



Contraceptives, Oral, Combined

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Drug Levels and Effects

Summary of Use during Lactation

Evidence on the safety and desirability of using combined oral contraceptives during lactation ranges in quality from poor to fair.[1][2][3]

The weight of current evidence seems to indicate that combination oral contraceptives probably do not affect the composition of milk substantially in healthy, well-nourished mothers and do not adversely affect long-term infant growth and development. Combined oral contraceptives might transiently affect growth negatively during the first month after introduction. The magnitude of the effect on lactation likely depends on the dose and the time of introduction postpartum. Ethinyl estradiol in doses greater than 30 mcg daily can suppress lactation and lead to more supplementation and possibly earlier discontinuation of breastfeeding than nonhormonal or progestin-only contraception. Additionally, introduction of an estrogen before 3 weeks postpartum may increase the risk of thromboembolism in postpartum women. Rare cases of reversible breast enlargement in breastfed infants have been reported, mostly with estrogen doses higher than are currently used.

Based on the available evidence, expert opinion in the United States states that postpartum women who are breastfeeding should not use combined hormonal contraceptives during the first 3 weeks after delivery because of concerns about increased risk for venous thromboembolism and generally should not use combined hormonal contraceptives during the fourth week postpartum because of concerns about potential effects on breastfeeding performance. Postpartum breastfeeding women with other risk factors for venous thromboembolism generally should not use combined hormonal contraceptives 4 to 6 weeks after delivery.[4] World Health Organization guidelines are more restrictive, stating that combined oral contraceptives should not be used in nursing mothers before 42 days postpartum and the disadvantages of using the method generally outweigh the advantages between 6 weeks and 6 months postpartum.[5]

Drug Levels

Combination contraceptives contain an estrogen and a progestin. Ethinyl estradiol is the most commonly used estrogen. Mestranol is an ethinyl estradiol pro-drug; 80 mcg of mestranol is equivalent to 50 mcg of ethinyl estradiol. The progestins are primarily 19-nor testosterone derivatives such as levonorgestrel, norgestrel, norethindrone and norethinodrel. They have varying degrees of androgenic activity.

Maternal Levels. Studies that measured ethinyl estradiol in breastmilk are reported here. Studies that reported progestin levels in milk (e.g., levonorgestrel, norethindrone) can be found in the records of those drugs.

Four women who were fully nursing their infants were given a contraceptive containing ethinyl estradiol 50 mcg and megestrol acetate 4 mg beginning at 2 months postpartum. Another 4 women who were 6 to 18 months postpartum were given a single dose of 500 mcg of ethinyl estradiol. After 10 days of therapy, ethinyl estradiol was undetectable (<50 ng/L) in the milk of women who received the 50 mcg dose at several times after the dose. In those who receive 500 mcg, peak milk levels usually were found in the 3-hour sample although the peak was found in the 7-hour sample in one. Peak milk levels ranged from about 170 to 300 ng/L; levels dropped rapidly and were usually undetectable by 23 hours after the dose. Based on the higher dose, the authors estimated that a fully breastfed infant whose mother was taking 50 mcg of ethinyl estradiol daily would receive a dose of about 10 ng daily.[6]

Milk was collected and pooled from 2 groups of women who were taking ethinyl estradiol 100 mcg 3 times daily either immediately postpartum or after 1 to 6 months postpartum. Milk samples were collected 2 hours after the dose. Pooled milk was bioassayed for estrogenic activity and compared with the milk from lactating mothers taking no exogenous estrogens whose milk was collected at various times postpartum. No estrogenic activity was detected (<10 ng/80 mL of pooled milk [<0.125 mcg/L]) from women taking ethinyl estradiol above background estrogenic activity found in control colostrum.[7]

Infant Levels. Relevant published information was not found as of the revision date.

Effects in Breastfed Infants

Bilateral breast enlargement was reported in a 3-week-old male breastfed infant whose mother began taking an oral contraceptive containing norethynodrel 2.5 mg and mestranol 100 mcg on day 3 postpartum. On the second cycle, she began taking norethynodrel 5 mg and mestranol 75 mcg in error and the breast enlargement became more pronounced. After discontinuation of breastfeeding, the breasts returned to normal within 2 to 3 weeks.[8] The contraceptive probably caused the breast enlargement.

Bilateral breast enlargement occurred in an otherwise normal 3-month-old male infant whose mother began a combination contraceptive containing 100 mcg of ethinyl estradiol for 21 days with the last 6 days also containing 5 mg of norethindrone. The woman stopped the contraception and the gynecomastia disappeared completely in about 4 weeks.[9] The contraceptive possibly caused the breast enlargement.

In a study of women given a combination of 50 mcg of ethinyl estradiol and 250 mcg of levonorgestrel, an infant (sex not stated) developed transient gynecomastia after 3 months of maternal therapy.[6] The contraceptive possibly caused the breast enlargement.

