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Etonogestrel

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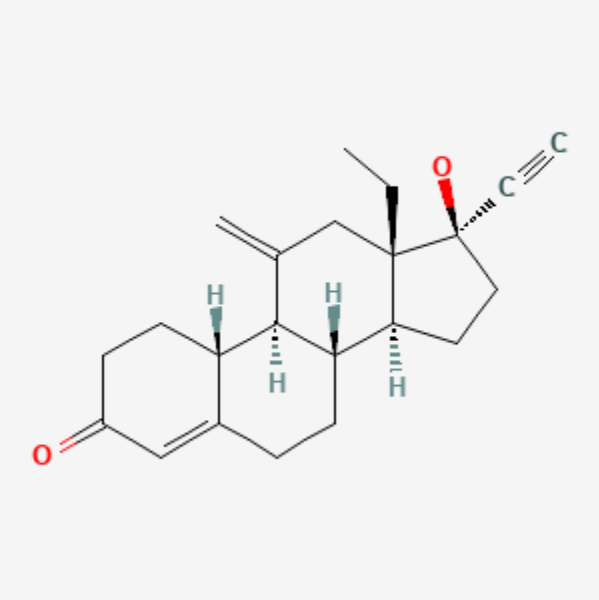

Drug Levels and Effects

Summary of Use during Lactation

Etonogestrel is available in the United States in a combination contraceptive vaginal ring (NuvaRing) that releases 120 mcg of etonogestrel and 15 mcg of ethinyl estradiol daily, and subcutaneous implants (Implanon, Nexplanon) that release etonogestrel at a decreasing rate over a 3-year period.

Based on the available evidence, expert opinion in the United States holds that postpartum women who are breastfeeding should not use combined hormonal contraceptives (e.g., NuvaRing) 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 until 6 weeks after delivery.[1,2] 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.[3] A decrease in milk supply can happen over the first few days of estrogen exposure.[4]

Expert opinion holds that the risks of progestin-only contraceptive products usually are acceptable for nursing mothers at any time postpartum.[2,3,5,6] A review of published data concluded that the etonogestrel implant appears to have a risk of lactation suppression of about 0.9%.[7] Low quality evidence indicates that there may be no difference in breastfeeding rates at 6 months between immediate and delayed insertion of progestin-releasing IUDs.[8] Some preliminary evidence indicates that secretory activation (lactogenesis II) might be delayed by the etonogestrel implant. However, other studies found no difference between immediate and delayed insertion of an etonogestrel implant.

Drug Levels

Maternal Levels. Forty-two women had an etonogestrel subcutaneous implant inserted implant inserted between 28 and 56 days postpartum. Breastmilk samples were obtained at 1, 2 and 4 months after insertion. The average breastmilk concentration of etonogestrel was 178 ng/L at 1 month (n = 41), 153 ng/L at 2 months (n = 38), and 131 ng/L at 4 months (n = 38) after insertion. The authors calculated that the infants would receive an average of 19.9 ng/kg daily at 1 month, 15.1 ng/kg daily at 2 months and 10.5 ng/kg daily at 4 months after insertion. The decreasing doses were caused by both a reduced quantity in milk and a lower breastmilk intake as time passed.[9]

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

Effects in Breastfed Infants

Forty-two women had an etonogestrel subcutaneous implant (Implanon) inserted between 28 and 56 days postpartum. Compared with the infants of 38 similar mothers who had a nonhormonal intrauterine device, no statistically significant difference was found in infant illnesses or growth rates between the groups, except for a statistically nonsignificant higher weight gain in the male infants, and respiratory conditions and skin disorders in the infants of women who received the implants.[6] Infants were followed up at 3 years of age; no differences in growth or psychomotor development were found.[10]

A non-blinded, randomized study of exclusively breastfeeding women compared those who received an etonogestrel implant 24-48 hours after delivery (n = 20) to those who received a 150 mg depot medroxyprogesterone acetate injection at 6 weeks postpartum (n = 20). No difference in infant weight gain was noted between the two groups.[11]

A randomized, prospective study compared the growth of infants of mothers who received an etonogestrel implant either within 48 hours (n = 50) of delivery or 6 weeks (n = 50) postpartum. Breastfeeding rates and growth of the infants were not significantly different between the groups over the first year of life.[12]

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.[13]

