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Safety of the etonogestrel-releasing implant during the immediate postpartum period: a pilot study

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Abstract

Background: The effects of etonogestrel (ETG)-releasing contraceptive implant during the immediate postpartum period on maternal safety are unknown.
Study design: Forty healthy women exclusively breastfeeding were randomized to receive either ETG-releasing implant 24–48 h after delivery (n=20) or depot medroxyprogesterone acetate (DMPA group; n=20) at the sixth week postpartum. We measured blood pressure, maternal and neonatal weight, body mass index (BMI; kg/m^2), waist circumference (WC), complete blood count, C-reactive protein, interleukin-6, tumor necrosis factor (TNF-alpha), lipid profile, fasting serum glucose and maintenance of exclusive lactation up to the 12th week postpartum.
Results: Decreases in mean maternal weight, BMI (kg/m^2) and WC were significantly greater in the ETG-releasing implant group than in the DMPA group during the first 6 weeks postpartum (-4.64±2.71 kg vs. -2.6±2.45 kg mean±SD, p=.017; -1.77±1.06 kg/m^2 vs. -0.97±0.95 kg/m^2, p=.026; -15.3±6.72 cm vs. -9.05±5.84 cm, p=.003, respectively). In addition, total cholesterol and HDL, were lower in DMPA users, and TNF-alpha and leukocytes were higher in DMPA users compared to in the implant group, between 6 and 12 weeks after delivery. The newborns of implant users showed a trend towards gaining more weight, as compared with the infants of the DMPA mothers during the first 6 weeks of life (implant group: +1460.50±621.34 g vs. DMPA group: +1035.0±562.43 g, p=.05). The remaining variables, including the duration of exclusive breastfeeding, were similar between the groups.
Conclusion: The insertion of ETG-releasing contraceptive implant during the immediate postpartum period was not associated with deleterious maternal clinical effects or with significant maternal metabolic alterations or decreased infant weight gain.

Keywords: Postpartum period; Breastfeeding; Contraceptive; Metabolism; Adverse effects; Etonogestrel

1. Introduction

Despite the great advances and options regarding contraceptive methods developed over the last few decades, about 50% of all pregnancies worldwide are not planned, with most of them occurring in developing countries [1]. This high rate of unplanned pregnancies is due to several reasons such as difficulty in obtaining contraceptives, failure of the chosen contraceptive method, lack of medical guidance for contraceptive users, difficulty in accessing health services and a lack of autonomy in the choice of a contraceptive method. Thus, long-acting reversible contraceptives such as the etonogestrel (ETG)-releasing implant represent a promising option for the reduction of unintended pregnancies, particularly for patients at risk for a short intergestational interval.

The immediate postpartum period is a window of opportunity for appropriate family planning in a population, as the woman is an inpatient at a health facility and is motivated to avoid a subsequent pregnancy in the near future. In addition, the importance of an adequate intergestational period (a mean of 2 years) in order to reduce neonatal, infant and maternal morbidity and mortality is well known [2–4].

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The World Health Organization (WHO) recommends starting the use of progestogen-only contraceptives (POCs) 6 weeks after delivery in breastfeeding women because there are insufficient data regarding neonatal safety before this time period [5]. However, for patients at a high risk for increased morbidity or mortality with a new pregnancy and/or who experience difficulty accessing health care, it is recommended that these contraceptives be initiated during the immediate postpartum period [5,6].

Some studies have assessed the early administration of progestogen-only pills and of depot medroxyprogesterone acetate (DMPA) started during the first postpartum week, with no differences being observed in newborn infant growth or in breastfeeding practices, such as the duration of lactation or the beginning of calorie supplementation [7–10].

The ETG-releasing implant is a highly effective long-acting, reversible contraceptive with annual pregnancy rates of 0.38% [11], and with no need for patient action or regular clinical assessment in order to maintain its efficacy. Additionally, fertility returns promptly after implant removal [5,11]. ETG is the active metabolite of desogestrel, which has been showed to be safe and effective for use by breastfeeding women and in the development of nursing infants [12,13]. However, there have been no studies regarding the maternal or neonatal safety when an ETG-releasing implant is inserted during the immediate puerperium period.

