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Norethindrone

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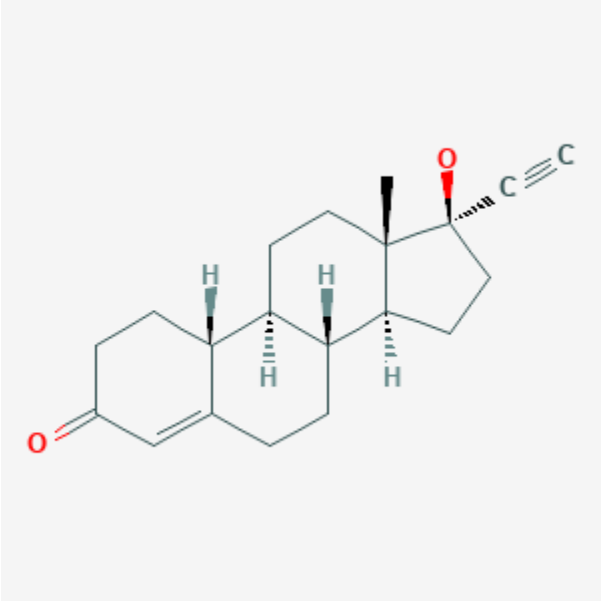

Drug Levels and Effects

Summary of Use during Lactation

This record contains information specific to norethindrone used alone. Readers with an interest in a combination oral contraceptive should consult the record entitled, "Contraceptives, Oral, Combined."

Poor to fair quality evidence indicates that norethindrone does not adversely affect the composition of milk, the growth and development of the infant or the milk supply.[1][2][3][4] Some evidence indicates that progestin-only contraceptives may offer protection against bone mineral density loss during lactation, or at least do not exacerbate it.[5][6][7]

Although nonhormonal methods are preferred during breastfeeding, progestin-only contraceptives such as norethindrone are considered the hormonal contraceptives of choice during lactation. Fair quality evidence indicates that norethindrone does not adversely affect the composition of milk, the growth and development of

the infant or the milk supply. Expert opinion holds that the risks of progestin-only contraceptive products usually are acceptable for nursing mothers at any time postpartum.[8][9]

Drug Levels

Maternal Levels. Five women with well-established lactation (exact time postpartum not stated) were given an oral dose of 350 mcg of norethindrone daily. Breastmilk levels were measured several times on the first day of treatment. Peak milk levels occurred at 2 or 4 hours after the dose in various individuals. Average milk levels were 0.747 mcg/L at 2 hours after the dose; 0.747 mcg/L at 4 hours; 0.396 mcg/L at 8 hours; 0.253 mcg/L at 12 hours; and, 0.174 mcg/L at 12 hours after the dose.[10]

Milk norethindone levels were measured in 4 women after daily ingestion of oral norethindrone 350 mcg started after 3 months postpartum. Peak milk norethindrone levels in the range of 0.4 to 0.5 mcg/L occurred between 1 and 3 hours after the dose and dropped slowly over the 6-hour study interval to about 0.15 to 0.4 mcg/L.[11]

At 6 to 20 weeks postpartum, 15 women received a single tablet of a combination oral contraceptive containing a dose of 3 mg of norethindrone. At 2 to 2.5 hours after the dose, a foremilk sample was taken. The mothers breastfed their infants and then a hindmilk sample was taken. The two samples were pooled for assay. Milk levels averaged 2.4 mcg/L (range 0.9 to 5.5 mcg/L).[12]

Infant Levels. At 6 to 20 weeks postpartum, 15 women received a single tablet of a combination oral contraceptive containing a dose of 3 mg of norethindrone. At 2 to 2.5 hours after the dose the mothers breastfed their infants; infant serum samples were taken 1.5 to 2 hours later at about 4 hours after the maternal dose. Infant serum levels averaged 0.19 mcg/L which was 0.8% of peak maternal serum levels drawn at 2 to 2.5 hours after the dose.[12]

Effects in Breastfed Infants

No consistent physical, mental, or radiologic differences have been found in infants whose mothers were using norethindrone enanthate (Norplant).[13][14] Some studies found increased infant weight gain among the infants of treated women.[13][15][16]

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). Infants of the implant users gained more than the infants of the DMPA mothers during the first 6 weeks of life.[17]

A short-term study of 12 women who received oral norethindrone 350 mcg daily starting 48 hours postpartum found no differences in infant weight gain over 14 days compared to 8 women taking a placebo.[18]

Effects on Lactation and Breastmilk

Studies of varying size and quality on the use of long-acting norethindrone injections (acetate or enanthate) have found that the use of levonorgestrel implants (Norplant or Norplant-2) as a contraceptive beginning at 6 weeks postpartum or later either has no clinically important negative effect on the quality of breastmilk and results in either no effect or an increase in the milk supply and duration of lactation [13][14][15][16] In one study, women who received the implant at 6 days postpartum, a transient decrease in milk protein occurred 2 weeks after implant insertion. A decrease in milk phosphorus content was also observed between 2 and 4 months after implant insertion in this group and at 3 months postpartum, the early insertion group had a higher rate of supplementation.[19] In another study, women given norethindrone enanthate depot injection less than 48 hours postpartum were 2.5 to 3 times more likely to have postpartum depression at 6 weeks postpartum. No differences were seen at 1 and 12 weeks postpartum.[20]

A short-term study of 12 women who received oral norethindrone 350 mcg daily starting 48 hours postpartum found no differences in milk production or milk composition over 14 days compared to 8 women taking a placebo.[18]

One small, nonrandomized study found that oral norethindrone 350 mcg daily decreased the quantity and quality (lower protein, lipids and calcium) compared to controls who received nonhormonal contraception.[21]

In a nonrandomized, nonblinded study comparing women who were breastfeeding at discharge, 102 postpartum women received depot medroxyprogesterone acetate (dosage not stated) in the early postpartum period (average 51.9 hours postpartum; range 6.25 to 132 hours), 181 received another progestin-only contraceptive and 138 used nonhormonal contraception. No differences in breastfeeding rates were seen at 2 and 6 weeks, but women receiving any hormonal contraceptive were breastfeeding at a lower rate (72.1% vs 77.6%) at 4 weeks postpartum. The authors concluded that progestin-only contraception initiated in the early postpartum period had no adverse effects on breastfeeding rates.[22]

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 a progestin-only oral contraceptive, such as norethindrone, were 3.15 times more likely to be breastfeeding (exclusive or nonexclusive) at 4 months than women who used a nonhormonal contraceptive. Women who said they would breastfeed for 3 to 4 months had 4-month breastfeeding rates equivalent to those using a nonhormonal contraceptive. These rates were much higher than those of women who were taking an estrogen-containing, combined oral contraceptive.[23]

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

Norethindrone

CAS Registry Number

68-22-4

Drug Class

Breast Feeding

Lactation

Contraceptive Agents, Female

Contraceptives, Oral, Synthetic