## Hormonal Contraceptives and Breastfeeding: A Review of Literature

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The use of hormonal contraceptives in a breastfeeding patient has been questioned by breastfeeding advocates. Their fear was that hormonal contraceptives will affect the milk production of the patient. This review of literature showed that progestins do not affect breastmilk supply whether it is the progestin only pill (POP), depot medroxyprogesterone acetate, levonorgestrel-containing intrauterine system (LNG-IUS) or the etonogestrel implant (ENG). The timing of administration of the progesterone derivative contraceptive method also does not affect milk production, whether immediately postpartum (within 48 hrs after delivery) or delayed (4 - 6 weeks postpartum). With this in mind, clinicians may safely advise these to breastfeeding patients to prevent unplanned pregnancies.

Keywords: contraception, progestin, breastfeeding, timing of contraceptive method

#### Introduction

Contraceptives have been used even in ancient times. In this modern era, hormonal contraceptives have become very popular. How hormonal contraceptives, specifically progesterone and its derivatives, affect breastfeeding has been a major cause of concern.

Breastfeeding as a form of contraception has been accepted on the basis of maternal physiology. At the sight and smell of the baby, the mother's anterior pituitary gland is stimulated causing the release of prolactin which is responsible for milk production. As the baby latches on the mother's nipple, the posterior pituitary gland is stimulated and there is the release of oxytocin. Oxytocin stimulates the myoepithelial cells of the breasts to contract resulting to milk let-down. This mechanism of milk production and milk letdown fulfills all the baby's nutritional requirement.<sup>1</sup>

With the release of prolactin and oxytocin, low levels of FSH and LH from the pituitary are secreted. Subsequently, low levels of estrogen and progesterone is produced. Thus, ovulation does not occur. When the infant starts to have solid food or complementary food, the periods of suckling will naturally decrease because the baby feels full already. Thus, at 4 to 6 months, when the release of prolactin and oxytocin decreases because of shorter periods of nursing, ovulation can occur.<sup>2</sup> During this period, unplanned pregnancy can occur. Hence, the use of natural methods (if the woman is already menstruating), barrier methods or hormonal contraception must be considered. The most ideal contraceptive method during breastfeeding would be the method that will not affect breast milk production and quality, does not have any effects on infant growth and development, and is cost effective, easy to use, with minimal physician follow-up/intervention. A Filipino woman's contraceptive preference usually depends on various factors which may include, among others, contraceptive efficacy and failure rates, ease of use, costs, adverse effects, religious and cultural beliefs, medical considerations, partner's attitude, previous contraceptive experience, and lactation status.

This paper will focus on the hormonal methods of contraception specifically Progesterone-onlypills, Levonorgestrel-containing intra-uterine system (LNG-IUS), depot medroxyprogesterone acetate (DMPA) and Etonogestrel (ENG) implant and their impact on breastfeeding.

## Methods

This review was restricted to published research articles that discussed hormonal methods of contraception specifically Progesterone-only-pills, Levonorgestrel-containing intra-uterine system, depot medroxyprogesterone acetate (DMPA) and Etonogestrel implant and their impact on breastfeeding.

In November 2020, the following databases were searched: WHO online resources, CDC online resources, PubMed, Wiley/Cochrane Library, Science direct, Google scholar, Uptodate and Ovid Wolters Kluwer. Keywords (and their vocabulary terms) included breastfeeding, hormonal/oral contraceptives, progestins, progestin only pills, levonorgestrel intrauterine system, depot medroxyprogesterone acetate, DMPA, and etonogestrel implant. Reference list of an article by WHO was reviewed in order to identify articles that could be included in this literature review. No limitations were placed on publication dates, publication type, or study design. Articles were chosen if they addressed breastfeeding and progestincontaining hormonal contraceptives mentioned above, and if they were written in English.

Proceedings of scientific meetings or conferences were not included. No attempt was made to identify unpublished studies nor contact any author.

Costs for each contraceptive method were derived from the prevailing market/pharmacy rates as of November 2020, and triangulated with inquiries to pharmaceutical representatives and end users.

## Results and Discussion

The literature search yielded 16 published works, including 2 textbook articles, 5 randomized controlled trials, 2 systematic reviews, 2 cross sectional studies,

2 prospective cohort studies, 1 case control and 2 website articles (CDC and WHO); These articles reported on the effect of progestin-containing hormonal contraceptives on breastmilk quality, infant outcomes, and timing of initiation.

#### **Hormonal Contraception**

The World Health Organization, twenty (20) years ago created the Medical Eligibility Criteria for contraceptive use. Now on its 5th edition<sup>3,4</sup>, it states that a contraceptive is categorized as 1 to 4 depending on the safety of the particular contraceptive.