The objective of this study was to assess maternal safety, in terms of clinical and metabolic parameters, with the use of an ETG-releasing implant during the immediate postpartum period; we compare this protocol with the traditional WHO-recommended time of initiating POCs in the postpartum period (after 6 weeks of delivery in breastfeeding women).

2. Materials and methods

This was a prospective, randomized, open pilot study comparing maternal clinical and metabolic safety data collected during two regimes of contraceptive administration (www.clinicaltrials.gov, NCT00828542). In the first regimen, an ETG-releasing contraceptive implant was inserted during the immediate puerperium period, while in the second DMPA, it was initiated 6 weeks after delivery. Women with both regimens were studied over a period of 12 weeks. The protocol was approved by the institutional review board of the Faculty of Medicine of Ribeirão Preto, University of São Paulo, Brazil.

Inclusion criteria were age between 18 and 35 years old, exclusively breastfeeding and a desire to receive long-acting contraception after delivery. Exclusion criteria were being a smoker, being alcoholic or using recreational drugs; having a body mass index (BMI kg/m^2) ≥30 or a systemic disease (*diabetes mellitus*, cardiovascular disease, liver disease, thyroid disease, autoimmune diseases); having a history (personal or family) of thromboembolic events; presenting alterations in hepatic enzymes and being allergic to local anesthetics (xylocaine). All women were invited to participate in this study during their participation in a prenatal care program. On the basis of these exclusion criteria, three out of 46 selected study participants were excluded due to hepatic enzyme alterations, and one was excluded due to obesity. Two women were lost to the study before the randomization due to moving to another address. Thus, a total of 40 volunteers were enrolled in the study after giving written informed consent to participate (Fig. 1).

The women were randomized immediately after giving birth, using a computer program (GraphPad Software, San Diego, CA, USA), in a ratio of 1:1, to two groups. Twenty women were allocated to receive the ETG-releasing contraceptive implant (Implanon®, NV Organon, Oss, The Netherlands) inserted 24–48 h after delivery (implant group), and 20 women received no contraceptives during the first 6 weeks after delivery, and at the 6th week, this group received IM 150 mg of DMPA (Contracept®, EMS Sigma Pharma, Hortolândia, Brazil) (DMPA group). The study participants were followed-up 6 and 12 weeks after delivery.

Evaluation during the immediate postpartum period was performed at the hospital 24–48 h after delivery, in the morning and after a 12-h fast. Women and newborns were both weighed, and the blood pressure, waist circumference (WC) and height of the women were each measured by the same observer. Peripheral blood samples (20 mL) were collected and processed within 2 h after being collected. After clotting the serum, samples were centrifuged at room temperature for 10 min, and the sera were stored at −80°C until they were used for the simultaneous determination of all variables except for the complete blood count, which was performed before clotting.

All women received a calendar to record their bleeding patterns and any possible side effects of the contraception, and they were instructed to abstain from sexual intercourse until the return visit (6 weeks after delivery). Information regarding the duration of exclusive lactation for 6 months or until menses occurred was provided to the study participants at the return visits, as defined by the Bellagio Conference [14]. Women were instructed to fast for 12 h prior to their return visits and to arrive at the hospital in the morning with their newborns, when the same procedures performed immediately postpartum were repeated.

