's studies (35%)[13-16]. Considering the worst-case scenario where all loss to follow-up cases were discontinued users, continuation rate was still higher (59.9%). The difference in continuation rate might be due to the difference in characteristics of study population. The proportion of teenager in the present study was about 43%, whereas Teunissen et al's and Asaye et al's studies had the proportion of teenager of 20% and 25%, respectively[13,16]. Teen participants were the group that prefer longer duration of birth spacing. This could contribute to the high continuation rate in the present study. Moreover, three-fourth of the subjects in the present study had at least one living child, whereas 94% of the participants in Obijaru et al's study were nulliparous women[15]. It is plausible that nulliparous women that were less certain about duration of birth spacing had more early implant discontinuation. From Kiriwat et al's study[23], 3-year continuation rate was 74.7%, which was not much different from the present study. However, Kiriwat et al's study aimed to evaluate

the efficacy of single rod implant over a period of four years and recruited a limited number of participants based on clinical feasibility. Therefore, the result could not represent the continuation rate in real-life.

Regarding the associated factors for implant continuation, only age group less than 20 years and over 40 years were associated with higher implant continuation rate. The present study result was similar to the previous studies[13,16], which found higher continuation rate in women in the age group over 35 and 40 years. Prior LARC use was not associated with implant continuation in the present study, whereas Teunissen et al's study found the highest continuation rate in prior implant users. Presence of living children was also not associated with implant continuation. The finding was in agreement with Asaye et al's study[16]. The difference in factors associated with implant continued use might be due to the difference in cultural context of contraceptive clients.

Unpredictable bleeding pattern is the most troublesome problem in progestin-containing implant, which can affect clients' acceptability[25]. In the present study, unscheduled bleeding was reported in 43.9% of implant users, which was similar to the previous studies[11,21,26]. Unscheduled bleeding was also the most common reason (43.8%) for implant early discontinuation in the present study. This was similar to those reported in most studies[12-16]. However, of the women who had unscheduled bleeding, only 16.9% underwent early implant removal. The low discontinuation rate could be the result of individual counseling prior to implant insertion, whereby information was given about possible adverse events including menstrual changes and weight changes. Weight gain was another adverse effect detected in about half of implant users in the present study, but did not affect implant continuation.

There were several strengths in the present study. First, the study had a high follow-up rate of 72% over 36 months. Second, the study included a wide range of age from teenage to advanced reproductive age. Therefore, all implant users would be included in the analyses. Third, standard contraceptive record form was used as contraceptive documentation for each client in the authors' family planning clinic. This could help increase data completeness. As the present study was a retrospective chart review study, bleeding pattern could not be categorized according to bleeding patterns for 90-day reference periods recommended by WHO[27]. The present study was conducted in a university hospital, therefore, the generalizability of the findings may be limited. To the authors' knowledge, the present study is the first study evaluating a three-year continuation of etonogestrel implant under real-life condition in Thailand.

The findings of the present study indicate the high three-year continuation rate of etonogestrel implant. Despite the high occurrence of common adverse events such as unscheduled bleeding and weight gain, it does not affect implant continuation. The present study can help health professionals offer the proper implant contraception to all contraceptive clients.

Conclusion

ESI is an highly effective and cost-effective method of contraception. Despite the problem of unpredictable bleeding pattern, a high continuation rate of ESI through three years after insertion in all age groups can indicate the high acceptability of the method. For women requesting long-term contraception, especially teenager, ESI should be offered as first-line contraceptive method.

What is already known on this topic?

ESI is highly effective long-acting reversible contraception. Common adverse events related to progestin implant include menstrual disruption and weight change. Unscheduled bleeding is the main reason for early implant removal in discontinued users.

What this study adds?

Teenagers had high implant long-term continuation rate. Menstrual irregularities and weight changes from implant use did not have effects on implant continuation. This study confirms the existing evidence that unscheduled bleeding is the main reason for early implant removal.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Bureau of Reproductive Health Ministry of Public Health. Abortion surveillance report, Thailand 2014 [Internet]. 2014 [cited 2016 Jul 1]. Available from: http://rh.anamai.moph.go.th/download/all_file/brochure/AbortionSurveillanceInThailandReport2014.pdf.
2. Finer LB, Zolna MR. Declines in unintended pregnancy in the United States, 2008-2011. N Engl J Med 2016; 374:843-52.
3. Power J, French R, Cowan F. Subdermal implantable contraceptives versus other forms of reversible contraceptives or other implants as effective methods of preventing pregnancy. Cochrane Database Syst Rev

