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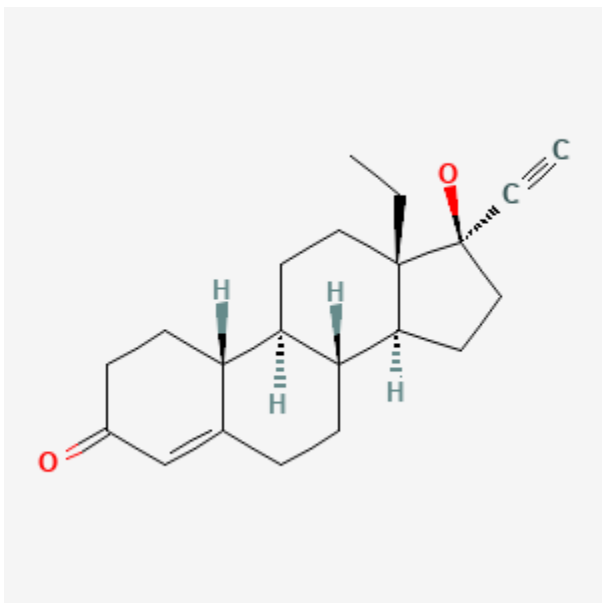
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Intrauterine Levonorgestrel

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Drug Levels and Effects

Summary of Use during Lactation

This record contains information specific to the levonorgestrel intrauterine device (IUD). Although nonhormonal methods are preferred during breastfeeding, progestin-only contraceptives such as levonorgestrel are considered the hormonal contraceptives of choice during lactation. Fair quality evidence indicates that levonorgestrel does not adversely affect the composition of milk, the growth and development of the infant or the milk supply. Expert opinion and a metaanalysis hold that the risks of progestin-only contraceptive products usually are acceptable for nursing mothers at any time postpartum.[1-6] There are no reports of adverse effects in breastfed infants with maternal use of progestin-only contraceptives. Low quality evidence indicates that there may be no difference in breastfeeding rates at 6 months between immediate and delayed insertion of progestin-

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releasing IUDs.[7] Some evidence indicates that progestin-only contraceptives may offer protection against bone mineral density loss during lactation, or at least do not exacerbate it.[8-10]

The World Health Association recommends that progestin-only intrauterine devices (IUDs) can be inserted before 48 hours postpartum and after 4 weeks postpartum, but should not be inserted between 48 hours and 4 weeks postpartum.[1] Other guidelines and product labeling consider delayed postpartum insertion acceptable if immediate insertion is not feasible.[4] Four small, randomized studies on this point differed in their outcomes. Three found that early insertion did not adversely affect breastfeeding,[11-13] and the other found that immediate IUD insertion markedly reduced the breastfeeding rate at 6 months postpartum.[14] A meta-analysis found that the risk of expulsion was no greater in breastfeeding mothers.[15] More recent prospective studies found an increase in the risk of expulsion of intrauterine devices with breastfeeding,[12,16] while a large retrospective study found a 29% lower risk of expulsion in breastfeeding women.[17] The American College of Obstetrics and Gynecology recommends that women be counseled that immediate postpartum insertion may have a higher expulsion rate than later insertion.[4]

Drug Levels

Levonorgestrel is a synthetic progestin that is the active isomer of the racemate norgestrel. It is considered to be twice as potent on a weight basis as the racemic mixture.

