



Cannabis

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Drug Levels and Effects

Summary of Use during Lactation

The main psychoactive component of cannabis, tetrahydrocannabinol (THC), is excreted into breastmilk in small quantities. The duration of detection of THC in milk has ranged from 6 days to greater than 6 weeks in various studies. A pharmacokinetic model predicted a half-life in milk of 39 hours which is consistent with a THC clearance from milk in about 8 days. Concern has been expressed regarding the possible effects of cannabis on neurotransmitters, nervous system development and endocannabinoid-related functions.[1,2] One preliminary study found a decrease in secretory IgA (SIgA) levels in the milk of cannabis users.[3] A 1-year study found that daily or near daily use might retard the breastfed infant's motor development, but not growth or intellectual development.[4] This and another study[5] found that occasional maternal cannabis use during breastfeeding did not have any discernable effects on breastfed infants, but the studies were inadequate to rule out all long-term harm. Although cannabis can affect serum prolactin variably, it appears not to adversely affect the duration of lactation. However, maternal perception that their use of cannabis is harmful to their infants are likely to discontinue breastfeeding earlier than mothers who do not believe it is harmful.[6] Other factors to consider are the possibility of positive urine tests in breastfed infants, which might have legal implications, and the possibility of other harmful contaminants in street drugs.

Because of insufficient long-term data on the outcome of infants exposed to cannabis via breastmilk, health professionals' opinions on the acceptability of breastfeeding by cannabis-using mothers varies. In general, professional guidelines recommend that cannabis use should be avoided by nursing mothers, and nursing mothers should be informed of possible adverse effects on infant development from exposure to cannabis compounds in breastmilk. In addition to possible adverse effects from cannabinoids in breastmilk, paternal cannabis use may also increase the risk of sudden infant death syndrome in breastfed infants. Cannabis should not be smoked by anyone in the vicinity of infants because the infants may be exposed by inhaling the smoke. [7-10]

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Drug Levels

The main active psychoactive component of cannabis is delta-9-tetrahydrocannabinol (THC), although it also contains other active compounds. THC is very fat soluble and persistent in the body fat of users and slowly released over days to weeks, depending on the extent of use.

Maternal Levels. Two women who smoked marijuana daily while nursing had their randomly collected milk analyzed. One mother who reported smoking marijuana once daily had a milk tetrahydrocannabinol concentration of 105 mcg/L; other metabolites were absent. The second mother who reported smoking marijuana 7 to 8 times daily had a milk concentration of 340 mcg/L; the metabolite 11-hydroxy-THC was found in a concentration of 4 mcg/L and 9-carboxy-THC was absent. A milk sample that was collected 1 hour after smoking marijuana contained 60.3 mcg/L of THC, 1.1 mcg/L of 11-hydroxy-THC and 1.6 mcg/L of 9-carboxy-THC.[11] One source used data in this case to estimate that the infant receives about 0.8% of the maternal weight-adjusted dosage.[12] However, a poorly characterized assay was used that might not be accurate and the portion of milk (i.e., foremilk versus hindmilk) that was collected by the mothers was not stated. This is important because of the high fat solubility of THC.

A woman who admitted to smoking cannabis (amount not stated) donated milk for analysis at an unknown time after the previous use. THC was present in a concentration of 86 mcg/L and 11-hydroxy-THC was present in a concentration of 5 mcg/L; 11-nor-carboxy-9-tetrahydrocannabinol was not detected.[13]

Eight exclusively nursing women who were 3 to 5 months postpartum and reported previous or current cannabis smoking were studied. After 24 hours of abstinence, each smoked a 100 mg of a standardized cannabis containing 23.18% THC. The product was smoked over 10 to 20 minutes from a glass pipe until it was fully consumed. Milk was pumped before smoking and at 20 minutes, 1, 2 and 4 hours after inhalation. THC and its metabolites, 11-OH-delta-9-tetrahydrocannabinol and 11-nor-9-carboxy-delta-9-tetrahydrocannabinol were measured in the milk samples. Six of the women had baseline THC concentrations of <2 mcg/L; the other two had 5.8 and 15.8 mcg/L of THC in their milk at baseline. The average THC concentration in breastmilk was 53.5 mcg/L (median 27.6 mcg/L; range 8.4 to 186.1 mcg/L), and the average peak THC concentration was 94 mcg/L (range 12.2 to 420.3 mcg/L) 1 hour after inhalation. The metabolites were not measurable (<0.097 mcg/L). The estimated daily THC intake for the infant was 8 mcg/kg, which corresponded to 2.5% (range 0.4 to 8.7%) of the weight-adjusted maternal dosage.[14]

