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Clomipramine

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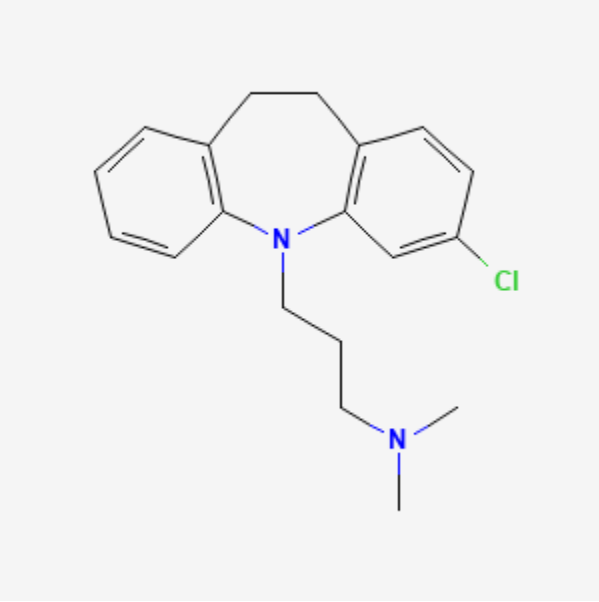

Drug Levels and Effects

Summary of Use during Lactation

Limited evidence indicates that use of clomipramine during breastfeeding is acceptable. For women who were taking clomipramine during pregnancy, the amount of drug in breastmilk may be insufficient to prevent neonatal withdrawal symptoms in breastfed infants. A safety scoring system finds clomipramine to be possibly used with caution during breastfeeding.[1] For use as an antidepressant, clomipramine may be less desirable than other antidepressants that have been studied more thoroughly.

Drug Levels

Maternal Levels. One woman took a dose of 125 mg of clomipramine daily during pregnancy and for 7 days postpartum, then increased to 150 mg daily. Milk levels taken 10 to 14 hours after the 125 mg dose on days 4 and 6 were 343 and 216 mcg/L, respectively. Milk levels taken 10 to 14 hours after the 150 mg dose on days 10, 14 and 35 were 270, 305 and 624 mcg/L, respectively. Using the average of the above concentrations, a fully breastfed infant would receive about 2.2% of the maternal weight-adjusted dosage of clomipramine in breastmilk.[2]

In a study of 2 mothers, concentrations of clomipramine were measured in the milk 12 to 15 hours after the dose. In one who was taking 100 mg daily, the level in foremilk was 60 mcg/L and in hindmilk was 226 mcg/L. The other woman was taking 75, 100 and then 125 mg daily. Three measurements of milk clomipramine on the 125 mg dose averaged 148 mcg/L (range 98 to 212 mcg/L) in foremilk and 202 mcg/L (range 136 to 250 mcg/L) in hindmilk. Using the average of the above fore- and hindmilk concentrations, a fully breastfed infant would receive about 1.3% of the maternal weight-adjusted dosage of clomipramine in breastmilk.[3]

A woman was treated with clomipramine 25 mg daily during pregnancy and postpartum. At 33 days postpartum, a breastmilk sample taken 12 to 15 hours after the dose contained clomipramine in a concentration of 55.1 mcg/L. Desmethylclomipramine concentration was undetectable (<50 mcg/L) in breastmilk.[4]

Infant Levels. An infant was born with a serum clomipramine level of 267 mcg/L because of transplacental passage. Breastfeeding was instituted on day 7 postpartum during maternal use of clomipramine 150 mg daily. Infant serum clomipramine levels 10 to 14 hours after the mother's dose on days 10, 14 and 35 were 45, 24 and 10 mcg/L, respectively.[2]

Two infants whose mothers were taking clomipramine from 1 and 3 weeks postpartum had plasma levels of clomipramine and its major active metabolites obtained at unspecified ages. The drugs were undetectable (< 0.1 mcg/L) in the plasma of an infant whose mother was taking 100 mg daily. In the infant whose mother was taking 75, 100 and then 125 mg daily, the infant had a combined drug and metabolite plasma level of 3.2 mcg/L with a maternal dosage of 75 mg daily. The infant plasma level was 5.5 mcg/L in one instance on a dose of 125 mg daily and undetectable in 3 instances with maternal dosages of 100, 125 and 125 mg daily.[3]

A newborn infant was exclusively breastfed by his mother who was taking clomipramine 25 mg daily. Infant serum obtained 12 to 15 hours after the mother's last dose contained undetectable (<50 mcg/L) amounts of clomipramine and its metabolite, desmethylclomipramine.[4]

