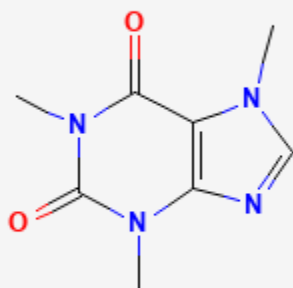




Caffeine

Revised: January 15, 2024.

CASRN: 58-08-2



Drug Levels and Effects

Summary of Use during Lactation

Caffeine appears in breastmilk rapidly after maternal ingestion. Insufficient high-quality data are available to make good evidence-based recommendations on safe maternal caffeine consumption.[1] Fussiness, jitteriness and poor sleep patterns have been reported in the infants of mothers with very high caffeine intakes equivalent to about 10 or more cups of coffee daily. Studies in mothers taking 5 cups of coffee daily found no stimulation in breastfed infants 3 weeks of age and older. A maternal intake limit of 300 to 500 mg daily might be a safe level of intake for most mothers, although European authorities set a likely safe level at 200 mg.[2-4] Maternal doses of caffeine greater than 130 mg daily may decrease weight gain in their exclusively breastfed infants, but this needs further confirmation.[5] However, preterm and younger newborn infants metabolize caffeine very slowly and may have serum levels of caffeine and other active caffeine metabolites similar to their mothers' levels, so a lower

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intake level preferable in the mothers of these infants.[2,6,7] Other sources of caffeine, such as cola and energy drinks, yerba mate or guarana, will have similar dose-related effects on the breastfed infant. Coffee intake of more than 450 mL daily may decrease breastmilk iron concentrations and result in mild iron deficiency anemia in some breastfed infants.[8]

Drug Levels

The half-life of caffeine in late pregnancy is much longer than in nonpregnant women; however, the maternal half-life returns to normal within the first week postpartum.[9] Smokers have more rapid clearance of caffeine and shorter half-lives than nonsmokers because smoking induces CYP1A2. Caffeine clearance is very low in preterm and newborn infants, but reaches adult values by 3 to 5 months of age.[6]

Maternal Levels. Caffeine appears in breastmilk with a peak usually occurring about 1 hour after a dose.[10-12] Most studies did not measure active metabolites in milk.

Five women who were 4 months to 1 year postpartum were given a dose of 150 mg of caffeine orally as caffeine sodium benzoate solution 2 hours after breakfast. Average caffeine levels at 30, 60 and 120 minutes after the dose were 1.6, 1.5, and 0.9 mg/L, respectively. One woman also received a 300 mg dose on a separate occasion and her milk caffeine levels were about double those after her 150 mg dose.[13]

Two nursing mothers who were 7 and 13 weeks postpartum ingested tablets containing a total of 128 mg of caffeine. Milk samples were taken over 12 and 48 hours in the 2 women, respectively. Peak milk levels of 1.3 and 1.6 mg/L occurred at 1.5 and 2 hours, respectively.[11]

A mother who drank 3 cups of coffee over a 1-hour period and then coffee at will throughout the day had milk caffeine concentrations ranging from 0.32 to 1.15 mg/L in 8 milk samples taken over a 10.5 hour period.[14]

Fifteen women ingested a caffeine-containing beverage of their choice (coffee or tea) containing caffeine in amounts ranging from 35 to 336 mg. Their breastfed infants ranged from 2 weeks to 9 months of age. Eleven of the women had caffeine detectable in their breastmilk with peak levels ranging from 2.1 to 7.2 mg/L. The 4 mothers with undetectable caffeine (<0.2 mg/L) had ingested less than 100 mg of caffeine. The mean half-life of caffeine in milk was 6.1 hours.[10]

Nine nursing mothers ingested 750 mg of caffeine (5 doses of 150 mg) in instant coffee daily for 5 days. Pooled 24-hour milk samples were collected on days 5 and 9 after no caffeine had been taken for 4 days. Caffeine concentration in the mothers' milk averaged 4.3 mg/L, ranging from undetectable (<0.25 mg/L) to 28.6 mg/L. By day 9, caffeine was undetectable in all milk samples. The authors estimated that at this caffeine intake, infants would receive 0.6 to 0.8 mg/kg daily.[15]

Eleven nursing mothers randomly consumed 5 cups of decaffeinated coffee or 5 cups of decaffeinated coffee with a total of 500 mg of added caffeine daily for 5 days in a randomized, double-blinded study. Their infants averaged 47 days (range 22 to 71 days) of age. During a 24-hour collection period on day 5, milk of the women who consumed caffeine contained an average of 3.1 mg/L, which amounted to an average of 2.4 mg or 0.5 mg/kg daily intake for the infants.[3]

Six women who were 3.5 to 17 weeks postpartum were given a single oral tablet of caffeine containing 100 mg of caffeine. Ten breastmilk samples from each breast were collected over the next 24 hours. The average peak milk levels from both breasts was 2.5 mg/L at 1 hour after the dose. Caffeine concentrations in milk from both breasts fell with an average half-life of 7.2 hours.[12] Using milk AUC data from 5 of the women, an exclusively breastfed infant would receive about 10% of the weight-adjusted maternal dose.