The following variables were analyzed: fasting serum glucose determined by the oxidase method and using a Konelab 60i apparatus (Wiener Lab®, Rosario, Argentina); total cholesterol (TC), high density lipoprotein (HDL) cholesterol, and triglycerides (TG) determined by an enzymatic method, using the BT 3000 Plus apparatus (Wiener Lab®); low-density lipoprotein (LDL) cholesterol calculated according to the Friedewald formula [15] [LDL cholesterol=total cholesterol−(HDL cholesterol+TG/5)], as none of the samples contained TG levels exceeding 400 mg/dL; ultrasensitive C-reactive protein (CRP) measured by

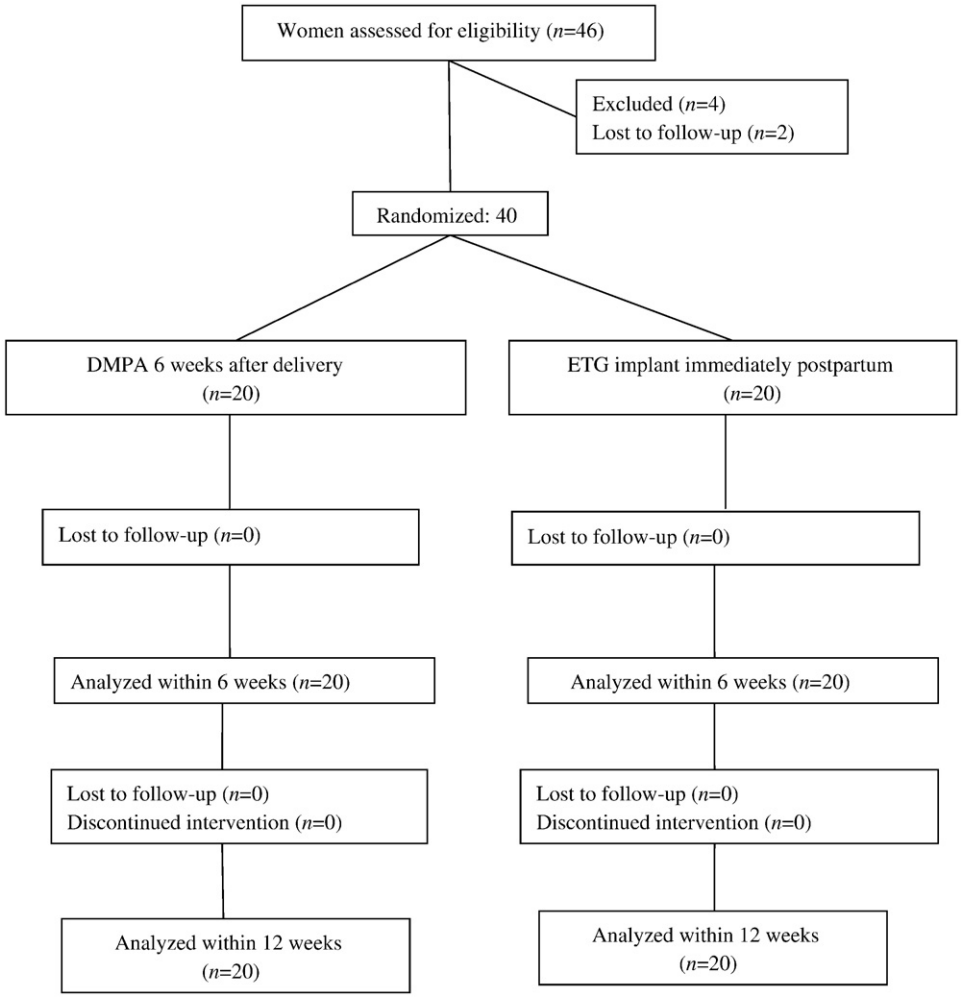

Fig. 1. Flow chart of study participants.

chemoluminescence with a DPC Immulite® 2000 apparatus (Diagnostic Products, Los Angeles, CA, USA®), and interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-alpha), as determined by chemoluminescence, using the DPC Immulite® 1000 apparatus (Siemens®, CA, USA). Complete blood counts were performed using an automated system (Coulter Gen-S, System 2; Beckman Coulter, Fullerton, CA, USA).