Infant serum levels were measured in 4 breastfed infants (one fully breastfed; extent not stated in the other 3) aged 2, 3, 18 and 19 weeks during maternal use of clomipramine 75 to 125 mg daily. Infant serum levels 10 to 12 hours after the maternal dose were undetectable (<10 mcg/L) for clomipramine and its 3 main active metabolites.[5]

Effects in Breastfed Infants

Follow-up for 1 to 3 years in a group of 20 breastfed infants whose mothers were taking various tricyclic antidepressants found no adverse effects on growth and development. One of the mothers whose infant was followed up at 24 months of age was taking clomipramine 175 mg daily.[6] Two small controlled studies indicate that other tricyclic antidepressants have no adverse effect on infant development.[3,7] In one of the studies, 2 mothers were taking clomipramine 100 mg daily in one and 75 to 125 mg daily in the other.[3]

In another study, 25 infants whose mothers took a tricyclic antidepressant during pregnancy and lactation were tested formally between 15 to 71 months and found to have normal growth and development. Some of the mothers were taking clomipramine.[8]

An infant was born to a mother who had taken clomipramine 25 mg daily during pregnancy. The infant exhibited inadaptation syndrome for the first few days of life. However, the infant was exclusively breastfed while the mother continued clomipramine at the same dose postpartum. At 33 days of life, the infant exhibited no clinical signs of clomipramine side effects.[4]

In an observational case series of 10 infants whose mothers were taking clomipramine in daily dosages ranging from 37.5 to 125 mg daily throughout pregnancy, all infants exhibited withdrawal symptoms after birth. Five of the 10 infants were breastfed, but no difference in withdrawal symptoms was seen between breastfed and non-breastfed infants. In 5 of the infants, 4 of whom were breastfed, the half-life was calculated to average 42 hours (range 27 to 68 hours). The half-life in the non-breastfed infant was 35 hours, which was not statistically different from the breastfed infants. The authors attribute the lack of differences in withdrawal and half-life between breastfed and non-breastfed infants to the small amount of drug that is excreted into breastmilk.[9]

Effects on Lactation and Breastmilk

Clomipramine has caused increased prolactin levels and galactorrhea in nonpregnant, nonnursing patients.[10-13] The clinical relevance of these findings in nursing mothers is not known. The prolactin level in a mother with established lactation may not affect her ability to breastfeed.

An observational study looked at outcomes of 2859 women who took an antidepressant during the 2 years prior to pregnancy. Compared to women who did not take an antidepressant during pregnancy, mothers who took an antidepressant during all 3 trimesters of pregnancy were 37% less likely to be breastfeeding upon hospital discharge. Mothers who took an antidepressant only during the third trimester were 75% less likely to be breastfeeding at discharge. Those who took an antidepressant only during the first and second trimesters did not have a reduced likelihood of breastfeeding at discharge.[14] The antidepressants used by the mothers were not specified.

A retrospective cohort study of hospital electronic medical records from 2001 to 2008 compared women who had been dispensed an antidepressant during late gestation (n = 575) to those who had a psychiatric illness but did not receive an antidepressant (n = 1552) and mothers who did not have a psychiatric diagnosis (n = 30,535). Women who received an antidepressant were 37% less likely to be breastfeeding at discharge than women without a psychiatric diagnosis, but no less likely to be breastfeeding than untreated mothers with a psychiatric diagnosis.[15] None of the mothers were taking clomipramine.

In a study of 80,882 Norwegian mother-infant pairs from 1999 to 2008, new postpartum antidepressant use was reported by 392 women and 201 reported that they continued antidepressants from pregnancy. Compared with the unexposed comparison group, late pregnancy antidepressant use was associated with a 7% reduced likelihood of breastfeeding initiation, but with no effect on breastfeeding duration or exclusivity. Compared with the unexposed comparison group, new or restarted antidepressant use was associated with a 63% reduced likelihood of predominant, and a 51% reduced likelihood of any breastfeeding at 6 months, as well as a 2.6-fold increased risk of abrupt breastfeeding discontinuation. Specific antidepressants were not mentioned.[16]

Alternate Drugs to Consider

Fluvoxamine, Nortriptyline, Paroxetine, Sertraline

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Substance Identification

Substance Name

Clomipramine

CAS Registry Number

303-49-1

Drug Class

Breast Feeding

Lactation

Milk, Human

Antidepressive Agents

Antidepressive Agents, Tricyclic