Fifty women who reported using cannabis in the prior 14 days donated milk samples for analysis of THC and its major metabolites. Four women donated two samples each for a total of 54 samples. THC was detectable in 63% of the samples. The median concentration of THC was 9.47 mcg/L (range 1 to 323 mcg/L). Only 5 samples had measurable concentrations of 11-OH-THC (range 1.3 to 12.8 mcg/L) and 5 samples had measurable concentrations of cannabidiol (range 1.3 to 8.6 mcg/L). Samples collected 140 hours (about 6 days) or longer after reported use contained no detectable (<1 mcg/L) THC and the sample with the highest cannabidiol concentration contained no detectable THC. Of the 34 milk samples from mothers who reported using cannabis, the half-life of THC in milk was estimated to average about 27 hours.[15] Using the median value, the median infant THC dosage would be 1.4 mcg/kg daily.

Twenty women in Oregon who admitted to using a cannabis product while breastfeeding their infants provided milk samples for analysis. The mothers reported using cannabis almost daily. Fifteen women provided milk samples at their infant's 2-week and 2-month checkup and 5 provided a sample at only one of the visits for a total of 35 milk samples. All but one milk sample contained at least one cannabinoid. None of the mothers reported using a cannabidiol (CBD) product, but 13 had detectable CBD in breastmilk. Median (IQR) concentrations in milk were as follows: THC 27.5 (0.8 to 190.5) mcg/L; 11-OH-THC 1.4 (0.7 to 5.2) mcg/L; THC-COOH 1.9 (0.5-16.6) mcg/L; CBD 1.2 (0.5 to 17) mcg/L. Three patients using edible products had similar cannabinoid levels as those who smoked cannabis. Fourteen mothers reported an increase in use of cannabis between the 2-week

and 2-month visit. Median breast milk THC concentrations were 16.7 mcg/L at visit 1 and 54.5 mcg/L at visit 2. The authors estimated that overall the breastfed infants received an average THC dose of 4.12 mcg/kg daily (range 0.52 to 123 mcg/kg daily) in milk.[16]

Seven women who used cannabis during pregnancy more than twice weekly, primarily by smoking, and were documented to be abstinent postpartum donated blood and milk levels 2 to 5 times weekly for 6 to 7 weeks. Maximum milk THC levels ranged from 2.8 to 26.1 mcg/L and the elimination half-life from milk averaged 17 days (range 12.2 to 21 days).[17]

Ninety lactating persons who reported using cannabis within the prior 48 hours donated 104 milk samples to a milk biorepository. THC, 11-hydroxy-THC, 11-COOH-THC, cannabidiol, and cannabinol were measured in the samples. The median concentration of THC was 22.7 mcg/L (range 0.1, 1620.0). The two main metabolites of THC, 11-OH-THC and 11-COOH-THC, were detected in 22 (21.2%) and 84 (80.8%) of samples, respectively. Cannabidiol was measurable in 44 (42.3%) of samples and cannabinol was measurable in 43 (41.3%) of samples. The number of hours since last use, route of use and number of puffs taken were significant predictors of the log of THC concentrations.[18] These samples and previously reported pharmacokinetic values from children taking cannabidiol were used to create a PBPK model of infant cannabidiol exposure from breastmilk with maternal cannabis use. Infant exposure was minimal compared to exposure from direct ingestion.[19]