An 18-month old partially breastfed girl developed bilateral breast enlargement 3 months after her mother began taking an oral contraceptive containing ethinyl estradiol 30 mcg and levonorgestrel 150 mcg. Breastfeeding was discontinued and the breast enlargement decreased over the next 6 months. The girl was growing and developing normally at 7 years of age.[10] The contraceptive possibly caused the breast enlargement.

A 10-month-old male infant presented after 3 weeks of vomiting, diarrhea and deterioration in nutritional status. Laboratory evaluation found folic acid deficiency and macrocytic anemia which responded well to folic acid. The mother had been taking a combination oral contraceptive (ingredients not specified) for 3 months. The authors attributed the folic acid deficiency to maternal contraceptive use.[11] The contraceptive possibly caused the folate deficiency.

Forty-eight children (20 boys and 28 girls) whose mothers used a combination oral contraceptive containing 50 mcg of ethinyl estradiol during lactation beginning 2 months postpartum were compared to age- and sex-matched control children whose mothers breastfed, but took no contraceptive. Using several different sources of

health records, no differences in the height or weight, illnesses, or intellectual development of the groups at several time points were found up to 8 years of age.[12]

Effects on Lactation and Breastmilk

High-dose estrogens, alone or in combination with an androgen, were formerly used to suppress lactation in women who did not wish to breastfeed.[13] Combination oral contraceptives containing mestranol 100 mcg daily has also been used as a method for decreasing postpartum breast engorgement in women who did not breastfeed.[14][15] In a randomized, double-blind study, 2 tablets twice daily for 5 days of a combination oral contraceptive containing 50 mcg of ethinyl estradiol had similar efficacy to bromocriptine (dosage not stated) in suppressing postpartum breast engorgement and lactation.[16]

Changes in milk composition of breastmilk (total and nonprotein nitrogen, alpha-lactalbumin, lactoferrin, and albumin) have been observed in women taking various combination contraceptives containing 30 to 50 mcg of ethinyl estradiol and levonorgestrel 150 to 250 mcg or megestrol acetate 4 mg. However, the changes were generally within the normal range of values for healthy women.[17] Similar results were reported by another group with similar combined contraceptives.[18] Another study found no clinically important changes in the composition in the milk of mothers taking a combination contraceptive containing 150 mcg of levonorgestrel and 30 mcg of ethinyl estradiol starting at 6 weeks postpartum. However, milk volume was decreased compared to women who used no hormonal contraception.[19][20]

In a partially randomized study, 25 postpartum women who want to breastfeed their infants were given an oral contraceptive containing mestranol 80 mcg and norethindrone 1 mg daily starting 6 weeks postpartum. The duration of lactation and the weight gain of the breastfed infants was reduced among the mothers who received the contraceptive compared to 25 mothers randomized to received a placebo or who took no tablets.[21]

In a double-blind trial (randomization not stated), mothers were given either placebo (n = 218) or a combination oral contraceptive containing mestranol 50 mcg and norethindrone 1 mg (n = 233) daily from the day after birth to day 8 postpartum. Although there was no difference in the percentage of mothers breastfeeding, women taking the active drug needed to provide supplementary feedings more frequently than placebo-treated patients (12% vs 3.5%). The authors concluded that mothers wishing to breastfeed should not receive this contraceptive.[22]

A nonrandomized study compared 100 women who were 4 to 24 weeks postpartum and were given a combination contraceptive containing mestranol 100 mcg and ethynodiol diacetate 1 mg to women who chose not to use oral contraception. Women who received the contraceptive produced less milk per week than control mothers in the 8 weeks after beginning the contraceptive.[23]

An observational report on 83 women who were given 1 of 9 combination oral contraceptives containing 50 mcg of ethinyl estradiol and 80 to 100 mcg of mestranol starting at 5 days postpartum found that 54% were still breastfeeding at 6 weeks postpartum. This was in comparison to 59% of women who were not taking an oral contraceptive. The authors noted that some mothers who wished to breastfeed had difficulty.[24] Because of the overall low breastfeeding rates, lack of randomization and high loss to follow-up, the results of this study are questionable.

In a randomized trial, 367 women receiving one of several methods of hormonal contraception and 249 women receiving nonhormonal contraception. Women receiving combination contraceptive containing ethinyl estradiol 50 mcg and norethindrone 1 mg beginning 1 month postpartum had a median duration of lactation shorter than control mothers who used no contraception (5.3 vs 4.6 months), but the difference was not statistically significant. Women who used oral contraceptives containing mestranol had a statistically shorter duration of lactation than those using nonhormonal contraception.[25]

One nonrandomized study of 6 women found that daily use of a combination contraceptive containing 10 mcg of ethinyl estradiol and 350 mcg of norethindrone experienced decreases in protein, lipids, calcium and phosphorus compared to 11 women who received nonhormonal contraception. However these changes were not statistically significant. Milk volume was similar in the two groups.[26]