Five nursing mothers who were 6 to 28 weeks postpartum received a single dose of 200 mg of caffeine as tablets. Blood and milk samples were taken over the next 24 hours for measurement of caffeine and 3 active caffeine

metabolites, paraxanthine, theobromine, and theophylline. The peak caffeine levels in milk occurred at about 1 hour, but peak metabolite levels in milk occurred later at about 5 to 10 hours for paraxanthine and 10 to 15 hours for theobromine and theophylline. The authors estimated that an exclusively breastfed infant would receive a caffeine dose of 7% and a total xanthine dose of 18% of the maternal weight-adjusted dosage.[7]

After one mother consumed a cup of espresso containing 80 mg of caffeine, breastmilk caffeine concentration had a peak value of 2.05 ng/L two hours after the espresso. Caffeine was undetectable (< 0.01 ng/L) in breastmilk after 24 hours. The authors estimated that the woman's 2-month-old infant ingested 167 mL/kg of milk and 0.1 mg/kg of caffeine daily which was 8.9% of the mother's weight-adjusted dosage. The half-life of caffeine in breastmilk was 4 hours.[16]

Four mothers anonymously donated milk samples for analysis. Caffeine was found in their milk samples in concentrations of 33, 35, 988 and 1011 ng/gram of milk.[17]

A study of 100 women in Poland found a strong correlation between caffeine ingestion based on 3-day food frequency questionnaires and milk caffeine content. There was also a strong correlation between caffeine and its primary metabolite paraxanthine in milk. Theobromine, and to a lesser extent theophylline, were also found in milk. The highest amount of caffeine in milk was found in hindmilk after 4 weeks of lactation.[18]

Milk obtained from a mother 30 minutes after consuming 500 mL of Coca-Cola Zero contained 30 micromoles/L (5.8 mg/L) of caffeine.[19]

Infant Levels. Nine breastfed infants aged 14 days to 19 weeks of age had saliva caffeine levels measured after maternal ingestion of 1 cup of coffee. All but 2 were completely breastfed. Among the 7 fully breastfed infants, saliva caffeine levels ranged from 0.21 to 0.75 mg/L between 1 and 6 hours after the maternal ingestion of caffeine.[20]

Fifteen nursing mothers ingested a beverage containing caffeine in amounts ranging from 35 to 336 mg. Caffeine was not detected (<0.2 mg/L) in the urine of any of their infants over the 5-hour collection period that began 2 hours after the maternal caffeine intake.[10]

A 7-day-old breastfed infant's urine contained 1 mg/L of caffeine about 24 to 40 hours after his mother took a combination of butalbital 50 mg with acetaminophen 325 mg and caffeine 50 mg every 6 hours for 24 hours.[21]

Effects in Breastfed Infants

Jitteriness in a 6-week-old breastfed infant reported by a mother who claimed to drink 4 to 5 cups of coffee and 2 to 3 bottles (about 480 mL each) of cola daily as well as occasional tea and cocoa. Upon examination, the infant was gaining weight appropriately, but had trembling and increased muscle tone. The infant's symptoms decreased markedly 2 weeks after his mother stopped all caffeine-containing beverages.[22]

Restlessness and irritability were reported in a breastfed (extent not stated) 5-month-old infant whose mother drank 20 cups of coffee a day.[14]

A physician who reported drinking at least 5 mugs of coffee, 4 mugs of tea and 1 can of cola daily breastfed 2 infants. The first slept for only brief periods and woke easily. The second baby was fretful and jumpy and also had poor sleep patterns until his mother stopped her caffeine intake.[23]

Another physician who reportedly drank 1.7 to 2 liters of decaffeinated coffee daily had premature twins (age and extent of nursing not stated) who both seemed to be irritable, although the larger infant was partially supplemented with formula and seemed less affected. When her coffee consumption increased further, the smaller infant suffered convulsive-like episodes. All symptoms resolved 24 hours after coffee consumption ceased.[24]

Parents of a 24-day old infant reported restlessness and irritability in their breastfed infant whose mother reported drinking about 0.5 liters of mate every other day.[25]

Eleven nursing mothers randomly consumed 5 cups of decaffeinated coffee or 5 cups of decaffeinated coffee with 500 mg of added caffeine daily for 5 days in a randomized, double-blinded study. Their infants averaged 47 days (range 22 to 71 days) of age; the extent of nursing was not reported. At the end of each 5-day period, no effects of caffeine on sleep time and heart rate were found.[3]

A cohort study of mothers' caffeine intake and its effect on nighttime awakening asked mothers to provide their caffeine intake during pregnancy and lactation and their infant's sleep pattern infant at 3 months of age. Women who ingested more than 300 mg of caffeine daily reported slightly more nighttime awakenings in their infants than those who ingested less than 300 mg daily, but the difference was not statistically significant. The authors concluded that a limit of 300 mg of caffeine daily is reasonable.[26]

In a study of low-income nursing mothers in Costa Rica, subjects were divided into high-intake (over 450 mL daily) and nondrinkers of coffee. Infants of coffee drinkers had a lower birth weight, and decreased concentrations of maternal and infant hemoglobin and hematocrit at birth. Iron levels in breastmilk were also lower among coffee drinkers and their infants' hemoglobin and hematocrit values were lower at 1 month postpartum.[8]

A survey of 56 exclusively breastfeeding mothers found that caffeine consumption of up to 130 mg daily was related to increasing weight percentile (52.3%), while consumption of more than 130 mg daily was related to decreasing weight percentile (44.6%) of their infants. Length, head circumference and stool frequency were not influenced.[5]

Effects on Lactation and Breastmilk

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

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Substance Identification

Substance Name

Caffeine

CAS Registry Number

58-08-2

Drug Class

Breast Feeding

Lactation

Milk, Human

Central Nervous System Stimulants

Phosphodiesterase Inhibitors

Purinergic P1 Receptor Antagonists

Xanthines