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Etonogestrel

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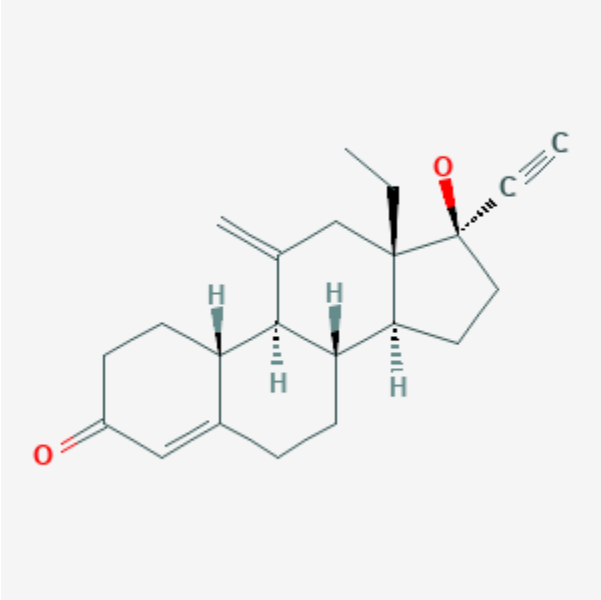

Drug Levels and Effects

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 because of the clotting risk, combination contraceptive products (e.g., NuvaRing) should not be used before 3 weeks postpartum. Between 3 weeks and 6 months postpartum, the advantages of using the method generally outweigh the theoretical or proven risks, although the evidence of lack of effect on lactation is poor and does not include preterm or ill infants. After 6 months postpartum, combination contraceptives, including oral tablets, the transdermal patch and vaginal ring, can be used, but progestin-only methods are preferred if breastfeeding will be continued.[1] 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.[2]

Expert opinion holds that the risks of progestin-only contraceptive products usually are acceptable for nursing mothers at any time postpartum.[2][3][4] A review of published data concluded that the etonogestrel implant appears to have a risk of lactation suppression of about 0.9%.[5] Several studies have found no difference in breastfeeding rates or infant growth between mothers who receive the implant within 48 hours of delivery or at 6 weeks postpartum.

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, 153 ng/L at 2 months, and 131 ng/L at 4 months 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.[6] With a milk intake of 150 mL/kg daily, the infant would receive 2.2% of the mother's weight-adjusted dosage at 1 month after insertion.

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.[7]

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.[8]

A randomized, prospective study compared the growth of infants of mothers who received an etonogestrel implant either within 48 hours (n = 50) of deliver 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.[9]

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.[6] 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.[7]

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). The rates of exclusive breastfeeding were similar between the groups at 6 and 12 weeks postpartum.[8]

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.[10]

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.[11]

A small study randomized postpartum women to either an etonogestrel implant (Implanon, Organon) 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.[12]

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. By 5 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.[5]

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.[13]

A randomized, prospective study compared the growth of infants of mothers who received an etonogestrel implant either within 48 hours (n = 50) of deliver or 6 weeks (n = 50) postpartum. Breastfeeding rates were not significantly different between the groups over the first year of life.[9]

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.[14]

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

Contraceptive Agents, Female