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Effects of the etonogestrel-releasing implant Implanon® and a nonmedicated intrauterine device on the growth of breast-fed infants

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Abstract

The study objectives were to compare the effects of an etonogestrel-releasing implant (Implanon) and a nonmedicated intrauterine device (IUD) on parameters of lactation in breast-feeding women and on the growth of their breast-fed infants over a 3-year period. Healthy lactating women (28–56 days postpartum) chose either the implant ($n=42$) or the IUD ($n=38$). Infant growth during a 3-year follow-up period is reported here. Total duration of breast-feeding coinciding with the mothers' treatment was 421.0 and 423.4 days in the Implanon and IUD groups, respectively. There were no differences between the infant groups in terms of body length, biparietal head circumference and body weight. No abnormalities were reported in psychomotor development or during physical examination. No treatment-related side effects were observed in either group. In conclusion, there were no differences in the growth of breast-fed infants of women treated with Implanon or a nonmedicated IUD. Implanon, therefore, appears to be a safe contraceptive option for breast-feeding women and their infants.

Keywords: Contraceptive implant; Nonmedicated IUD; Breast-feeding; Etonogestrel; Infant growth; Adverse events

1. Introduction

The benefits of breast-feeding are well-known, particularly in developing countries, where the health of breast-fed infants tends to be better and their survival higher compared with non-breast-fed infants. Breast-feeding also provides mothers with contraceptive protection, which is important because a short interval between pregnancy results in a discontinuation of breast-feeding and may adversely affect the mother's health. When women are fully breast-feeding and amenorrheic, they tend to be protected from pregnancy [1–3]. However, when supplementary feeding and weaning are introduced, lactating women need to use additional contraceptive protection as the contraceptive and bleeding-controlling effects of breast-feeding diminish.

Combined methods of hormonal contraception are unsuitable for lactating women because the estrogen component adversely affects the quantity and composition of breast milk. Conversely, estrogen-free hormonal contraceptive methods, however, do not appear to adversely affect breast milk and are therefore suitable for women from 6 weeks postpartum [4,5].

Implanon (NV Organon, Oss, The Netherlands) is a single-rod etonogestrel-releasing contraceptive implant designed to provide contraceptive efficacy for three years mainly by ovulation inhibition [6]. Etonogestrel is the biologically active metabolite of desogestrel, which is widely used in oral contraceptives, including an estrogen-free pill (desogestrel 75 μg/day). Desogestrel 75 μg/day provides consistent ovulation inhibition [7] and has been shown to be effective and safe for use by breast-feeding mothers and safe for infant development [8].

The efficacy and safety of Implanon in nonlactating women have previously been established [9]. The present study investigated the effects of Implanon on lactation parameters and on the growth of breast-fed infants. Women were free to choose between Implanon and a nonmedicated

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intrauterine device (IUD); the nonmedicated IUD was a good comparator in this type of study because it does not release pharmacoactive components and will, therefore, not affect lactation or have an effect on the breast-fed infant. Effects on breast-feeding parameters (milk volume, milk composition and transfer of etonogestrel in breast milk), as well as the occurrence of adverse events in the children during the first 4 months of the study, have been reported previously [10]. No differences were found between the implant and IUD groups with regard to the volume or composition of the women's breast milk. The present report focuses on the development of the breast-fed children for 3 years since birth and the comparative safety of the two contraceptive methods for the infants of mothers who had used them.

2. Methods

2.1. Design

The study was an open, nonrandomized, group comparative study of two non-oral long-term contraceptive methods in breast-feeding women. The study was conducted at the Department of Obstetrics and Gynaecology of Chulalongkorn Hospital (Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand). Women were free to choose between an etonogestrel-releasing contraceptive implant (Implanon, NV Organon) and a nonmedicated IUD (Multiload® Cu 375 SL; NV Organon).

The study protocol was approved by the Ethics Committee of Chulalongkorn Hospital and the Ministry of Public Health. The study was performed in compliance with the declaration of Helsinki and guidelines on good clinical practice.