One group of investigators studied lactational performance in a randomized controlled trial of fully nursing mothers given an oral contraceptive containing levonorgestrel 150 mcg and ethinyl estradiol 30 mcg daily beginning at 30 to 35 days postpartum. Comparison groups were mothers who received no hormonal contraception. Of the mothers evaluated at 91 days postpartum (contraceptive n = 103; placebo n = 188), the contraceptive group had a lower percentage of exclusively breastfeeding mothers (81% vs 92%) and lower average daily infant weight gain during the first month of use and lower absolute weights at 61 and 91 days compared to the control groups.[27] The negative effect of the hormonal contraceptives continued to be seen during postpartum months 4 to 10. Infant weight gain was lower than that of control women who used the lactation amenorrhea method, but not compared to women who used an IUD.[28] The same group studied the same contraceptive in 59 mothers compared to 82 mothers using nonhormonal contraception all of whom were fully breastfeeding at 90 days postpartum. The oral contraceptive was initiated at 90 to 95 days postpartum. At all times from months 6 to 12 postpartum, the percentage of fully breastfed infants in the oral contraceptive group was lower and the percentage of infants receiving supplements was greater, although the average time of complete weaning did not differ between the groups. During the first month of therapy, infants whose mothers were taking the oral contraceptive gained weight at a lower rate than those in the nonhormonal group. However, the absolute weights of the infants were not significantly different at 12 months postpartum.[29] The authors concluded that low-dose combination contraceptives are not a good choice during breastfeeding and that if they are used, they should be instituted as late as possible, and particularly not during the first month postpartum.

In a multicenter, double-blind study, well-nourished women wishing hormonal contraception were randomized to contraceptive containing 30 mcg of ethinyl estradiol and 150 mcg of levonorgestrel (n = 86) or 75 mcg of racemic norgestrel (n = 85) beginning at 6 weeks postpartum. One hundred eleven women who received either no or nonhormonal contraception comprised the control group. Infant growth and maternal milk volume were measured periodically up to 24 weeks postpartum. The decline in milk volume was statistically significantly greater at all time periods from week 6 to 24 for the combined oral contraceptive group (42% vs 17% in the control group and 12% with progestin-only tablets). No differences were seen between groups in average infant growth. The authors concluded that low-dose combined oral contraceptives can be used in well-nourished mothers postpartum, but that they should be warned that their milk volume might be decreased.[30]

A case-control study compared the children of 48 women who used a combination oral contraceptive containing 50 mcg of ethinyl estradiol during lactation beginning at 2 months postpartum. There was a statistically significant difference in the duration of lactation between the contraceptive users and nonusers, 3.7 and 4.6 months, respectively.[12]

A retrospective cohort study compared 371 women who received high-dose estrogen (either 3 mg of diethylstilbestrol or 150 mcg of ethinyl estradiol daily) during adolescence for adult height reduction to 409 women who did not receive estrogen. No difference in breastfeeding duration was found between the two groups, indicating that high-dose estrogen during adolescence has no effect on later breastfeeding.[31]

A prospective, nonrandomized trial compared 4 contraceptives in 10 women each to assess their effect on milk production. One of the following were begun on day 42 postpartum as chosen by the mother: combined ethinyl estradiol 30 mcg plus levonorgestrel 150 mcg (Microvlar), etonogestrel implant (Implanon), levonorgestrel intrauterine system (Myrena), or a copper IUD (Optima). Milk intake was measured using deuterium oxide given to the mother and measured in the infants' saliva as well as numbers of wet diapers per day. Infants were also weighed and measured to assess growth. No differences in milk intake or infant growth were observed between the methods from days 42 through 63.[32]

A study analyzed data from a prospective cohort study of U.S. women from May 2005 through June 2007. Women were followed from the third trimester of pregnancy throughout the first year postpartum. Data from the subset of women who intended to breastfeed for 3 months or longer postpartum during their third trimester of pregnancy and who were using a contraceptive at 3 months postpartum were analyzed (n = 1349). Women who intended to breastfeed for at least 4 months and were taking an estrogen-containing combined oral contraceptive were only 17% as likely to be breastfeeding (exclusive or nonexclusive) at 4 months as women who used a nonhormonal contraceptive. Women who said they would breastfeed for 3 to 4 months were 34% as likely to be breastfeeding rates as those using a nonhormonal contraceptive. These rates were much lower than those of women who were taking a progestin-only oral contraceptive.[33]

Alternate Drugs to Consider

Etonogestrel, Intrauterine Copper Contraceptive, Oral Levonorgestrel, Intrauterine Levonorgestrel, Levonorgestrel Implant, Medroxyprogesterone Acetate, Progesterone

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Substance Identification

Substance Name

Contraceptives, Oral, Combined

Drug Class

Breast Feeding

Lactation

Contraceptive Agents, Female

Contraceptives, Oral, Synthetic