There were no statistical differences in participants with regard to parity [primiparous=implant group: 35% (7/20) and DMPA group: 60% (12/20); multiparous (2 or more)=implant group: 65% (13/20) and DMPA group: 40% (8/20)], current delivery (implant group: 80% vaginal birth and 20% cesarean section vs. DMPA group: 85% vaginal birth and 15% cesarean section), years of formal education (≤11 years: 90% and ≥12 years: 10%, in both groups), percentage of prior breastfeeding women (implant group: 60% vs. DMPA group: 40%) and family income (implant group: 45% earn <2 minimum wages/month and 55% earn 0–6 minimum wages/month *vs.* DMPA group: 40% earn <2 minimum wages/month and 50% earn 2–6 minimum wages/month). Brazilian minimum wage in this period was US $247 per month.

2.1. Statistical analysis

The sample size was calculated, considering the body weight as the main variable. To detect a difference of at least 1 S.D. between the groups during the first 6 weeks, 16 women per group were be necessary; 20 subjects per group were selected due to the possibility of participant loss during the study.

Data were tested for normality using Kolmogorov–Smirnov and Shapiro–Wilk tests. Continuous variables with normal distributions were compared within groups using analysis of variance followed by the Tukey post hoc test, while variables that were continuous but not normally distributed were compared with the Friedman test, followed by the Dunn posttest. For intergroup comparisons, continuous variables with normal distributions were compared with the unpaired Student's *t* test, while variables that were continuous but not normally distributed were

compared with the Mann–Whitney *U* test. The Fisher's Exact test or the chi-square test was used for categorical variables. The level of significance was set at 5%. Data were analyzed statistically with SPSS 16.0 for Windows (SPSS, Chicago, IL, USA) and GraphPad 5.0 for Windows (GraphPad Software, San Diego, CA, USA) software. The results are reported as means±S.D.

3. Results

Participants in the two groups were similar with regard to age [(mean±S.D.) 22.5±2.5 vs. 22.9±4.4 years for the implant and DMPA groups, respectively].

Although women were instructed to avoid sexual intercourse until the first return visit, 40% of the women in the ETG-releasing implant group and 45% in the DMPA group reported having had sexual intercourse before the end of the 42 days of puerperium.

There was no difference in the maintenance of exclusive lactation between the groups. In the first follow-up (6 weeks after delivery), 95% (19/20) of women in the implant group and 85% (17/20) of women in the DMPA group were in exclusive breastfeeding. In the second follow-up (12 weeks after delivery), 85% (17/20) of women in the implant group and 75% (15/20) of women in the DMPA group reported exclusive breastfeeding. Study participants that were not in exclusive lactation had started supplementing their newborn, but none of the participants had completely ceased breastfeeding.

The most frequently reported side effect in the ETG-releasing implant users was headache [45% (9/20) vs. 10% (2/20), for the implant vs. DMPA group, p=.03]. Implants users also reported nervousness (25%), hair loss (10%), and nausea (5%). The women in the DMPA group reported acne (5%), abdominal cramps (10%) and nausea (5%).

There was no difference in bleeding patterns between the two groups. The mean and S.D. of postpartum lochial bleeding days was 13±3 days for the implant group and 12±4 days in the DMPA group. In the remaining days until the 6-week follow-up, only one woman in the implant group reported 3 days of spotting; all other study participants reported they were amenorrheic. From 6 to 12 weeks post delivery, 40% of women in the implant group and 35% of women in the DMPA group were amenorrheic (p=.47). However, most participants had bleeding/spotting, with a mean of 10±3 days in the implant group and 8±2 days in the DMPA group.

At baseline, all clinical and metabolic variables were similar between both groups, with the exception of the HDL levels (Table 1). Changes in the clinical and metabolic variables were described in two ways: variation between baseline and six week values (comparison of ETG-releasing implant vs. no hormonal contraceptive) and variation between 6 and 12 weeks after delivery (comparison of ETG-releasing implant vs. DMPA).