The primary objective of the study was to compare the effects of both contraceptive methods on the volume and quality of lactation and to determine the concentrations of etonogestrel in breast milk and compare them to the mothers' serum concentrations. The results of these assessments have been reported previously [10]. The present publication focuses on the secondary study objective, that is, to study the growth of the children up to the age of 3 years and to study the comparative safety in the children by means of regular examinations and assessment of adverse events.

Inclusion criteria for the mothers have been previously described [10]. Infants were included if they were healthy singletons born at 259–294 days of gestational age (based on ultrasound measurements during pregnancy), had a birth weight that did not deviate by more than 2 SDs of normal (reference Chulalongkorn Hospital) and were 28–56 days postpartum at the start of treatment.

2.2. Treatment

Implanon, a single-rod implant, was inserted under local anesthesia, subdermally on the inner side of the upper nondominant arm 6–8 cm above the elbow in the groove between the biceps and triceps (sulcus bicipitalis medialis). The implant was to remain in situ for 3 years.

Multiload Cu 375 SL, a copper IUD, was inserted according to the instructions given in the package insert. Users of the IUD could continue using the device after the 3-year study period if they wished to do so.

2.3. Assessments

The children's growth and development was studied by measuring anthropometric parameters (body weight, body height and biparietal head circumference) and by assessing psychomotor development and physical examination at baseline and at the end of months 1, 2, 4, 12, 18, 24, 30 and 36. Infant adverse events were monitored by active interviewing of the mothers at the end of months 1, 2, 4 and 9, and at 3-month intervals thereafter.

2.4. Statistical analysis

Statistical analyses were performed by the Biometrics Department at NV Organon using SAS version 6.12 under Windows NT. A random coefficients model (longitudinal analysis) was used to test for treatment effects on the anthropometric measurements of the infants — body length, body weight and biparietal head circumference.

3. Results

3.1. Subject disposition

Eighty women were enrolled in the study: 42 in the implant group and 38 in the IUD group. Eighty infants were also included in the study, and 38 (81.0%) infants in the Implanon group and 33 (86.8%) infants in the IUD group completed the study as planned. The primary reasons for infant discontinuation were all unrelated to treatment (mother not willing or able to cooperate further or lost to follow-up).

The baseline demographic data of the infants are presented in Table 1. There were no significant differences between the two treatment groups. The number of baby girls in the study population was higher than the number of boys, but the sexes were equally distributed over the groups.

Table 1
Infant demographic data at baseline (all-subjects-treated group)

	Implant group (n=42)			IUD group (n=38)		
	Mean	SD	Range	Mean	SD	Range
Age (days)	41.1	7.0	31–57	44.0	7.4	30–61
Body length (cm)	54.8	1.8	51–60	55.3	2.0	51–61
Body weight (g)	4722	446	3940–5590	4688	540	3500–6000
Body mass index (kg/m^2)	15.7	1.2	13–19	15.3	1.2	13–18
Biparietal head circumference (cm)	37.3	1.0	35–39	37.4	1.2	35–40
Sex, n (%)						
Female	25 (59.5)			23 (60.5)		
Male	17 (40.5)			15 (39.5)		

Table 2
Duration of breast-feeding (days) coinciding with Implanon/IUD use (all-subjects-treated group)

	Implant group ($n=42$)	IUD group ($n=38$)
Mean	421.0	423.4
SD	189.7	262.6
Range	34–876	1–1099

Data on the extent of infant exposure are presented in Table 2. Mean duration of breast-feeding coinciding with treatment of the mothers was 421.0 days (SD=189.7) in the Implanon group and 423.4 days (SD=262.6) in the IUD group.

3.2. Growth and development

There were no remarkable differences in body length between the treatment groups during the 3-year study (Fig. 1). Statistical testing revealed that average body length was comparable for both treatment groups and both sexes during the 3-year study period, and that there were no differences in growth rates between the two treatment groups.

