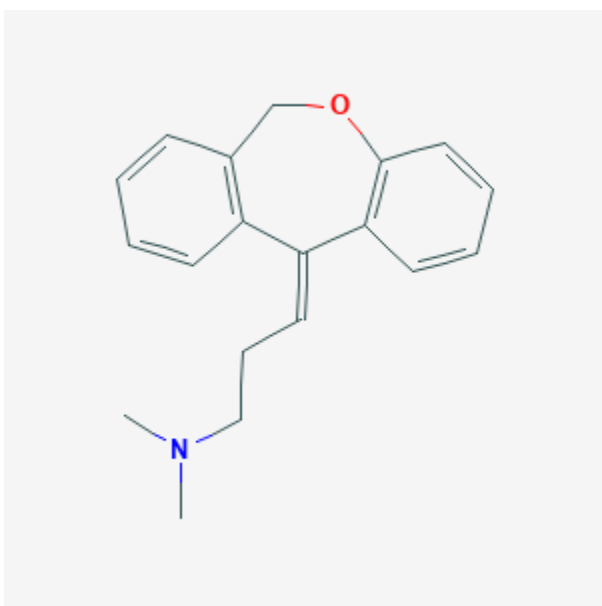




Doxepin

Revised: March 16, 2020.

CASRN: 1668-19-5



Drug Levels and Effects

Summary of Use during Lactation

Because of its sedating potential, active metabolite, presence in infant serum, two reports of adverse effects in breastfed infants, and only one report of use without apparent adverse reactions, doxepin is a poor choice and other agents may be preferred, especially while nursing a newborn or preterm infant. Other agents are preferred, especially while nursing a newborn or preterm infant.

Maternal use of topical doxepin cream is unlikely to pose a problem for a breastfed infant as long as it is applied away from the breasts so that the infant cannot ingest the drug directly.

Drug Levels

Doxepin is metabolized to N-desmethyldoxepin which has antidepressant activity equal to that of doxepin.[1]

Maternal Levels. In one patient taking doxepin 25 mg three times daily, milk doxepin levels ranged from 7 to 29 mcg/L at various times throughout the day, with peaks occurring at about 4 to 5 hours after the dose. N-desmethyldoxepin levels ranged from trace to 11 mcg/L.[2]

A mother who was taking 150 mg daily at bedtime, had milk doxepin and metabolite levels measured 8 times before and after feeding her infant over a 92-day postpartum period at about 18 hours after her dose. Her doxepin plus N-desmethyldoxepin milk levels averaged 141 mcg/L prefeed and 214 mcg/L postfeed. The authors estimated that the infant received about 2.2% of the maternal weight-adjusted dosage.[3]

A mother who was taking doxepin 35 mg daily had breastmilk doxepin and N-desmethyldoxepin measured 3 times 11 to 13 days postpartum from 13 to 15 hours after the dose. The combined milk levels were 60, 100 and 100 mcg/L.[4]

Infant Levels. An 8-week-old exclusively breastfed infant whose mother was taking doxepin 25 mg three times daily had serum levels of N-desmethyldoxepin of 58 and 66 mcg/L on 2 occasions that were almost as high as maternal serum. The infant's doxepin serum level was 3 mcg/L.[2]

An infant whose mother was taking 150 mg of doxepin a bedtime daily had an undetectable (<5 mcg/L) serum doxepin level and 15 mcg/L of N-desmethyldoxepin at 43 days of age, which was 15% of the mother's serum N-desmethyldoxepin level.[3]

An 11-day-old infant whose mother was taking 35 mg daily of doxepin had combined doxepin plus N-desmethyldoxepin plasma levels that were undetectable (<40 mcg/L). Doxepin concentration was about 10 mcg/L and N-desmethyldoxepin was undetectable (<10 mcg/L) 2 hours after feeding.[4]

Effects in Breastfed Infants

One infant was breastfed (extent not stated) over a 2-month period during maternal use of doxepin 150 mg at bedtime, beginning at 30 days postpartum. The infant experienced no apparent adverse reactions.[3]

One infant had an adverse reaction that was probably caused by doxepin in breastmilk. An 8-week old breastfed infant was found pale, limp, somnolent and almost not breathing 4 days after the maternal dosage had been increased from 10 mg daily to 25 mg three times daily. The infant returned to normal 24 hours after discontinuing breastfeeding.[2]

A 9-day-old breastfed infant had poor sucking and swallowing, hypotonia, vomiting, and weight loss. The reaction was probably caused by doxepin in breastmilk. The infant's mother was taking 35 mg of doxepin at bedtime daily.[4]

Effects on Lactation and Breastmilk

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.[5] 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.[6] None of the mothers were taking doxepin.

Alternate Drugs to Consider

Nortriptyline, Paroxetine, Sertraline

References

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Substance Identification

Substance Name

Doxepin

CAS Registry Number

1668-19-5

Drug Class

Breast Feeding

Lactation

Antidepressive Agents

Antidepressive Agents, Tricyclic