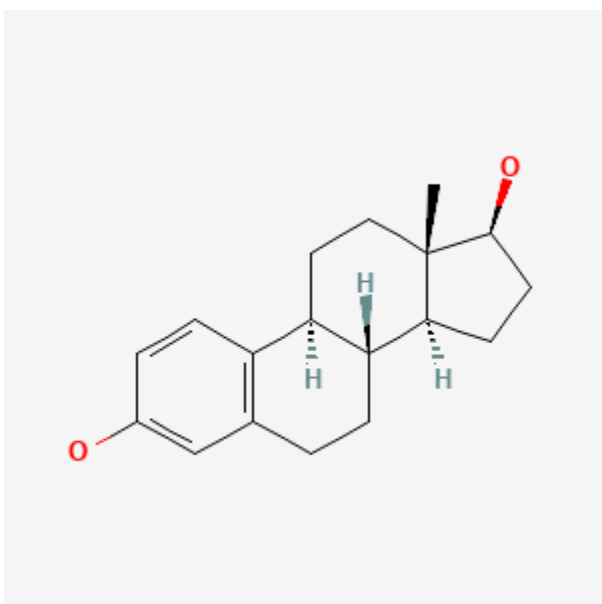




Estradiol

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CASRN: 50-28-2



Drug Levels and Effects

Summary of Use during Lactation

Limited information on the use of estradiol during breastfeeding indicates that the route of administration and dosage form have influences on the amount transferred into breastmilk. Vaginal administration results in measurable amounts in milk, but transdermal patches do not. Maternal doses of up to 200 mcg daily transdermally do not increase estradiol or estriol in breastfed infants or cause any adverse effects in breastfed infants. Vaginal administration results in unpredictable peak times for estradiol in breastmilk, so timing of the dose with respect to breastfeeding is probably not useful. Milk estradiol levels have not been studied after use of the estradiol gel, but maternal blood levels only increase slightly in a dose-dependent manner.

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Estrogens can decrease the milk supply, especially if started before the milk supply is well established at about 6 weeks postpartum. The decrease can happen over the first few days of estrogen exposure.[1] A case report of inadequate milk production and inadequate infant weight gain was possibly caused by transdermal estradiol initiated on the first day postpartum, but 2 small studies found no such effect when the drug was initiated after lactation was well established.

Drug Levels

Maternal Levels. Six women who were 6 or more months postpartum were given a vaginal suppository containing 50 or 100 mg of estradiol. In 3 of the 6 women, peak milk levels occurred 3 hours after the dose. In 2 others, the peak level occurred 7 hours after the dose and in the sixth, the peak occurred 11 hours after the dose. Peak milk levels were about 100 ng/L in 4 women, in one it was 300 ng/L and in the sixth, it was 1000 ng/L.[2]

Twenty-one women who were 20 weeks postpartum and breastfeeding their infants were randomized to receive a transdermal patch that released estradiol 50 mcg (n = 7), 75 mcg (n = 5) or 100 mcg (n = 6) daily or placebo (n = 4) for 2 weeks. Breastmilk and serum samples were collected at the beginning and end of the study. Serum estradiol levels increased slightly from baseline, but the differences were not statistically significant; serum levels were in the range of 25 to 45 ng/L. Estradiol was undetectable (<6.8 ng/L) in all breastmilk samples.[3]

Infant Levels. Six nursing mothers received transdermal estradiol as part of a study comparing estradiol to sertraline and placebo for postpartum depression. The mothers received estradiol dosages between 50 and 200 mcg daily (mean 133 mcg daily) at the time of serum level analysis at 4 and 8 weeks of therapy. Four of the 6 infants were exclusively breastfed and the other two were more than 50% breastfed. All infants had undetectable (<2.5 ng/L) serum estradiol concentrations and 4 of the 6 had undetectable (<2.5 ng/L) serum estradiol concentrations. The other two had estradiol concentrations of 7 and 7.1 ng/L. The serum estradiol and estradiol concentrations were not significantly different from breastfed infants in the placebo or sertraline arms of the study. No correlation was found between maternal and infant serum concentrations of estradiol or estradiol.[4]

