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Zidovudine

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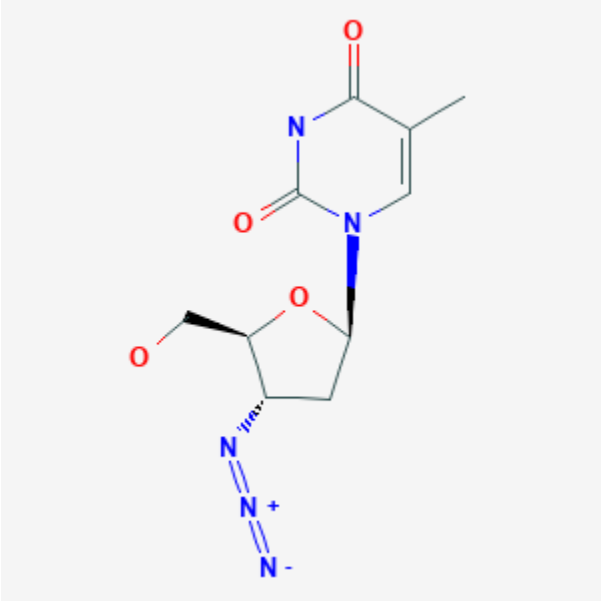

Drug Levels and Effects

Summary of Use during Lactation

In the United States and other developed countries, HIV-infected mothers should generally not breastfeed their infants. Zidovudine has been well studied during breastfeeding. In countries in which no acceptable, feasible, sustainable and safe replacement feeding is available, World Health Organization guidelines recommend that all women with an HIV infection who are pregnant or breastfeeding should be maintained on antiretroviral therapy for at least the duration of risk for mother-to-child transmission. Mothers should exclusively breastfeed their infants for the first 6 months of life; breastfeeding with complementary feeding should continue through at least 12 months of life up to 24 months of life.[1] The first choice regimen for nursing mothers is tenofovir, efavirenz and either lamivudine or emtricitabine. If these drugs are unavailable, alternative regimens include: 1) zidovudine, lamivudine and efavirenz; 2) zidovudine, lamivudine and nevirapine; or 3) tenofovir, nevirapine and either lamivudine or emtricitabine. Exclusively breastfed infants should also receive 6 weeks of prophylaxis with

nevirapine.[2][3] Breastfed infants whose mothers receive a highly active antiretroviral (HAART) regimen containing zidovudine have higher rates of neutropenia during the first month and severe anemia during the first 6 months of life.

Drug Levels

Maternal Levels. Six women were given a single oral dose of 200 mg of zidovudine. Milk samples were collected 1, 2, 4 and 6 hours after the dose. The peak milk concentration occurred 1 to 2 hours after the dose in 4 women and occurred 1 hour later in the others. The average peak milk concentration was 857 mcg/L (range 472 to 1043 mcg/L).[4]

Eighteen women who were receiving oral zidovudine 300 mg twice daily as part of a combination antiretroviral regimen had their milk analyzed at either 2 or 5 months postpartum. Milk samples were provided at a median of 4 hours (range 1 to 8.5 hours) after the last dose. The median zidovudine concentration in breastmilk was 207 mcg/L.[5]

Forty women were given postpartum prophylaxis with unstated dosages of lamivudine, nevirapine and zidovudine (or stavudine if the hemoglobin <8 g/dL). Blood and milk samples were collected once during the first 3 days postpartum and once at 7 days postpartum. The median times after a dose that samples were collected were 5.3 hours (range 0 to 99 hours) for the first sample and 6 hours (range 4.3 to 20 hours) for the 7-day sample. Average breastmilk zidovudine concentrations were calculated only for samples that had detectable (>20 mcg/L) concentrations of zidovudine. The mean breastmilk concentrations were 130 (n = 11) and 150 mcg/L (n = 13), respectively, at the two sampling times, which was equal to the simultaneous maternal serum concentrations.[6]

Fifty-eight mothers who were taking a combination regimen of lamivudine, nevirapine and zidovudine had their serum and breastmilk analyzed for the presence of these drugs. Mothers took zidovudine 200 mg twice daily starting at 34 to 36 weeks postpartum and continuing until 6 months postpartum. Breastmilk was collected within 24 hours after delivery and at 2, 6, 14 and 24 weeks postpartum at variable times after the previous dose. The median breastmilk zidovudine concentration in 35 selected samples across all visits was 9 mcg/L.[7]

Thirty-eight mothers who were receiving zidovudine 300 mg twice daily as part of a combination antiretroviral regimen provided a total of 114 milk samples at birth, 1 month, 3 months and/or 6 months postpartum. Milk samples were collected at a median of 4.5 hours (range 3.5 to 6 hours) after the previous dose. The median breastmilk zidovudine concentration was 33 mcg/L (range 5 to 117 mcg/L).[8]

Fifteen women had been taking zidovudine 300 mg twice daily for 53 to 182 days as part of a drug combination that included ritonavir, zidovudine, and lamivudine. Breastmilk samples were collected at just before a dose at a median of 1 month postpartum. Whole breastmilk levels contained a median of 7 mcg/L of zidovudine.[9]