Category 1 is a condition wherein there is no restriction for the use of the contraceptive method. With good resources for clinical judgement and with limited resources for clinical judgement, the method can be used.<sup>3,4</sup>

Category 2 of the Medical Eligibility Criteria (MEC) is a condition wherein contraceptive's benefit outweighs the theoretical or proven risk. With good resources for clinical judgement and with limited resources for clinical judgement, the contraceptive could be used.<sup>3,4</sup>

Category 3 of the MEC is a condition wherein the contraceptive has a theoretical or proven risk that outweighs the advantages of using the method. With good resources for clinical judgment, the use of this contraceptive method is not recommended unless other appropriate methods are not available. With limited resources for clinical judgment, the patient is advised not to use this method.<sup>3,4</sup>

Category 4 of the MEC is a condition wherein the contraceptive is an unacceptable health risk if this contraceptive will be used. With good resources and limited resources, this method must not be used as a contraceptive. An example is combined oral contraceptives (COC) when it is given less than 21 days from delivery (category 4) because of the risk of thromboembolism. Also, those COC given more than 21 days from delivery (category 3) wherein the risk outweighs the benefit.<sup>3,4</sup>

# Hormonal Contraceptive Method: Progestin-only Contraceptives

There has always been a theoretical concern related to breastmilk supply when progestincontaining options are initiated during the first 48 hours postpartum, as a drop in progesterone levels after birth is necessary for secretory differentiation and lactogenesis to occur. Hypothetical concerns also have been raised regarding the impact of exposure to progestins on neonates, particularly in the first 6 weeks of life. However, evidence from a systematic review generally found no adverse effects of progestin-only contraceptives on breastfeeding outcomes through 12 months of age, infant immunoglobulins, or infant sex hormones.

Locally available progestin-only contraceptives include the progestogen-only pill ("minipill"), etonogestrel implant, depot medroxyprogesterone acetate (DMPA), and the Levonorgestrel intrauterine system.

#### Progesterone Only Pills (POP)

WHO MEC re-classified Progesterone-only Pills (POP) to category 2. Unlike combined hormonal contraceptives (Estrogen and Progesterone) which have been found to be associated with venous thromboembolism, POP has been found to be safe and does not interfere with breastfeeding performance, maternal health and infant growth parameters.<sup>6,7</sup> There is no change in the volume of milk flow and infant satisfaction.

In a study by Perheentupa, et al.<sup>8</sup>, 2 groups of postpartum women were compared. One group used a barrier method (BM) of contraception and another group used progestin-only pills (POP). They were followed up 6 weeks postpartum up to 18 weeks postpartum. Results showed that there was little change in the serum FSH and LH in both groups. There is no difference between the BM and POP in terms of serum estradiol and the levels of inhibin. The size of the follicle was the same for both groups. There was note of increased endometrial thickness in the POP group. The authors surmised that the contraceptive effect of POP lies in its effect on the endometrium and cervix.

In a 2015 Cochrane review<sup>9</sup>, results regarding POP affecting milk flow were inconsistent. The studies reviewed had low to moderate quality of evidence, and as a whole, there was no significant difference between users of POP and non- users of POP, in terms of lactation.<sup>7</sup>

Cost: Php 165.75 for 500 mcg x 28s (Common locally available brands: Daphne, Exluton, Cerazette)

#### Depot Medroxyprogesterone Acetate (DMPA)

In the category of immediate postpartum (IPP) contraception is the long-acting reversible contraception or LARC. A common LARC that is safely administered immediately postpartum is the injectable progestin-only contraceptive depot medroxyprogesterone acetate (DMPA) which is given every 12 weeks.

Traditionally, injectable contraceptives like DMPA, are started at 6 weeks postpartum up to 4 months postpartum. This is so because of the mistaken notion that IPP LARC like DMPA can affect breastfeeding by decreasing milk flow. Another concern is the possibility of the steroid hormone being present in the mother's milk. Due to this belief, a good number of postpartum mothers miss their 6-week visit and resume sexual intercourse. Thus, unplanned pregnancy can occur.

The first DMPA injection can be given at any time, including immediately postpartum (U.S. MEC 2 if <1 month postpartum and U.S. MEC 1 if  $\geq 1$ month postpartum) if it is reasonably certain that the woman is not pregnant.<sup>10</sup> It does not affect breastmilk production. If the woman is <6 months postpartum, amenorrheic, and fully or nearly fully breastfeeding, no additional contraceptive protection is needed. Otherwise, a woman who is  $\geq 21$  days postpartum and has not experienced return of her menstrual cycle needs to abstain from sexual intercourse or use additional contraceptive protection for the next 7 days. If her menstrual cycles have returned and it has been >7 days since menstrual bleeding started, she needs to abstain from sexual intercourse or use additional contraceptive protection for the next 7 davs.10

Cost: Php 90.00-150.00 (Locally available brands: Depot Trust, Depot Femme, Lyndavel)

#### Levonorgestrel Intrauterine System (LNG-IUS)

In a randomized controlled trial by Averbach, et al.<sup>11</sup> 183 women were given the Levonorgestrel intrauterine system (LNG IUS) immediately postpartum and 183 women had the LNG IUS inserted at a delayed time (4-6 weeks postpartum). Infants were followed up at 3 and 6 months. Results of this study showed that exclusive breastfeeding was similar in the immediate postpartum group and the delayed group (74% vs 71% p= 0.84) There was no report of lactogenesis failure. There was no significant difference in the infant parameters in the immediate and delayed group. For infants' weight, it was 4623+/-1020 grams in the immediate group versus 4407 +/-957.3 grams in the delayed group (p=0.26). For the infants' head circumference, values were 9.3 + / - 2.6 cm in the immediate group versus  $9.5 \pm 2.7$  cm (p=0.7). For the baby's length, for the immediate group babies' length were 14.7+/-5.3 cm and the delayed insertion of LNG group 15.2 +/-5.1 cm (p=0.63). The preterm infants in this study showed increase in weight in the immediate group versus the delayed group. (6033 vs. 4563 g. (p=0.006). This study has good results but there was poor follow up of the infants at 6 months.