Effects in Breastfed Infants

A mother who had severe postpartum depression with 2 previous infants was prescribed a transdermal estradiol patch that released 50 mcg daily beginning on day 1 postpartum to prevent recurrence of depression. At 11 days of age, the infant was jaundiced and had gained only 60 grams since birth. With more frequent nursing, weight gain improved, but remained inadequate until day 28 when the estradiol was discontinued. The infant then experienced above average weight gain through day 66 postpartum. The delayed and reduced weight gain was possibly caused by estradiol.[5]

Six nursing mothers received transdermal estradiol as part of a study comparing estradiol to sertraline and placebo for postpartum depression. The mothers received estradiol dosages between 50 and 200 mcg daily (mean 133 mcg daily) at the time of serum level analysis at 4 and 8 weeks of therapy. Four of the 6 infants were exclusively breastfed and the other two were more than 50% breastfed. There was no difference in infant length, weight, and head circumference nor in the average daily gains in any of these parameters between treatments.[4]

Effects on Lactation and Breastmilk

Thirteen women who were 12 weeks postpartum and fully breastfeeding their infants were given a transdermal patch that released 100 mcg of estradiol daily. The average number of breast feeds per day did not change significantly during 3 days of patch application.[6]

Nineteen women who were 6 weeks postpartum, using a barrier contraceptive method and breastfeeding their infants were randomized to transdermal patches that released estradiol 50 mcg daily or placebo patches for 12

weeks. An additional control group received no patches. The number of breast feeds per day decreased in all groups over the course of the study, but there were no important differences among the groups.[7]

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.[8]

A transgender woman took and spironolactone 50 mg twice daily to suppress testosterone, domperidone 10 mg three times daily, increasing to 20 mg four times daily, oral micronized progesterone 200 mg daily and oral estradiol to 8 mg daily and pumped her breasts 6 times daily to induce lactation. After 3 months of treatment, estradiol regimen was changed to a 0.025 mg daily patch and the progesterone dose was lowered to 100 mg daily. Two weeks later, she began exclusively breastfeeding the newborn of her partner. Breastfeeding was exclusive for 6 weeks, during which the infant's growth, development and bowel habits were normal. The patient continued to partially breastfeed the infant for at least 6 months.[9]

A transgender woman was taking sublingual estradiol 4 mg twice daily, spironolactone 100 mg twice daily and progesterone 200 mg at bedtime for gender-affirming therapy. In order to prepare for the birth of the infant being carried by her partner, sublingual estradiol was increased to 6 mg twice daily and progesterone was increased to 400 mg at bedtime. Domperidone 10 mg twice daily was also started to increase serum prolactin levels and later increased to 20 mg 4 times daily. Before the delivery date, progesterone was stopped, spironolactone was decreased to 100 mg daily and estradiol was changed to 25 mcg per day transdermally. At day 59 postpartum, estradiol was changed to 2 mg per day sublingually and spironolactone was increased to 100 mg twice daily. The patient was able to produce up to 240 mL of milk daily. The patient was able to produce up to 240 mL of milk daily containing typical macronutrient and oligosaccharide levels.[10]

A transgender woman who wished to breastfeed was given estradiol transdermal patch 150 mcg daily and progesterone 100 mg daily by mouth. Later estradiol spray 100 mcg and domperidone 10 mg 4 times daily were added. Domperidone dosage was then doubled to 20 mg 4 times daily and progesterone was doubled to 100 mg twice daily. After further adjustment of estradiol and progesterone dosages, 7 mL of milk was produced with pumping, but 2 weeks after the infant's birth, lactation induction was discontinued at the patient's request.[11]

A 50-year-old transgender woman wished to breastfeed her grandchild was taking baseline treatment with estradiol 0.3 mg transdermal patch every 72 hours and micronized progesterone 200 mg oral once daily. To initiate lactation, her estradiol dose was increased to a 0.4 mg transdermal patch every 72 hours and nipple stimulation was initiated. Later the patient's progesterone was increased to 300 mg daily and metoclopramide oral 10 mg three times daily was initiated. She lactated for a total of two weeks and nursed the four-month-old infant on multiple occasions. Her peak milk production was 30 mL from her larger right breast, and 8 mL from her smaller left breast.[12]

Alternate Drugs to Consider

Ethinyl Estradiol

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Substance Identification

Substance Name

Estradiol

CAS Registry Number

50-28-2

Drug Class

Breast Feeding

Lactation

Milk, Human

Estrogens

Hormones