2007;(3):CD001326.
4. Trussell J. Contraceptive failure in the United States. Contraception 2011;83:397-404.
5. Hohmann H, Creinin MD. The contraceptive implant. Clin Obstet Gynecol 2007;50:907-17.
6. Fischer MA. Implanon: a new contraceptive implant. J Obstet Gynecol Neonatal Nurs 2008;37:361-8.
7. Mansour D. Nexplanon(®): what Implanon(®) did next. J Fam Plann Reprod Health Care 2010;36:187-9.
8. Rai K, Gupta S, Cotter S. Experience with Implanon in a northeast London family planning clinic. Eur J Contracept Reprod Health Care 2004;9:39-46.
9. Agrawal A, Robinson C. An assessment of the first 3 years' use of Implanon in Luton. J Fam Plann Reprod Health Care 2005;31:310-2.
10. Lakha F, Glasier AF. Continuation rates of Implanon in the UK: data from an observational study in a clinical setting. Contraception 2006;74:287-9.
11. Arribas-Mir L, Rueda-Lozano D, Agrela-Cardona M, Cedeno-Benavides T, Olvera-Porcel C, Bueno-Cavanillas A. Insertion and 3-year follow-up experience of 372 etonogestrel subdermal contraceptive implants by family physicians in Granada, Spain. Contraception 2009;80:457-62.
12. Weisberg E, Bateson D, McGeechan K, Mohapatra L. A three-year comparative study of continuation rates, bleeding patterns and satisfaction in Australian women using a subdermal contraceptive implant or progestogen releasing-intrauterine system. Eur J Contracept Reprod Health Care 2014;19:5-14.
13. Teunissen AM, Grimm B, Roumen FJ. Continuation rates of the subdermal contraceptive Implanon(®) and associated influencing factors. Eur J Contracept Reprod Health Care 2014;19:15-21.
14. Diedrich JT, Zhao Q, Madden T, Secura GM, Peipert JF. Three-year continuation of reversible contraception. Am J Obstet Gynecol 2015;213:662-8.
15. Obijuru L, Bumpus S, Auinger P, Baldwin CD. Etonogestrel implants in adolescents: experience, satisfaction, and continuation. J Adolesc Health 2016;58:284-9.
16. Melkamu Asaye M, Syoum Nigussie T, Mequannt Ambaw W. Early Implanon discontinuation and associated factors among Implanon user women in Debre Tabor Town, Public Health Facilities, Northwest Ethiopia, 2016. Int J Reprod Med 2018;2018:3597487.
17. The Ministry of Social Development and Human Security. Contraceptive uses in women of reproductive age (15-49 years) [Internet]. 2014 [cited 2016 Dec 26]. Available from: http://healthcaredata.moph.go.th/report/std18report/rep_J03_thailand.php?year=2557.
18. Gold MA, Coupey SM. Young women's attitudes toward injectable and implantable contraceptives. J Pediatr Adolesc Gynecol 1998;11:17-24.
19. National Statistical Office and United Nations Children's Fund, Thailand. Multiple indicator cluster survey 2015-2016, Final report, NSO and UNICEF [Internet[. 2016. [cited 2016 Dec 26]. Available from: https://www.unicef.org/thailand/sites/unicef.org.thailand/files/2018-06/Thailand_MICS_Full_Report_EN_0.pdf.
20. Chaovisitsaree S, Piyamongkol W, Pongsatha S, Morakote N, Noium S, Soonthornlimsiri N. One year study of Implanon on the adverse events and discontinuation. J Med Assoc Thai 2005;88:314-7.
21. Thamkhantho M, Jivasak-Apimas S, Angsuwathana S, Chiravacharadej G, Intawong J. One-year assessment of women receiving sub-dermal contraceptive implant at Siriraj Family Planning Clinic. J Med Assoc Thai 2008;91:775-80.
22. Suntipap M. Implant discontinuation rate among teenage pregnancy in 2015-2017. J Prev Med Assoc Thai [Internet]. 2018 [cited 2018 Sep 23];8(1):81-7. Available from: https://www.tci-thaijo.org/index.php/JPMAT/article/view/126531.
23. Kiriwat O, Patanayindee A, Koetsawang S, Korver T, Bennink HJ. A 4-year pilot study on the efficacy and safety of Implanon, a single-rod hormonal contraceptive implant, in healthy women in Thailand. Eur J Contracept Reprod Health Care 1998;3:85-91.
24. Bahamondes L, Brache V, Ali M, Habib N. A multicenter randomized clinical trial of etonogestrel and levonorgestrel contraceptive implants with nonrandomized copper intrauterine device controls: effect on weight variations up to 3 years after placement. Contraception 2018;98:181-7.
25. Affandi B. An integrated analysis of vaginal bleeding patterns in clinical trials of Implanon. Contraception 1998;58(6 Suppl):99S-107S.
26. Darney P, Patel A, Rosen K, Shapiro LS, Kaunitz AM. Safety and efficacy of a single-rod etonogestrel implant (Implanon): results from 11 international clinical trials. Fertil Steril 2009;91:1646-53.
27. Belsey EM, Farley TM. The analysis of menstrual bleeding patterns: a review. Contraception 1988;38: 129-56.