A small study randomized postpartum women to either an etonogestrel implant (Implanon) within 48 hours postpartum (n = 12) or no contraception for the first 6 weeks postpartum (n = 12). Breastmilk intake was measured in the first 48 hours postpartum and on day 29 postpartum. No difference in milk intake was found between the two groups and no difference was seen in the weight gain of newborns during the follow-up period.[14]

Effects on Lactation and Breastmilk

Forty-two women had an etonogestrel subcutaneous implant (Implanon) inserted between 28 and 56 days postpartum. Compared with 38 similar mothers who had a nonhormonal intrauterine device, no difference was found in milk volume, or in milk lactose, protein or fat content.[9] No difference was seen between the two groups in duration of lactation, averaging 421 days in the Implanon group and 423 days in the IUD group.[10]

A non-blinded, randomized study of exclusively breastfeeding women compared those who received an etonogestrel implant 24 to 48 hours after delivery (n = 20) to those who received a 150 mg depot medroxyprogesterone acetate injection at 6 weeks postpartum (n = 20). The rates of exclusive breastfeeding were similar between the groups at 6 and 12 weeks postpartum.[11]

A randomized, controlled study compared etonogestrel implant insertion at 1 to 3 days postpartum (n = 35) to insertion at 4 to 8 weeks postpartum (n = 34). Several outcome parameters were measured: time to lactogenesis II, prevalence of lactation failure, use of formula supplementation and milk composition at 6 weeks postpartum. No differences were found in any of the outcomes between the two groups.[15]

A woman was breastfeeding a newborn successfully with good infant growth. On day 39 postpartum, an etonogestrel implant (Nexplanon) was inserted. By day 70 postpartum, the mother reported a decrease in milk supply and infant had lost weight, going from the 44th percentile to the 6th percentile for growth. Five weeks later, the mother had transitioned completely to formula feeding. The authors requested reports on etonogestrel from the FDA and found a similar case of loss of milk supply. From a review of 4 published studies, the authors estimated that there is about a 0.9% (range 0.2 to 5.4%) chance of lactation suppression with the etonogestrel implant.[7]

A randomized, nonblinded trial compared the insertion of an etonogestrel contraceptive implant (brand not specified) in postpartum women 14 to 24 years old either before discharge or at 6 weeks postpartum. Breastfeeding rates at 3 and 6 months postpartum were slightly higher in the women who had immediate placement of the insert, but the differences were not statistically significant.[16]

A randomized, prospective study compared the growth of infants of mothers who received an etonogestrel implant either within 48 hours (n = 50) of delivery or 6 weeks (n = 50) postpartum. Breastfeeding rates were not significantly different between the groups over the first year of life.[12]

A study in Malawi compared the breastfeeding rates between women who received an etonogestrel (n = 28) or levonorgestrel (n = 112) implant immediately postpartum. Mothers chose the method and were followed for 2 years postpartum. Most women breastfed for 2 years. No difference was seen in the exclusive breastfeeding rate at 6 months between the groups nor in the continuation of breastfeeding to 2 years.[17]

A study of women who expressed a desire to breastfeed randomized them to receive a progestin implant (presumably etonogestrel) either in the delivery room or at 24 to 48 hours after delivery. The time to lactogenesis II was not significantly different between the two groups.[18]

A small, nonrandomized, prospective pilot study compared the time to secretory activation in women who received an etonogestrel implant (Nexplanon; n = 8) to those receiving no contraception (n = 24). Women who received the etonogestrel implant had a delay in secretory activation compared to those who did not, as measured by biochemical markers.[19]

A noninferiority study randomized postpartum women to insertion of an etonogestrel implant at either 0 to 2 hours (n = 35) or 24 to 48 hours (n = 34) post-delivery. No significant difference was found between the two groups in the time to lactogenesis II.[20]

A study randomized postpartum women to receive the etonogestrel implant either within 30 minutes of placental delivery, 24 to 72 hours postpartum, or 6 or more weeks postpartum. There was no significant difference in time to lactogenesis II with an average time of 62 hours. Duration and exclusivity of breastfeeding, satisfaction with the implant, and reports of heavy or irregular bleeding were similar among all groups.[21]

A woman reported persistent galactorrhea after implantation of Nexplanon 2 months after delivery and breastfeeding her infant. The galactorrhea persisted for 2 years until the Nexplanon implant was removed. Her galactorrhea was improved 1 and 7 months after removal.[22]

Alternate Drugs to Consider

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

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Substance Identification

Substance Name

Etonogestrel

CAS Registry Number

54048-10-1

Drug Class

Breast Feeding

Lactation

Milk, Human

Contraceptive Agents, Female