Thirteen milk samples were collected from 12 women who reported cannabis use post-delivery, and one sample was collected from a woman who did not indicate the period of cannabis usage. Among the 14 samples, 13 milk samples had detectable levels of THC (median 22 mcg/L), 5 milk samples contained carboxy-THC levels (median 2.6 mcg/L), 3 milk samples contained 11-OH-THC levels (median 6 mcg/L), 2 milk samples contained cannabinol levels (median 7.15 mcg/L), and 1 milk sample contained 9.3 ng/mL of CBD.[3]

A physiologically based pharmacokinetic model of THC following smoking of cannabis predicted relative infant dose of 0.59, 0.71, 0.60, and 0.39% for infants up to 1, 3, 6, and 12 months old, respectively. The predicted half-life in milk was about 39 hours.[20]

Infant Levels. The urine of 2 breastfed infants whose mothers smoked marijuana found none of the 9-carboxy-THC metabolite. One mother reported smoking marijuana once daily and the other reported smoking marijuana 7 to 8 times daily. Analysis of the feces of the latter mother's infant revealed a higher proportion of metabolites than THC, indicating that THC was probably absorbed from the milk, metabolized by the infant, and excreted in feces.[11]

A 6-month-old infant was exclusively breastfed by a mother who was a chronic cannabis user. She presented to the emergency department with somnolence after falling off a couch and developed seizure-like activity and minimally responsive dilated pupils. Laboratory values and a head CT scan were normal except for carboxy-THC found in urine. Specimens drawn 24 to 36 h post-exposure showed carboxy-THC levels of 189 mcg/L in blood and 423 mcg/L in urine.[21]

A mother reported smoking about 4 cannabis resin joints daily sometimes just before breastfeeding. She reported starting when her breastfed infant was 4 months old. At 9 months of age after a tonic-clonic seizure, the infant's plasma contained delta-9-THC 2.2 mcg/L, delta-9-THC-COOH 1.1 mcg/L, and 11-OH-THC 0.4 mcg/L. [22]

A physiologically based pharmacokinetic model of THC following smoking of cannabis predicted that in the worst-case scenario of maternal cannabis use six times daily during lactation, the maximum infant plasma concentration ranged between 0.084 and 0.167 ng/mL for infants between 1 and 12 months, with one-month-old infants having higher levels. These concentrations were orders of magnitude lower than maternal plasma levels. Neonates up to 1 month old had the highest THC exposure, probably because of the incomplete maturation of metabolizing enzymes.[20]

Effects in Breastfed Infants

Twenty-seven mothers reported smoking marijuana during breastfeeding. Twelve of them smoked once a month or less, 9 smoked weekly, and 6 smoked daily. Six of their infants were compared at 1 year of age to the infants of mothers who did not smoke marijuana during pregnancy or breastfeeding. No differences were found in growth, or on mental and motor development.[5]

Sixty-eight infants whose mothers reported smoking marijuana during breastfeeding were compared to 68 matched control infants whose mothers did not smoke marijuana. The duration of breastfeeding varied, but the majority of infants were breastfed for 3 months and received less than 16 fluid ounces of formula daily. Motor development of the marijuana-exposed infants was slightly reduced in a dose-dependent (i.e., number of reported joints per week) manner at 1 year of age, especially among those who reported smoking marijuana on more than 15 days/month during the first month of lactation. No effect was found on mental development.[4]

A small, case-control study found that paternal marijuana smoking postpartum increased the risk of sudden infant death syndrome. In this study, too few nursing mothers smoked marijuana to form any conclusion.[23]

A study of women taking buprenorphine for opiate substitution during pregnancy and lactation found that 4 of the women were also using cannabis as evidenced by positive urine screens for THC between 29 and 56 days postpartum. One was also taking unprescribed benzodiazepines. One infant was exclusively breastfed and the other 3 were mostly breastfeeding with partial supplementation. Infants had no apparent drug-related adverse effects and showed satisfactory developmental progress.[24]

Fifty women who reported using cannabis in the prior 14 days donated milk samples for analysis of THC and its major metabolites. THC was detectable in 66% of the samples and below the limit of quantification in 32% of samples. Preliminary evidence found no differences in infant adverse reactions, postnatal growth, or neurodevelopmental outcomes were found between the groups with quantifiable and nonquantifiable THC in breastmilk.[25]