A similar study done by Turok et al, compared 259 women, 132 women had the LNG-IUS inserted immediately postpartum and 127 had the LNG IUS inserted 4-12 weeks postpartum (delayed group). The infants were followed up at 8 weeks and 6 months. Results showed that breastfeeding at 8 weeks in the immediate group was 79% versus 84% in the delayed group (p=0.28). On follow-up at 6 months, immediate group was 33% versus 40% in the delayed group (0.27). There is no difference in the mothers' breastfeeding duration whether the LNG IUS was inserted immediately postpartum or delayed. However, 2 women in the immediately postpartum group reported lactogenesis failure.

Cost Php13,500 per LNG IUS (Locally available brand: Mirena - Bayer)

#### Etonogestrel (ENG) implant

A randomized study conducted by Braga, et al. determined the impact of etonogestrelreleasing implants in breastfeeding patients who are in the immediate post-partum period. A group of 24 postpartum patients and their infants, were randomized into 2 groups of 12 mother-infant pairs. One group had their ENG implanted within 48 hours from delivery and the other group is the control group where no contraceptive method was initiated. The primary outcome is the amount of breastmilk intake of the newborn infants. Their results showed comparable amount of breastmilk in both the ENG group and the control group. On day 0, the ENG group had 340 ml/day (240-420 ml/day) breastmilk and the control group had 330 ml/day (300-530 ml/day) of breastmilk. On Day 29, the ENG group had 845 ml/ day (770-980) of breastmilk and the control had 785 ml/day (680-980 ml/day) of breastmilk as estimated by spectrometry. Their conclusion was ENG implant inserted immediately postpartum does not affect the volume of breastmilk intake by newborn infants.

A randomized controlled trial was conducted by Carmo, et al.<sup>14</sup> comparing the timing of early insertion of ENG implants (within 48 hours from delivery) versus conventional ENG implant insertion (6 weeks postpartum) and its effect or non-effect in the growth of breastfed infants. A total of 100 patients were included in the study, with the primary outcome being the infant's weight at 12 months. The secondary outcomes were the infants' height, head and arm circumference, measured at 14,40,90, 180,270 and 360 days. Results showed there was no significant difference in the weight of the infants in both early and conventional ENG insertion at 360 days. The authors noted that there was no difference between the early and conventional group in terms of height, head and arm circumferences of the infants. The authors concluded that there was no difference in the growth of the infants at 12 months in both the early and the conventional postpartum insertion of ENG group.<sup>12</sup>

A study by Reinprayoon, et al.<sup>15</sup> in 2000 studied the effects of ENG-releasing contraceptive implant (Implanon<sup>R</sup>) on parameters of breastfeeding in one group, compared with the breastmilk of mothers with non-hormonal IUD. In this study, 80 healthy fully breastfeeding postpartum women were the participants, 42 chose the ENG releasing implant and 38 chose the non-hormone containing IUD. One month after insertion of Implanon, the amount of ENG in the blood of the baby was determined. It was determined to be at 19.86 ng/kg/day, which decreased to 10.45 ng/kg/day at the end of the study period (month 4). Infants were 259 -294 days old when they were included in the study. The volume of breastmilk produced was not affected by Implanon<sup>R</sup>. Between groups, there was no significant difference between the milk content, total fat, total protein, and lactose. For female infants, no significant differencees were noted in terms of body weight, height and head circumference. The same observations were noted for the male infants except that they seems to be larger in terms of body weight. The authors noted this especially in babies whose mothers were on  $Implanon^{R}$ . From this paper, the authors concluded Implanon did not change the volume and composition of breastmilk.<sup>13</sup>

Another randomized controlled trial by Brito, et al.<sup>16</sup> concluded that the insertion of ENG-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.

Cost: Php 2400-3000 (Locally available brand: Implanon)

## Conclusion

Progesterone derivatives used in conjunction with breastfeeding does not affect the quality, quantity and over-all composition of the breastmilk. Except for some published literature that reported a small number of patients with lactation failure, there is sufficient evidence to state that progestins, whether in the form of progestin-only-pill (POP), depot medroxyprogesterone acetate, Levonorgestrel Intrauterine system or Etonogestrel implant, are safe for breastfeeding mothers.

#### Disclosure:

Dr. Stella Marie Legaspi-Jose is the chair of the Breastfeeding Committee of the Philippine General Hospital from 1996-present.

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