Table 1
Baseline clinical and metabolic variables in immediate postpartum period

Variable	Implant group mean (±S.D.)	DMPA group mean (±S.D.)	Intergroup comparison (p)
Weight (kg)	62.2 (9.4)	64.2 (6.8)	.44
BMI (kg/m^2)	24.1 (3.1)	25.4 (2.1)	.14
SAP (mmHg)	114 (12.3)	110 (9.7)	.26
DAP (mmHg)	68 (8.3)	68 (7.7)	1
WC (cm)	91.0 (7.8)	93 (4.3)	.35
NB weight (g)	3248 (422)	3143 (543)	.5
Hb (g/dL)	11.5 (1.4)	11.5 (1.7)	.94
Plat (×10^3/μL)	250.1 (82.0)	268.6 (77.9)	.47
Leu (×10^3 cells/μL)	15.8 (4.5)	13.7 (4.1)	.13
Glu (mg/dL)	67.1 (9.7)	70.9 (7.9)	.18
TG (mg/dL)	169.2 (59.9)	157.2 (5.6)	.5
TC (mg/dL)	225.6 (55.5)	224.7 (47.3)	.95
HDL (mg/dL)	60.7 (13.2)	72.7 (17.7)	.02
LDL (mg/dL)	131.0 (45.1)	120.5 (40.6)	.44
CRP (mg/L)	60.21 (55.9)	55.78 (46.2)	.79
IL-6 (pg/mL)	16.87 (20)	9.39 (6.7)	.12
TNF-alpha (pg/mL)	13.64 (5.05)	13.34 (3.62)	.83

NB, newborn; Hb, hemoglobin; Plat, platelets; Leu, leukocytes; Glu, serum glucose.

3.1. Variation between baseline and 6 weeks (Δ0–6):

Reductions were observed in mean maternal weight, BMI (kg/m^2) and WC in both groups; however, this reduction was greater in women in the implant group than in the DMPA group (Table 2). Statistical analysis conducted after excluding women who had discontinued exclusive breastfeeding showed greater reductions in mean of variation in maternal weight [(mean±S.D.) in implant group: −5.12±2.45 kg vs. DMPA group: −2.94±2.31 kg, p=.015] and decreased BMI [(mean±S.D.) implant group: −1.94±0.89 vs. DMPA group: −1.1±0.97, p=.018] continued to be greater in the implant group, as compared with DMPA group.

The newborns of implant users showed a trend towards gaining more weight, as compared with the infants of the DMPA mothers [(mean±S.D.) implant group: +1460.50±621.34 g vs. DMPA group: +1035.0±562.43 g, p=.05] (Table 2). A greater reduction in IL-6 levels was observed in implant group compared with DMPA group (Table 3). There was no difference in the remaining variables between the two groups. In both groups, there was a reduction in mean in blood pressure (systolic and diastolic) (Table 2), leukocytes, lipid profile and levels of the remaining inflammatory markers (Table 3) and an increase in hemoglobin, platelets and fasting serum glucose levels (Table 3).

3.2. Variations between 6 and 12 weeks (Δ6–12)

The variations in clinical parameters did not differ between the groups during the 6–12-week time period. Mean change in maternal weight, BMI (kg/m^2) and WC were reduced and mean of variation in infant weights were enhanced in both treatments groups. The mean change in systolic arterial blood pressure (SAP) increased in women in the DMPA group, and decreased in women in the implant

Table 2
Comparison of the clinical effects, during the first 12 weeks postpartum, of the etonogestrel-releasing implant, inserted in the immediate postpartum period, versus DMPA started six weeks after delivery

