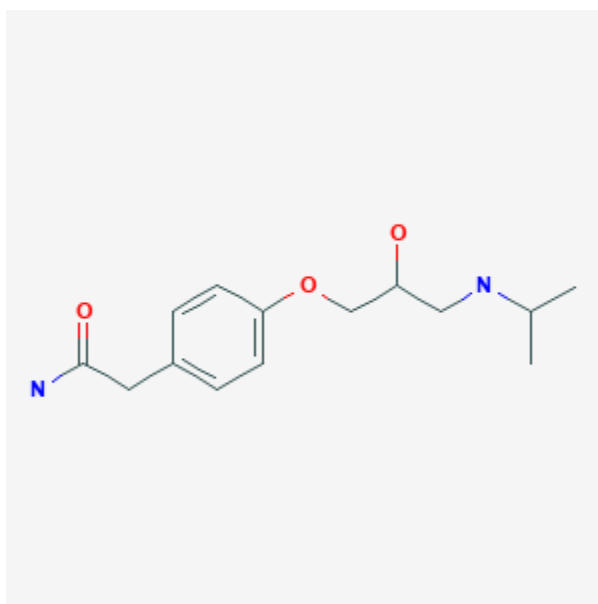




Atenolol

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CASRN: 29122-68-7



Drug Levels and Effects

Summary of Use during Lactation

Because of atenolol's relatively extensive excretion into breastmilk and its extensive renal excretion, other agents may be preferred while nursing a newborn or preterm infant or with high maternal dosages.[1][2] Infants older than 3 months of age appear to be at little risk of adverse effects from atenolol in breastmilk. Timing breastfeeding with respect to the time of the atenolol dose appears to be of little benefit in reducing infant atenolol exposure because the time of the peak is unpredictable.[3]

Drug Levels

The excretion of beta-adrenergic blocking drugs into breastmilk is largely determined by their protein binding. Those with low binding such as atenolol at 10% are more extensively excreted into breastmilk. Accumulation of

the drugs in the infant is related to the fraction excreted in urine. With 85% renal excretion, atenolol presents a high risk for accumulation in infants, especially neonates.

Maternal Levels. The time of the peak milk level of atenolol varied between 2 and 8 hours after the dose in 5 women.[4][5][6] In one woman a peak level of 1.6 mg/L occurred 4 hours after a single 50 mg dose.[5] After a single dose of 100 mg of atenolol in 4 women 4 to 12 days postpartum, peak milk levels ranged from 1.4 to 2.1 mg/L.[6] In 6 women taking atenolol 100 mg/day, two milk samples were taken in one day at unstated times after the dose. Milk levels ranged from 0.025 to 2.1 mg/L (average 0.7 mg/L).[7]

In a study of 5 early postpartum women, single milk levels taken 2 hours after a dose ranged from 0.38 to 1.04 mg/L (average 0.63 mg/L) with a dosage of 100 mg/day.[8] Because of the single early sample taken, these probably do not represent the peak milk levels in these women. Another woman taking atenolol 50 mg twice daily had an atenolol milk levels of 469 mcg/L 1.5 hours after a dose which probably does not represent the peak milk level.[9] It is estimated that a fully breastfed infant would receive between 5.7 and 19.2% of the maternal weight-adjusted dosage of atenolol.[10]

Nine women taking atenolol in dosages ranging between 25 and 200 mg daily (average not stated) in 2 divided doses had milk atenolol levels averaging 464 mcg/L at 2 hours after a dose. There was a 53% coefficient of variation in the levels measured, in part due to the wide range of dosages.[11]

Breastfeeding women taking oral atenolol for hypertension were studied during 3 time periods: 2-4 weeks postpartum, 3-4 months postpartum and 6-8 months postpartum. Seventeen women were evaluated at all time periods, 22 at the two earlier times, and 32 at 2-4 weeks postpartum. The excretion of atenolol into breastmilk decreased over time, with the average weight-adjusted percentages of maternal dosage of 9%, 5.1% and 3.2% at the 3 time periods, respectively. The highest percentages in individual infants were 34.8% at 2-4 weeks and 17.8% at 3-4 months of age. The absolute dose that breastfed infants received were proportional to the maternal dosage. Peak concentrations of atenolol in breastmilk occurred at an average of 4.4 hours after the dose, but in some individuals, the peak concentration occurred as late as 12 hours after the previous dose just before the next dose. [3]