Maternal Levels. Ten women had IUDs that released either 10 mg or 30 mcg of levonorgestrel daily placed at 6 weeks postpartum. Milk was analyzed for levonorgestrel at various times over a 12-month period. All milk levels were less than 0.1 mcg/L, regardless of the dose that the mother was receiving.[18]

A study of levonorgestrel IUDs compared levonorgestrel milk levels in women who had the IUD placed either within 30 minutes of delivery (immediate: n = 12) or at 4 to 8 weeks postpartum (delayed: n = 10). At 4 to 8 weeks postpartum, the median milk levonorgestrel level in the immediate group was 32.5 ng/L and the median in the delayed group's milk levels was 17.5 ng/L before IUD placement. Four weeks later, the two groups had similar median levels: 26.2 ng/L in the immediate group and 28 ng/L in the delayed group. It was not clear why the delayed group had measurable levonorgestrel levels before having the IUD placed. Measurements of milk creatinocrit found no effect of levonorgestrel on milk fat.[19]

Infant Levels. A study compared women who received levonorgestrel as a contraceptive via Norplant-2 (n = 14), an IUD that released 20 mcg daily (n = 14) or oral tablets containing 30 mcg of levonorgestrel (n = 10) at 4 to 6 weeks postpartum. The levonorgestrel serum levels averaged 0.03 mcg/L in infants whose mothers used the IUD. Infant serum levels averaged 6.7% of maternal serum levels.[20]

Effects in Breastfed Infants

One study found serum thyroid stimulating hormone levels to be lower in the infants exposed to levonorgestrel than in control infants.[21]

IUDs that released levonorgestrel were inserted 6 weeks after delivery. IUDs released 10 mcg per day (n = 30) or 30 mcg per day (n = 40); copper-releasing IUDs (n = 40) were used as controls. No differences were seen in infant height, weight, development, respiratory infections or blood chemistries up to 12 months of age between the levonorgestrel and copper IUD groups.[22]

Three hundred twenty lactating women were randomized to either an IUD containing levonorgestrel (Mirena; n = 163) or the copper-containing IUD Cu T380A group (n = 157). Follow-up of infants for 1 year found no differences in growth and development or in duration of breastfeeding.[23]

Effects on Lactation and Breastmilk

IUDs releasing levonorgestrel were inserted 6 weeks after delivery. IUDs released 10 mcg per day (n = 30) or 30 mcg per day (n = 40); copper-releasing IUDs (n = 40) were used as controls. The rate of breastfeeding discontinuation was higher with the levonorgestrel groups than in the copper IUD group at 75 days, but not at other times.[22]

In a small prospective study, forty-six women were randomized to have an IUD containing levonorgestrel (Mirena) inserted either within 10 minutes after placental delivery (n = 15), between 10 minutes and 48 hours after placental delivery (n = 15), or after 6 weeks postpartum (n = 16). At 6 months postpartum, no statistical difference in the rates of continued breastfeeding (extent not stated) was found among the groups.[11]

Women who gave birth were offered contraception with a levonorgestrel-containing IUD and randomized to have the IUD placed immediately following delivery (n = 46) or at 6 to 8 weeks postpartum (n = 50). Women randomized to later IUD insertion were more likely to be nursing at 6 months postpartum (24% vs 6%) and tended to have a longer median duration of exclusive breastfeeding.[14]

A noninferiority trial compared breastfeeding in women who received a levonorgestrel IUD (product and dose not specified) immediately postpartum (n = 132) or at 8 weeks postpartum (n = 127). At 8 weeks, women who received the IUD immediately postpartum had a 5% lower rate of any breastfeeding (79% vs 84%), which fell within the predetermined 15% noninferiority margin. Exclusive breastfeeding was slightly lower at 8 weeks in the immediate group (33% vs 40%), but the difference was not statistically significant. The time to lactogenesis in the immediate group was noninferior to that of the delayed group (65.3 vs 63.6 hours). Twenty-four device expulsions occurred in the immediate group compared to 2 in the delayed group (19% vs 2%), which was statistically significant.[12]

Alternate Drugs to Consider

Etonogestrel, Intrauterine Copper Contraceptive, Medroxyprogesterone Acetate, Norethindrone

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Substance Identification

Substance Name

Intrauterine Levonorgestrel

CAS Registry Number

797-63-7

Drug Class

Breast Feeding

Lactation

Milk, Human

Contraceptive Agents, Female

Contraceptives, Oral, Synthetic