A 6-month-old infant was exclusively breastfed by a mother who was a chronic cannabis user. She presented to the emergency department with somnolence after falling off a couch and developed seizure-like activity and minimally responsive dilated pupils. Laboratory values and a head CT scan were normal except for carboxy-THC found in urine and blood. The infant returned to baseline in 72 hours.[21]

A 9-month-old girl was hospitalized for a first tonic-clonic seizure. Brain scan and magnetic resonance imaging showed nonspecific right focal frontal cortical hypodensity, without bleeding or traumatic lesion. The electroencephalogram was normal and no infection was found. Delta-9-THC, delta-9-THC-COOH and 11-OH-THC were found in the infant's blood. Diazepam and its metabolites were also found in the infant's blood and the urine screening found cotinine. Her mother explained she smoked cannabis resin since her child was 4 months old, sometimes just before breastfeeding, and on average 5 joints daily. Since then her child had three spasms. She did not report any cannabis or other drugs use during pregnancy. Breastfeeding was replaced by formula and 1.5 months later, the child had not had a recurrence.[22] The infant's symptoms were probably caused by cannabis, but direct exposure to cannabis smoke and diazepam and tobacco use could have contributed.

The infant of a woman who used cannabis edibles for anxiety during pregnancy and during breastfeeding had several episodes of apnea. At 1 week of age while undergoing treatment for a urinary tract infection, the infant required intubation because of apneic episodes. At 5 weeks of age, the mother noticed the infant was having irregular breathing and apneic episodes and took the infant to the hospital. There the infant was having more apneic episodes and a urine positive for THC, although the mother reported not using cannabis for the prior 3 days.[26]

Effects on Lactation and Breastmilk

Acute one-time marijuana smoking suppresses serum concentrations of luteinizing hormone and prolactin in nonpregnant, nonlactating women.[27-29] The effects of long-term use is unclear, with some studies finding no effect on serum prolactin.[30-32] However, hyperprolactinemia has been reported in some chronic cannabis users,[33-35] and galactorrhea and hyperprolactinemia were reported in a woman who smoked marijuana for over 1 year.[35] The prolactin level in a mother with established lactation may not affect her ability to breastfeed.

Of 258 mothers who reported smoking marijuana during pregnancy, 27 who had smoked marijuana during breastfeeding were followed-up at 1 year. No difference was found in the age of weaning between these mothers and 35 who reported not smoking marijuana during pregnancy or breastfeeding.[5]

The US state of Colorado legalized medical cannabis in 2001 and recreational cannabis in 2012. A cross-sectional survey conducted in Colorado in 2014 and 2015 found that both prenatal and postnatal cannabis use were associated with a shorter duration of breastfeeding. Among women who reported using cannabis during pregnancy, 64% breastfed for 9 or more weeks compared with 78% of women who did not use cannabis during pregnancy. Among women who reported postpartum cannabis use, 58% breastfed for 9 or more weeks compared with 79% of women who did not use cannabis postpartum. Both differences were statistically significant.[36]

A study using a database of 4969 postpartum women found that those who reported using marijuana were more likely to smoke cigarettes, experience postpartum depressive symptoms, and breastfeed for less than 8 weeks.[37] Tobacco smoking is known to decrease the duration of breastfeeding, so the effect of marijuana is not clear. Most of the women who smoked marijuana postpartum also used it during pregnancy.

Among a group of 14 women who used cannabis postpartum by inhalation, lactose levels were higher in the milk of cannabis users compared to the milk of non-users. The milk of cannabis users had lower levels of sIgA relative to non-users; however, when adjusted for BMI, there was no difference in sIgA levels between the groups. Subjects who used both cannabis and cigarettes had lower carbohydrate levels and greater crude protein and true protein levels in their milk. Cannabis-using mothers reported lower levels of milk production in the first, second, fourth, and sixth weeks postpartum, compared to non-users.[3]

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Substance Identification

Substance Name

Cannabis

CAS Registry Number

8063-14-7

Drug Class

Breast Feeding

Lactation

Milk, Human

Cannabinoids

Street Drugs