Variables	Δ0–6 weeks		Δ6–12 weeks	
	Absolute variation mean (S.D.)	% Change from baseline	Absolute mean (S.D.)	% Change variation from 6 weeks
Weight (kg)				
Implant	−4.64 (2.71)	−7.46	−0.17 (1.22)	−0.30
DMPA	−2.60 (2.45)	−4.04	−0.76 (1.71)	−1.23
Implant × DMPA (p)	.017		.22	
BMI (kg/m^2)				
Implant	−1.77 (1.06)	−7.34	−0.06 (0.49)	−0.27
DMPA	−0.97 (0.95)	−3.81	−0.30 (0.69)	−1.23
Implant×DMPA (p)	.026		.21	
SAP (mmHg)				
Implant	−8.0 (11.05)	−7.02	−1.0 (9.12)	−0.94
DMPA	−9.0 (12.93)	−8.19	+2.50 (10.19)	+0.99
Implant×DMPA (p)	.794		.26	
DAP (mmHg)				
Implant	−6.0 (9.94)	−8.82	+1.50 (9.88)	+2.41
DMPA	−6.0 (8.21)	−8.82	−1.50 (3.66)	−2.41
Implant×DMPA (p)	1.0		.211	
WC (cm)				
Implant	−15.30 (6.72)	−16.81	−1.85 (3.09)	−2.44
DMPA	−9.05 (5.84)	−9.73	−1.70 (3.66)	−2.03
Implant×DMPA (p)	.003		.889	
NB weight (g)				
Implant	+1460.50 (621.34)	+45	+366.38 (88.86)	+25.09
DMPA	+1035.0 (562.43)	+33	+636.72 (170.17)	+35.14
Implant×DMPA (p)	.05		.068	

Δ, variation during the period; Data are shown as absolute variation mean (±S.D.).

group; in contrast, the mean of variation in diastolic arterial blood pressure (DAP) increased in women in the implant group and decreased in women in the DMPA group. However, there was no significant difference in these variables between the two groups (Table 2).

The mean change in white cell counts were increased in women in the DMPA group compared with the implant group (Table 3). Mean change in HDL and TC levels declined in both groups over time, but the decrease was significantly greater in women in the DMPA group (Table 3). Mean change in TNF-alpha levels increased in women in the DMPA group but decreased in the implant group (Table 3).

Changes in the other variables did not differ significantly between the groups. There was a decrease in mean change in mean LDL, TG, CRP and IL-6 in both groups and in platelets in the implant group. Further, we recorded an increase in mean change in newborn weight, hemoglobin, and fasting serum glucose in both groups during the 6–12 weeks interval after delivery, however, there were no significant differences between the two groups (Table 3).

4. Discussion

Previous studies have found maternal and infant safety to be present when the ETG-releasing implant was inserted after the 28th day of delivery. However, as far as we know, the present study is the first to evaluate maternal safety with the insertion of the ETG-releasing contraceptive implant in the immediate postpartum period. Breastfeeding leads to ovarian suppression, but the resumption of ovulation is unpredictable and depends on breastfeeding pattern, maternal biological variables and nutritional, geographic, cultural and socioeconomic factors [16]. More than 50% of the first menstruations after delivery are preceded by ovulation, and 50% of these cycles have included an active luteal phase [17], which highlights the need for effective contraception in the postpartum period.

Nearly 50% of the participants in our study engaged in sexual intercourse before the 6 weeks postpartum, despite the explicit instructions provided to them to abstain from sexual activity during this period. Thus, the availability of an effective, long-acting contraceptive after delivery will offer a useful opportunity to prevent unwanted pregnancy.

Studies evaluating adverse effects in users of the ETG-releasing implant outside of the puerperium period have observed weight gain in these women [18]. However, in the present study, there was a surprisingly greater reduction of weight, BMI (kg/m^2) and WC in women in the ETG-releasing implant group, during the first 6 weeks of delivery, compared with women not taking hormonal contraception in this time. The literature has shown that it is difficult to interpret weight changes that are supposedly related to contraceptive methods, since most studies of the long-term use of any contraceptive (even nonhormonal methods) have reported weight gain among users; these data suggest that

Table 3
Comparison of the metabolic effects, during the first 12 weeks postpartum, of the etonogestrel-releasing implant, inserted in the immediate postpartum period versus the DMPA started 6 weeks after delivery