Growth of infant body weight is depicted in Fig. 2. During the first 12 months, the mean body weight of the infants in the Implanon group was somewhat higher than of those in the IUD group; but from month 18 onward, the mean body weight of the children in the IUD group was higher. Statistical testing showed that the average body weight was comparable for both treatment groups and both sexes during the 3-year study period.

Growth of biparietal head circumference is presented in Fig. 3. Again, there were no differences between the two treatment groups during the 3-year study period. Statistical testing indicated that there were no significant differences between the two treatment groups or sexes. There was also no difference in growth rate between the two groups.

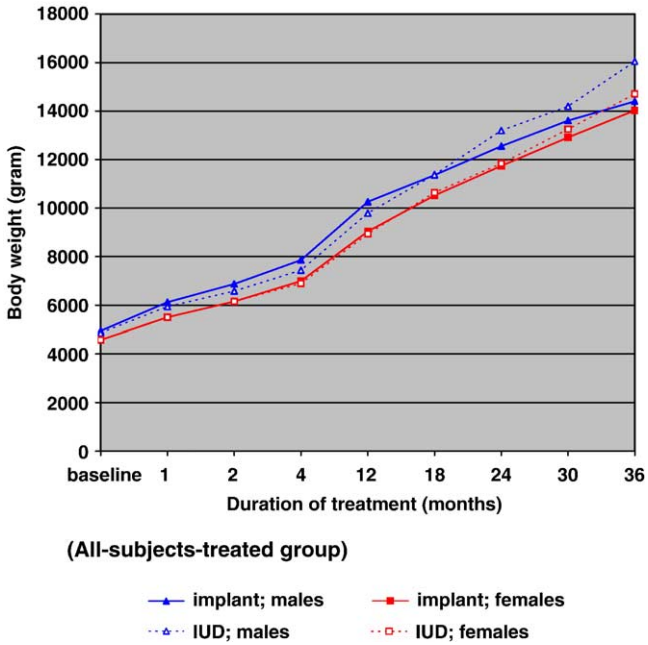

Fig. 2. Growth of body weight of the infants.

No abnormalities were reported for psychomotor development in either of the two treatment groups.

3.3. Adverse events

There were no treatment-related adverse events during the study and no discontinuations due to adverse events in either of the infant groups. The majority of infants presented with adverse events during the study period, with the most

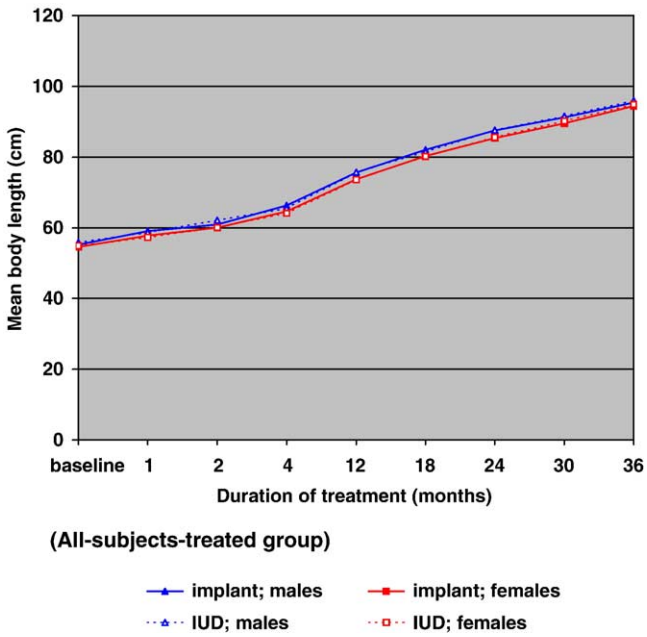

Fig. 1. Growth of mean body length of the infants.

