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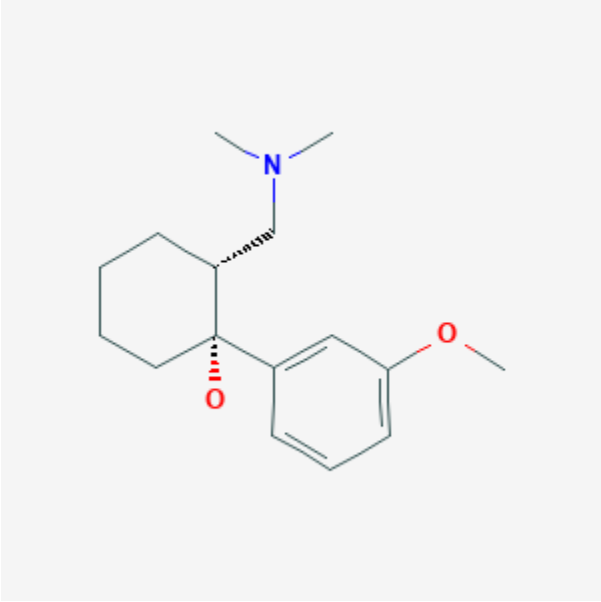
Tramadol

Revised: June 3, 2019.

CASRN: 27203-92-5



Drug Levels and Effects

Summary of Use during Lactation

The excretion of tramadol into milk is low and even lower amounts of the active metabolite, O-desmethyltramadol, are excreted. With usual maternal dosage, the amount excreted into breastmilk is much less than the dose that has been given to newborn infants for analgesia. A study of breastfeeding in breastfed newborn infants found no adverse effects attributable to tramadol. Although tramadol is unlikely to adversely affect nursing infant,[1] the U.S. Food and Drug Administration and the manufacturer recommend against the use of tramadol during breastfeeding.[2] If tramadol is used, monitor infants for increased sleepiness (more than usual), difficulty breastfeeding, breathing difficulties or limpness, and contact a physician immediately if any of these occur.

Drug Levels

In adults, tramadol has 70 to 100% oral bioavailability and is metabolized to the active O-desmethyltramadol (M1). Tramadol has a more potent monoamine reuptake inhibitory effect while M1 has a more potent opioid mu-agonist effect.[3] M1 is about 10% as potent as morphine in mu-opiate binding, although some investigators have reported a 450-fold potency difference.[4] Women who are extensive metabolizers of tramadol may have higher than expected serum levels of M1, potentially leading to higher levels of M1 in breastmilk. The capacity of preterm and newborn infants to metabolize tramadol to M1 is limited.[5]

Maternal Levels. The manufacturer reports that in the 16 hours following a 100 mg intravenous dose of tramadol, the cumulative excretion into breastmilk was 100 mcg of tramadol and 27 mcg of M1. No further details are provided.

Detectable levels (>12 mcg/L) of tramadol were found in samples of breastmilk collected 10 hours after a 50 mg maternal dose of intravenous or oral tramadol.[6] No other clinical details or milk levels were reported.

One mother was taking oral tramadol 300 mg daily during pregnancy and presumably the same dose postpartum for chronic back pain. On approximately day 3 postpartum (time not specified), the breastmilk concentration of tramadol was 1.8 mg/L.[7]

Seventy-five mothers who were 2 to 4 days postpartum provided 3 milk samples from both breasts during the 6 hours following a dose of 100 mg of oral tramadol after taking at least 4 doses. The average milk concentration of tramadol was 748 mcg/L and of M1 was 203 mcg/L. These values translate to an average infant dosage of 112 and 30 mcg/kg daily of the drug and metabolite, respectively. An exclusively breastfed infant would receive maternal weight-adjusted dosages of 2.24% of tramadol and 0.64% of its metabolite.[8]

Reanalysis of the above data using a pharmacokinetic model with first-pass conversion rates based on literature values and simulating a maternal dosage of 100 mg every 6 hours yielded average milk tramadol levels of 0.82 mg/L in extensive metabolizers and 0.99 mg/L in poor metabolizers. Average M1 milk levels were 0.36 mg/L and 0.18 mg/L, respectively. Infant exposure to tramadol and M1 was the same in both phenotype groups and represented 3.1% of the maternal weight-adjusted tramadol dose.[9] Based on this analysis, the average daily dosage of tramadol excreted in milk in poor metabolizers would be 0.15 mg/kg, which is 2.6% of the maternal weight-adjusted tramadol dose, and 1.5% of the recommended daily intravenous neonatal tramadol dose of 10 mg/kg.[5] The average daily dosage of M1 excreted in milk in extensive metabolizers would be 0.054 mg/kg, which represents 2% to 3 % of the normal daily neonatal intravenous morphine equivalent dosage.

Infant Levels. An infant was born to a mother who as taking 300 mg of tramadol daily for chronic back pain. By day 3, the infant was exclusively breastfeeding and a serum concentration was obtained (time not specified). The infant's tramadol serum concentration was 2 mcg/L. A typical serum tramadol level in neonates given tramadol intravenously for pain is 200 mcg/L.[7]

Effects in Breastfed Infants

Seventy-five breastfed infants whose mothers were breastfeeding and taking tramadol 100 mg every 6 hours following a cesarean section were compared to 75 matched infants at 2 to 4 days of age. Forty-nine percent of the mothers taking tramadol and all of the control mothers were taking other opiates (primarily oxycodone) and 61% of and 58%, respectively, also were taking a nonsteroidal antiinflammatory agent (primarily diclofenac). Examination by a pediatrician revealed no difference between the groups using the Neurologic and Adaptive Capacity Score.[8]

Effects on Lactation and Breastmilk

Tramadol can increase serum prolactin.[10] However, the prolactin level in a mother with established lactation may not affect her ability to breastfeed.

A randomized study compared tramadol and naproxen for post-cesarean section pain. Patients received the drugs either on a fixed schedule or as needed. No difference in breastfeeding rates were seen among the groups.[11]

In a study in China, women with a scheduled cesarean section were randomized to receive intravenous patient-controlled analgesia with either sufentanil or tramadol. Postpartum prolactin levels were higher in the tramadol group (348 mcg/L) than in the sufentanil group (314 mcg/L). The onset of lactation was sooner in the tramadol group (21.4 hours) than in the sufentanil group (25.1 hours). Both of these difference were statistically significant.[12] Injectable tramadol is not available in the United States.

Alternate Drugs to Consider

Acetaminophen, Ibuprofen, Morphine

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Substance Identification

Substance Name

Tramadol

CAS Registry Number

27203-92-5

Drug Class

Breast Feeding

Lactation

Analgesics, Opioid

Narcotics