Variables	Δ0–6 weeks		Δ6–12 weeks	
	Absolute variation mean (S.D.)	% Change from baseline	Absolute variation mean (S.D.)	% Change from 6 weeks
Hb (g/dL)				
Implant	+1.10 (1.30)	+9.56	+0.19 (0.70)	+1.50
DMPA	+1.15 (1.44)	+10.0	+0.02 (0.65)	+0.15
Implant×DMPA (p)	.918		.420	
Plat ($\times 10^3/\mu L$)				
Implant	+39.90 (51.03)	+15.95	−7.80 (46.74)	−2.69
DMPA	+15.45 (48.11)	+5.75	+4.10 (41.17)	+1.44
Implant×DMPA (p)	.127		.398	
Leu ($\times 10^3$ cells/μL)				
Implant	−6.72 (3.99)	−42.53	−0.44 (1.13)	−6.47
DMPA	−6.96 (5.66)	−50.80	+2.54 (3.77)	+36.28
Implant×DMPA (p)	.875		.005	
Glu (mg/dL)				
Implant	+10.50 (11.42)	+15.64	+1.70 (7.30)	+2.19
DMPA	+9.0 (8.58)	+12.68	+1.50 (5.71)	+1.88
Implant×DMPA (p)	.641		.924	
TG (mg/dL)				
Implant	−98.0 (48.26)	−57.91	−8.60 (37.50)	−12.07
DMPA	−76.75 (63.32)	−48.82	−24.85 (34.05)	−30.87
Implant×DMPA (p)	.240		.160	
TC (mg/dL)				
Implant	−53.15 (48.50)	−23.56	−7.4 (15.01)	−4.29
DMPA	−38.05 (49.41)	−16.93	−28.55 (17.71)	−15.30
Implant×DMPA (p)	.336		.001	
HDL (mg/dL)				
Implant	−8.10 (13.46)	−13.34	−0.15 (5.02)	−0.28
DMPA	−7.25 (15.79)	−9.97	−12.45 (7.32)	−19.0
Implant×DMPA (p)	.856		<.0001	
LDL (mg/dL)				
Implant	−25.45 (36.65)	−19.43	−5.53 (12.67)	−5.24
DMPA	−15.45 (36.41)	−12.87	−11.13 (16.13)	−10.60
Implant×DMPA (p)	.392		.230	
CRP (mg/L)				
Implant	−52.91 (55.50)	−87.87	−4.09 (9.59)	−66.40
DMPA	−49.71 (48.97)	−89.12	−0.69 (16.24)	−18.96
Implant×DMPA (p)	.848		.424	
IL-6 (pg/mL)				
Implant	−14.22 (20.07)	−84.29	−0.08 (1.90)	−3.64
DMPA	−5.67 (9.17)	−60.38	−0.42 (3.06)	−16.15
Implant×DMPA (p)	.045		.676	
TNF-alpha (pg/mL)				
Implant	−0.51 (5.29)	−3.74	−0.55 (2.46)	−7.30
DMPA	−0.87 (3.37)	−6.52	+2.21 (3.18)	+17.85
Implant×DMPA (p)	.799		.001	

Plat, platelets; Δ, variation during the period. Data are shown as absolute variation mean (±S.D.).

this weight gain may be related to other, external factors [19]. Considering that exclusively lactating women had a more rapid weight loss than nonexclusively lactating women, even after nonexclusively lactating women were excluded, the greater reduction in weight among implant users was maintained.

The side effects typically reported by the users of POCs are irregular bleeding, acne, mood swings and breast pain [18,19]. All of the women studied herein reported similar symptoms, except for more frequent complaints of headache in the implant group, a symptom known to be associated with implant use. In previous studies, headache was the main adverse effect reported by implant users (15%), but only 1.6% of the women reported headache as the cause of discontinuation of the method [11]. The safety and tolerability of levonorgestrel (LNG)-releasing contraceptive implant in the immediate puerperium (<48 h after delivery) were evaluated in 121 women and compared with those observed in 120 women receiving the implant after 4–6 weeks. No significant changes were observed regarding

weight, blood pressure, nausea or mood swings. However, as was also observed herein, headaches were more frequent when the implant insertion occurred in the immediate postpartum period (15% vs. 2.8%) [20].