Thirty women were studied at 6, 12 or 24 weeks postpartum (10 at each time). Each mother was taking zidovudine 300 mg, lamivudine 150 mg, lopinavir 400 mg, and ritonavir 100 mg twice daily by mouth starting at delivery. On the study day, at a median of 14.9 hours after the previous evening's dose, maternal plasma and breastmilk samples were obtained prior to the morning dose and 2, 4 and 6 hours after the dose. Ninety-eight of the 121 breastmilk samples contained detectable quantities (10 mcg/L or greater) of zidovudine, with a median breastmilk concentration of 0.2 mg/L over the 6 hours.[10]

Nine HIV-positive women about to undergo cesarean section received 3 doses of lopinavir 200 mg, ritonavir 150 mg, zidovudine 300 mg, lamivudine 50 mg at 3 hour intervals before the procedure. Breastmilk samples were collected at a mean of 25 hours postpartum. The average milk concentration of zidovudine was 101mcg/L (range 20 to 448 mcg/L).[11]

Infant Levels. Eighteen nursing mothers were receiving oral zidovudine 300 mg twice daily as part of a combination antiretroviral regimen. Their infants had serum concentrations determined at either 2 or 5 months postpartum. Serum samples were provided at a median of 4 hours (range 1 to 8.5 hours) after the last dose. The infants were also receiving oral zidovudine 4 or 6 mg/kg 3 times daily, depending on their age. The median infant serum zidovudine concentration was 123 mcg/L (range 14 to 3302 mcg/L). The average value was 25 times the IC50 for HIV.[5]

Fifty-eight infants whose mothers were taking a combination regimen of lamivudine, nevirapine and zidovudine had their serum analyzed for the presence of these drugs. Mothers took zidovudine 200 mg twice daily starting at 34 to 36 weeks postpartum and continuing until 6 months postpartum and were instructed to exclusively breastfeed for 5.5 months. Serum samples were collected within 24 hours after delivery and at 2, 6, 14 and 24 weeks postpartum. Median serum concentration of 16 selected dried blood spot samples was 24 mcg/L. At later times postpartum, zidovudine was not detectable (<30 mcg/L) in 66 infant dried blood spots.[7]

Breastfed infants of 38 mothers who were receiving zidovudine 300 mg twice daily as part of a combination antiretroviral regimen had a total of 34 blood samples analyzed at 1 month, 3 months and/or 6 months postpartum. Samples were collected at a median of 4.5 hours (range 3.5 to 6 hours) after the previous maternal dose and a median of 30 minutes (range 20 to 60 minutes) after the previous nursing. The infants' zidovudine plasma concentrations ranged from 0 to 2.5 mcg/L, which was a median of 2% (range 0 to 5%) of the maternal serum concentration.[8]

Thirty-three infants were breastfed either partially or exclusively by their mothers who had been taking zidovudine 300 mg twice daily as part of a drug combination. Infant blood was collected at a median of 1 month postpartum for 24 infants and at 3 months postpartum for 9 infants at various times after the last dose and a median of 1 hour (range 6 minutes to 35 hours) after the last breastfeeding. None of the infants had detectable zidovudine levels in their serum (<45 mcg/L).[9]

Thirty nursing mothers were studied at 6, 12 or 24 weeks postpartum (10 at each time). Each mother was taking zidovudine 300 mg twice daily by mouth starting at delivery. Infant plasma samples were obtained before their mother's first dose and at 2, 4 and 6 hours after the mother's dose. Infants were allowed to breastfeed *ad libitum* during the study period. Zidovudine was undetectable (<10 mcg/L) in all of the 115 infant plasma samples.[10]

Effects in Breastfed Infants

A study assigned pregnant women to zidovudine alone or highly-active antiretroviral therapy (HAART: zidovudine, lamivudine and nevirapine) to prevent maternal-to-child transmission of HIV infection. After delivery, All infants received one month of zidovudine prophylaxis; some infants were breastfed and others were formula fed. A higher percentage of infants in the HAART-exposed group had neutropenia than those in the unexposed group at 1 month of age (15.9 and 3.7%, respectively). Hematologic toxicity was transient and asymptomatic. From 2 to 6 months postpartum, no differences in hematologic toxicity were seen between breastfed and formula-fed infants. No statistical difference in hepatic toxicity was seen between the breastfed and formula-fed infants.[12]

A study compared the rates of severe anemia in 3 groups of infants who received postpartum prophylaxis with zidovudine for prevention of maternal-to-child transmission of HIV infection. Through 6 months of age, breastfed infants whose mothers received HAART had a higher rate of severe anemia (7.4%) than breastfed infants whose mothers received only zidovudine (5.3%). Formula-fed infants had the lowest rate of severe anemia (2.5%). The anemia generally responded well to iron and multivitamin supplementation, and discontinuation of zidovudine.[13]

Effects on Lactation and Breastmilk

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

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Substance Identification

Substance Name

Zidovudine

CAS Registry Number

30516-87-1

Drug Class

Breast Feeding

Lactation

Anti-Infective Agents

Anti-HIV Agents

Antiviral Agents

Anti-Retroviral Agents

Reverse Transcriptase Inhibitors