Three nursing mothers who were 1 to 4.25 months postpartum and taking atenolol for hypertension each provided 8 milk samples over a 12- to 24-hour period. Their dosages were 100 mg each night, 25 mg twice daily and 25 mg daily. Peak milk concentrations occurred 4 hours after the dose in the women taking the drug once daily. Milk levels were relatively constant in the woman taking the drug twice daily. Average milk concentrations were 1.348 mg/L with 100 mg daily, 0.8 mg/L with 50 mg daily, and 0.35 mg/L with 25 mg daily. The weight-adjusted percentages of maternal dosage ranged from 14% to 18%.[12]

Infant Levels. After a single 50 mg maternal atenolol dose, the serum level in one 2-week-old infant was undetectable (<10 mcg/L) 4 hours after nursing when the milk concentration was 1.8 mg/L.[5] Another 2-week-old infant had serum levels of 0, 0 and 69 mcg/L just prior to nursing at three times: before, 2.25 hours and 6.25 hours after the maternal dose of atenolol 100 mg/day.[13][14]

One infant had undetectable (assay limits not stated) whole blood and plasma levels of atenolol at 3 and 8 days of age, respectively, with a maternal dose of 100 mg/day, although sampling times were not stated.[15] In 3 infants, atenolol serum levels ranged from undetectable (<27 mcg/L) to 116 mcg/L 4 and 8 hours after a 100 mg maternal dose of atenolol.[6]

In one 10-day-old infant with symptoms of beta-blockade, serum atenolol levels were 2 mg/L 48 hours after the last nursing and 0.14 mg/L 72 hours after nursing was discontinued. The infant's mother was taking atenolol 50 mg twice daily.[9]

Urine atenolol levels of 20, 30 and 435 mcg/L were found in 3 infants whose mothers were taking 100 mg/day.[7] [16] In another 8-day-old breastfed infant, a urine atenolol level of 440 mcg/L was measured during maternal use of atenolol 100 mg/day.[15]

Atenolol serum concentrations were below the lower limit of the assay (10 mcg/L) in 22 breastfed (extent not stated) infants aged 3 to 4 months whose mothers were taking atenolol in an average oral dosage of 49 mg daily. [3]

A 4.25-month-old infant was breastfed (extent not stated) by a mother who was taking atenolol 100 mg daily at bedtime. Simultaneous maternal and infant blood samples were obtained (time with respect to dose not stated). The infant's plasma level was 18.9% of the mother's plasma level.[12]

Effects in Breastfed Infants

A study of mothers taking beta-blockers during nursing found a numerically, but not statistically significant increased number of adverse reactions in those taking any beta-blocker. Although the ages of infants were matched to control infants, the ages of the affected infants were not stated. Of 13 mothers taking atenolol, one reported lethargy in her breastfed infant; she was also taking other unspecified drugs for hypertension.[17]

Cyanosis, bradycardia and hypothermia occurred in a 5-day-old infant probably because of atenolol in breastmilk. Her mother was taking atenolol 50 mg twice daily. Symptoms continued until day 8 when breastfeeding was discontinued.[9]

No difference between resting and crying heart rates were observed in 22 breastfed (extent not stated) infants aged 3 to 4 months whose mothers were taking atenolol in an average oral dosage of 49 mg daily. This finding indicated that the infants were experiencing no beta-adrenergic blockade from atenolol in breastmilk.[3]

Other authors have reported 15 infants aged 3 days to 2 weeks exposed to atenolol in breastmilk with no signs of adverse effects. Maternal dosages were 50 or 100 mg daily.[5][6][7][13][15][16][18]

Effects on Lactation and Breastmilk

One unusual case of oligomenorrhea, hyperprolactinemia and galactorrhea was reported in a 38-year-old woman who had been taking atenolol for about 18 months. Prolactin values returned to normal within 3 days of discontinuation of atenolol. Galactorrhea slowly lessened and disappeared one month after atenolol discontinuation.[19]

Alternate Drugs to Consider

Propranolol, Labetalol, Metoprolol

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Substance Identification

Substance Name

Atenolol

CAS Registry Number

29122-68-7

Drug Class

Breast Feeding

Lactation

Antihypertensive Agents

Adrenergic Beta-Antagonists

Antiarrhythmics