In previous reports, the main cause of discontinuation of contraceptive implants was menstrual changes [21]. The main menstrual change reported in these studies by users of the ETG-releasing implant was infrequent bleeding (33.3%), amenorrhea (21.4%) and prolonged bleeding (16.9%) [11,22]. In the present study, we found no difference in lochial bleeding and in bleeding patterns after the lochia stopped between the two groups. Phemister et al. [20] observed more bleeding days when LNG-releasing contraceptive implants were inserted prior to 48 h after delivery, compared to the insertion of this implant at 4–6 weeks post delivery. However, hemoglobin levels between the two groups were similar, so these data were not clinically significant.

Any medication administered during the puerperium should be evaluated in terms of its effects on women's health, lactation and on the newborn infant. Indeed, the beneficial effects of breastfeeding are unquestionable. As also observed in previous studies [12,13], we did not detect a difference in the rate of maintenance of exclusive lactation between implant users and women who initiated the DMPA 6 weeks after delivery. Although there were no previous reports of the effects of using the ETG-releasing implant after the immediate postpartum period on lactation, studies comparing the use of the ETG-releasing implant inserted between the 28th and 56th day of delivery with the use of a copper intrauterine device (IUD) detected no difference in volume or composition of milk (total fat, total protein, and lactose), the duration of lactation or newborn weight gain during 3 years of use of the contraceptives [12,13]. Related to the tendency toward increased weight gain in newborns during the first 6 weeks after delivery in the ETG-releasing group greater than nonhormonal users in our study, Karim et al. [10] observed a greater weight gain in infants of mothers treated with DMPA administered during the first week of puerperium, as compared with women in a control group (without hormonal contraceptive). Patel et al. [23] showed that 4-week-old infants could neither absorb nor metabolize LNG, and that 12-week-old infants could metabolize this hormone more efficiently than absorb it. However, there are no studies in the literature that evaluate the absorption of ETG by newborns.

During the physiological puerperium, there is a reduction in the lipid profile values to pregestational levels, as observed in the present study. We detected a reduction in the entire lipid profile (TC, LDL, HDL, TG) during a period of 12 weeks after delivery, with a more marked reduction of HDL in the implant group during the first 6 weeks. This marked reduction is likely due to the action of the ETG during this period, although the HDL levels remained within normal ranges. A longitudinal study previously evaluated the effect of ETG- and LNG-releasing implants versus the copper IUD on lipid metabolism outside of the postpartum period. Data from this study reflected fluctuations in the serum concentrations of TC, TG, HDL and LDL in the 3 groups studied over a period of 3 years, with a tendency toward decreased TC and LDL levels among the users of both implants [24]. In contrast, another study evaluating 70 users of the ETG-releasing implant detected increased, but still normal, TC and TG levels after 3 years of using the device, as compared with preinsertion levels, with no changes in HDL, LDL or fasting serum glucose [25].

As observed in the literature, fasting serum glucose, while slightly elevated, was within normal range in both groups [26]. This increase is probably due to the restoration of blood gestational hemodilution.

No deleterious maternal or neonatal effects were observed after the insertion of the ETG-releasing implant in the immediate postpartum period, and the changes in clinical and metabolic variables detected were similar to those observed at the beginning of DMPA treatment after 6 weeks. Additional studies involving other issues of neonatal safety with the early use of ETG-releasing implant after delivery should provide further data.

In conclusion, the use of the ETG-releasing implant in the immediate postpartum period was not associated with deleterious maternal clinical or metabolic effects or effects on newborn growth. In addition, users of the ETG-releasing implant showed greater reductions in BMI (kg/m^2) and weight within 6 weeks after delivery. Considering that many women in our study reported sexual intercourse before their first return follow-up visit, there is a clear need for early contraceptive prescription following delivery and the use of the ETG-releasing implant can provide safe, effective, long-acting contraception in women, independent of their breastfeeding status. Furthermore, the immediate postpartum initiation of a long-acting reversible contraception can increase a woman's intergestational interval, thereby reducing neonatal/infant and maternal morbidity and mortality related to short intervals between pregnancies.

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