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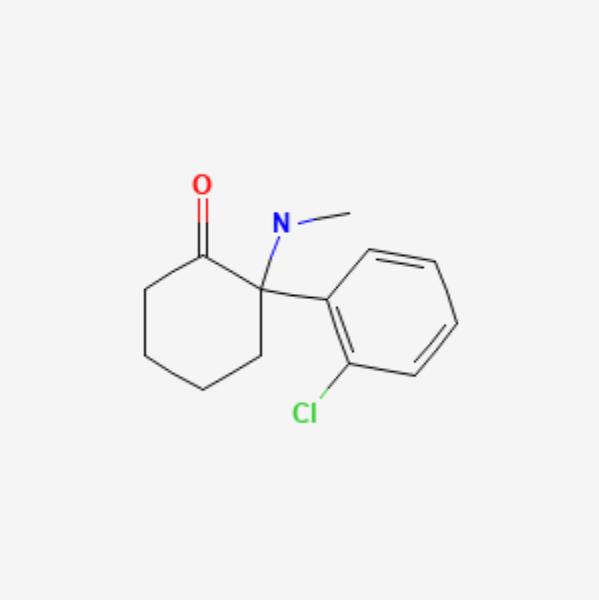
Ketamine

Revised: September 15, 2023.

CASRN: 6740-88-1



Drug Levels and Effects

Summary of Use during Lactation

Ketamine and its active metabolite appear in milk in very low levels and its oral bioavailability is low, indicating a low risk to breastfed infants. Available data indicate that ketamine use in nursing mothers may not affect the breastfed infant or lactation. Until more data are available, ketamine should be used with careful infant monitoring of the infant for sedation, poor feeding and poor weight gain.[1,2]

Drug Levels

Ketamine is metabolized to norketamine, dehydronorketamine and hydroxynorketamine. Of the metabolites, only norketamine is active, but it has only about one-third the activity of ketamine.

Maternal Levels. Four women with well-established lactation were given two doses of ketamine intramuscularly, 0.5 and 1 mg/kg with 5 to 14 days between doses. Complete milk expressions were collected at 3, 6, 9 and 12 hours after a dose. The average peak levels of ketamine in milk were 51 mcg/L after the 0.5 mg/kg dose and 125 mcg/L after the 1 mg/kg dose, both at 3 hours after the dose. Very little drug was detected in milk of one mother after 12 hours. The authors calculated relative infant doses of 0.65% after the 0.5 mg/kg dose and 0.77% after the 1 mg/kg dose. The metabolites norketamine, dehydronorketamine and hydroxynorketamine had similar patterns of excretion into milk, with norketamine having levels similar to those of ketamine.[3]

A participant in a clinical study who was about 6 months postpartum was given a sub-anesthetic ketamine infusion at 0.1 mg/kg per hour for 12 hours. She collected 7 milk samples over 20 hours after the start of the infusion. The peak ketamine level of about 115 mcg/L occurred at about 8 hours after the start of the infusion. Norketamine and dehydronorketamine concentrations were fairly constant over the study duration with a peak norketamine concentration of about 45 mcg/L occurring at about 12 hours and peak dehydronorketamine of 15 mcg/L occurring at about 2 hours after the start of the infusion.[4]

Four women who were receiving ketamine infusions at varying intervals collected milk samples over a 24-hour period beginning just before the infusion was begun. The maximum concentrations of both ketamine and norketamine were observed at 1 hour after the start of the infusion and their concentrations declined over 24 hours. Their dosages ranged from 0.61 to 4.17 mg/kg. The estimated daily infant dosage of ketamine ranged from 0.003 mg/kg to 0.017 mg/kg, and the estimated daily infant dosage of norketamine ranged from 0.005 mg/kg to 0.018 mg/kg. The relative infant dosage of ketamine ranged from 0.34% to 0.57%, and relative infant dosage of norketamine was 0.29% to 0.95%.[5]

Infant Levels. Relevant published information was not found as of the revision date.

Effects in Breastfed Infants

Four mothers who received epidural analgesia with lidocaine and bupivacaine for cesarean section also received general anesthesia with ketamine and midazolam (dosages not specified). Their infants were either breastfed or received their mother's breastmilk by bottle. No adverse effects were reported in the infants.[6]

A retrospective chart review of 298 mothers and infants born at 37 weeks or beyond was conducted to determine the effects of ketamine and diazepam on breastfed infants after maternal tubal ligation surgery. Surgery occurred on a median of day 2 (range 1 to 6) postpartum. Most infants were fully breastfed, with breastfeeding resumed 2 to 4 hours after the procedure. No differences were found in weight loss or phototherapy requirements of infants whose mothers received low dose (<1.16 mg/kg) and high dose (1.16 mg/kg or more) ketamine.[7]

Effects on Lactation and Breastmilk

A pregnant woman sustained 28% body surface area burns near term. She underwent an emergency cesarean section on her due date under ketamine anesthesia. Although the infant required vigorous resuscitation, the infant began breastfeeding immediately. The infant had transient jaundice that resolved in a few days.[8]

A study compared women undergoing cesarean section who received either placebo or S-ketamine (esketamine) 0.5 mg/kg intramuscularly, followed by a continuous infusion of 2 mcg/kg/minute for 12 hours. This low dose was used to enhance analgesia and reduce residual pain rather than to provide anesthesia. All women received intraspinal bupivacaine 8 to10 mg and sufentanil 5 mcg for analgesia, as well as midazolam 0.02 mg/kg intravenously before the S-ketamine or placebo injection. Postoperatively, patients received patient-controlled intravenous morphine for 24 hours, followed by acetaminophen, oral ketorolac and a single dose of ondansetron 8 mg intravenously as needed. Of the 56 patients enrolled in the study (28 in each group), 13 in each group were contacted at 3 years postpartum. Patients who received placebo reported breastfeeding for an average of 10.5

months and those who received S-ketamine reported breastfeeding for an average of 8 months; however, the difference was not statistically significant.[9]

A randomized, double-blind study compared the effects of intravenous propofol 0.25 mg/kg, ketamine 0.25 mg/kg, ketamine 25 mg plus propofol 25 mg, and saline placebo for pain control in mothers post-cesarean section. A single dose was given immediately after clamping of the umbilical cord. The time to the first breastfeeding was 58 minutes in those who received placebo, 31.9 minutes with ketamine and 25.8 minutes with propofol plus ketamine. The time was significantly shorter than the other groups with the combination.[10]

A small preliminary study of the use of ketamine for the prevention of postpartum depression after cesarean section gave mothers ketamine 0.5 mg/kg by either subcutaneous or intravenous injection or a placebo. No statistical difference in the breastfeeding rates were seen; however, the numbers of patients in each group was small (7 or 8), so the study was underpowered to make a final determination.[11]

Alternate Drugs to Consider

Dexmedetomidine, Etomidate, Methohexital, Propofol, Thiopental

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Substance Identification

Substance Name

Ketamine

CAS Registry Number

6740-88-1

Drug Class

Breast Feeding

Lactation

Milk, Human

Anesthetics, Intravenous

Hypnotics and Sedatives

Anesthetics, Dissociative

Excitatory Amino Acid Antagonists