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Imipramine

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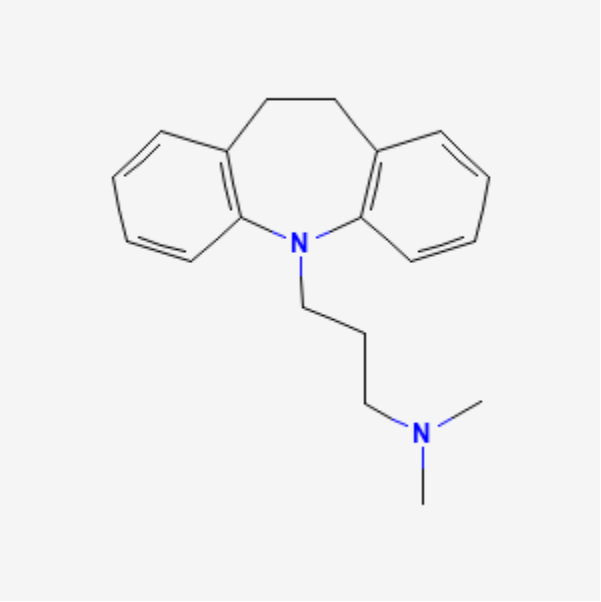

Drug Levels and Effects

Summary of Use during Lactation

Milk levels of imipramine and its metabolite are low and have not been detected in the serum of breastfed infants. Immediate side effects have not been reported and a limited amount of follow-up has found no adverse effects on infant growth and development. Imipramine use during breastfeeding would usually not be expected to cause any adverse effects in breastfed infants, especially if the infant is older than 2 months. A safety scoring system finds imipramine use to be possible during breastfeeding.[1] Some experts consider imipramine one of the antidepressants of choice for nursing mothers.[2] However, other agents may be preferred when large doses are required or while nursing a newborn or preterm infant.

Drug Levels

Imipramine is metabolized to desipramine which has antidepressant activity equal to that of imipramine. Desipramine is metabolized to 2-hydroxydesipramine which has antidepressant activity equal to that of desipramine.[3]

Maternal Levels. Two women who were taking imipramine 50 mg daily for panic disorder had imipramine and desipramine breastmilk levels measured 1 month postpartum (time after dose not stated). In one, levels of impramine and desipramine were 91 and 185 mcg/L, respectively. In the other only trace quantities were detected.[4]

A mother who was 1 month postpartum began taking imipramine for depression. Sixteen days after initiation, milk imipramine plus desipramine levels ranged from 21 to 59 mcg/L at various times while taking a dose of 200 mg daily. There was no clear-cut relationship of milk levels to the time since the dose.[5]

Four mothers who were taking imipramine in doses of 75 to 150 mg daily had milk samples taken 12 to 15 hours after their daily dose. Milk imipramine plus desipramine levels ranged from 48 to 622 mcg/L, with little correlation to dosage. Foremilk levels were lower than hindmilk levels.[6] Using the hindmilk data from this study, an exclusively breastfed infant would receive an estimated maximum of 2.9% of the maternal weight-adjusted dosage.

Infant Levels. Two infants had serum level measurements of imipramine plus desipramine while breastfeeding. One infant whose mother began imipramine 75 mg daily 2 weeks postpartum and was breastfed for 7 weeks had a serum level of 0.6 mcg/L. Another infant was breastfed for 17 weeks after his mother began imipramine 100 mg daily 8 weeks postpartum and later decreased to 75 mg daily. His average of 3 serum levels was 5.5 mcg/L (range 3.3 to 7.4 mcg/L). Time after the dose was not stated.[6]

One 5.9-week-old infant who was breastfed 10 to 12 times daily had no detectable serum imipramine or desipramine (both <25 mcg/L) during maternal use of imipramine 75 mg daily. Another 17-week-old infant who was breastfed 10 to 12 times daily had no detectable serum imipramine (<20 mcg/L) or desipramine (<35 mcg/L) during maternal use of imipramine 150 mg daily.[7]

Effects in Breastfed Infants

No behavioral or physical changes were noted in a 6-week-old breastfed infant whose mother had been taking imipramine 200 mg daily at bedtime for 15 days.[5]

Follow-up for 1 to 3 years in 14 breastfed infants whose mothers were taking imipramine in an average dosage of 161 mg daily (range 125 to 225 mg daily) found no adverse effects on growth and development.[8]

Four infants were breastfed for 7 to 18 weeks during maternal use of imipramine 75 to 150 mg daily starting at 2 weeks (3 infants) and 8 weeks (1 infant) postpartum. Formal testing indicated no adverse effects on infant development up to 30 months of age. The mother of 1 infant was taking haloperidol along with imipramine 150 mg daily.[6]

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 imipramine.[9]

Six postpartum mothers diagnosed with panic disorder were successfully treated with imipramine 25 to 35 mg (mean 28 mg) daily starting at a mean of 5.9 weeks postpartum. Mothers were treated for a mean of 9.3 weeks. All mothers reported that no adverse effects occurred in their infants.[10]

Effects on Lactation and Breastmilk

Imipramine has caused increased prolactin levels and gynecomastia in nonpregnant, nonnursing patients.[11,12] Galactorrhea has been reported rarely.[13,14] 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.[15] 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.[16] None of the mothers were taking imipramine.

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.[17]

Alternate Drugs to Consider

Nortriptyline, Paroxetine, Sertraline

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Substance Identification

Substance Name

Imipramine

CAS Registry Number

50-49-7

Drug Class

Breast Feeding

Lactation

Milk, Human

Antidepressive Agents

Antidepressive Agents, Tricyclic