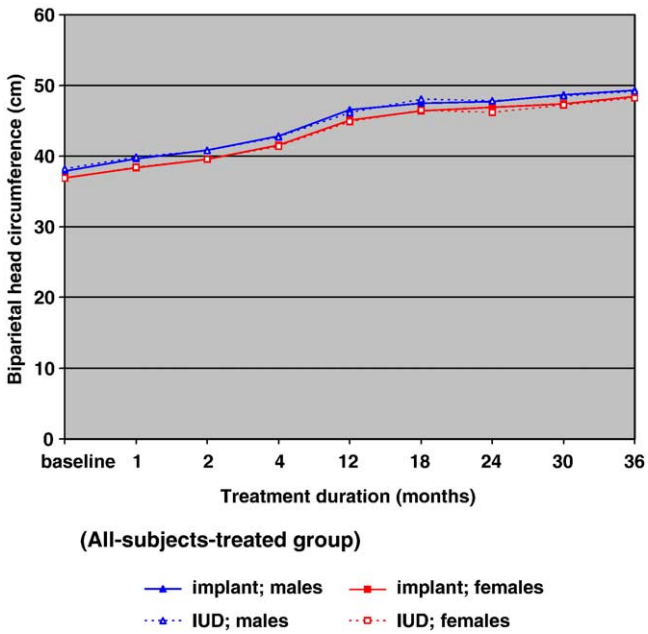

Fig. 3. Growth of biparietal head circumference of the infants.

frequently reported events being "respiratory tract disorders" (more than 60% for both groups) and "skin and appendages disorders" (more than 30% for both groups).

4. Discussion

Before a contraceptive method can be recommended for use during breast-feeding, it is important to know if lactation parameters or growth of the breast-fed child is adversely affected. The present study compared the effects of an etonogestrel-releasing implant (Implanon) to those of a nonmedicated IUD on lactation parameters and growth of the breast-fed infants.

Implanon releases etonogestrel at an initial rate of 60–70 μg per day, decreasing to 35–45 μg per day at the end of the first year of use. These levels of etonogestrel do not appear to affect the volume or quality of mothers' breast milk [10]. Analysis of maternal serum revealed that even during the initial period of use, when maternal serum concentrations are relatively high due to a "burst effect" of the implant, the transfer of etonogestrel to the mother's milk was low. With a mean concentration of 177.7 pg/mL in the first month, the mean dose ingested by the infant was calculated at 19.86 ng/kg a day. At months 2 and 4, etonogestrel concentrations in milk had decreased to 153.1 and 131.4 pg/mL, and the calculated doses ingested by the infants had decreased to 15.08 and 10.45 ng/kg a day at months 2 and 4, respectively. This decrease was caused both by the lower etonogestrel concentrations in milk and by the smaller volume ingested due to increased supplementary feeding.

The data reported here show that the etonogestrel ingested by the infants did not adversely affect their growth or development. Body length, body weight and biparietal head circumference increased to a similar degree as for infants whose mothers had used the IUD during breast-feeding, and there were no abnormalities in psychomotor or physical development. None of the adverse events reported in the infants were considered to be related to the ingestion of etonogestrel.

It should be noted that the number of women and children included in this study was based on the primary objective of determining the effects on lactation and the etonogestrel concentrations in milk. For the follow-up of infant growth, the numbers are limited for detailed analysis of effects on growth and development or for the study of comparative safety. However, it would appear that the results are in line with those reported previously for oral desogestrel and other comparative studies on the use of progestogen-only pills and nonmedicated IUDs on breast-feeding [8,11,12]. When oral desogestrel (75 μg/day) was compared with a nonmedicated IUD, there were no adverse effects on quantity or quality of breast milk or on the growth (body length, body weight and biparietal head circumference) of children followed up to the age of 2.5 years [8].

In conclusion, there were no differences in the growth of breast-fed infants of women using Implanon or a non-medicated IUD. There were no differences in safety-related parameters between the two groups. Implanon, therefore, appears to be a safe contraceptive option for breast-feeding women and, consequently, their infants.

Acknowledgments

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