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Infliximab

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Drug Levels and Effects

Summary of Use during Lactation

Infliximab is usually either not detectable in breastmilk or detectable at very low levels in milk. Absorption of the drug from milk by the infant is minimal. Follow-up of infants exposed in utero and breastfed during maternal infliximab therapy have found no adverse effects and normal development. The measurement of minute concentrations in the milk of some women raises the possibility of local immune suppression in the gastrointestinal tract, but levels were not high enough to be of concern for systemic immunosuppression.[1] In mothers who received infliximab during pregnancy, continued use while breastfeeding does not prolong infliximab elimination by the infant.[2] Numerous experts and professional guidelines have stated that the drug is a low risk to the nursing infant and acceptable to use during breastfeeding.[3-13] Waiting for at least 2 weeks postpartum to resume therapy may minimize transfer to the infant.[14]

Drug Levels

Maternal Levels. A nursing mother with Crohn's disease (time postpartum not stated) was given a single 5 mg/kg dose of infliximab by intravenous infusion. Milk samples taken 24 hours and 1 week after the dose had undetectable (<60 mcg/L) levels of infliximab.[15]

A woman who was 4 months postpartum received 2 doses of infliximab. Milk levels were measured after the first dose of 160 mg and second dose of 165 mg, but the time between the 2 doses was not stated. The first milk sample was obtained 10 days after the first dose. Milk infliximab levels increased gradually (values not stated) over the next 10 days. After the second dose, milk infliximab levels increased further, with the highest infliximab concentration of 473 mcg/L measured one day after the second dose.[16]

A woman with Crohn's disease received infliximab 10 mg/kg at 2 and 10 weeks postpartum. Infliximab was not detectable in breastmilk with an ELISA assay (assay sensitivity not specified) at 6, 10 or 13 weeks postpartum.[17]

A woman with severe Crohn's disease received infliximab 1000 mg (10 mg/kg) intravenously every 4 weeks during pregnancy and lactation. She received a dose on an unstated day postpartum, then breastmilk samples were collected daily (times not stated) once before and daily for 30 days after the dose. None of the samples had detectable infliximab (<5 mcg/L) using an ELISA assay.[18]

Three women with Crohn's disease received infliximab during pregnancy and postpartum. Single breastmilk samples were obtained from each woman after a postpartum dose of 5 mg/kg of infliximab. Samples were collected 7, 5, and 43 days, respectively, after their prior dose. Infliximab was undetectable (<100 mcg/L) in all breastmilk samples.[19]

Three women with Crohn's disease received an intravenous infusion of infliximab 5 mg/kg postpartum for a disease flare and discontinued nursing. Milk samples were obtained before and after the infusion. Milk samples were also obtained from 8 nursing mothers who did not receive infliximab. Infliximab was undetectable (<10 mcg/L) in all of the pre-infusion samples and in those from the untreated mothers. Infliximab was detected in breastmilk samples obtained after the infusion in all 3 women. Infliximab was detectable 12 hours after the infusion and peaked at 75 to 105 mcg/L at 2 to 3 days after the infusion in 2 patients. In a third, one sample obtained 2 days after the infusion was about 20 mcg/L. The assay used in this series was more sensitive than those used previously and allowed the very low infliximab concentrations to be measured.[1]

Two mothers received infliximab 300 mg intravenously for inflammatory bowel disease. Breastmilk infliximab was 200 mcg/L in one mother (time after dose not stated), which was about 4.3% of her serum concentration. The second mother began infliximab at 3 months postpartum. Her breastmilk infliximab levels were 94.6 mcg/L on day 1 after the first dose and 119.7 mcg/L on day 4 after the dose.[20]

Three women with inflammatory bowel disease who received postpartum infliximab infusions (doses not specified) had milk samples analyzed for the drug for 5 days after the infusion. The assay method was somewhat unreliable in this study. In the first patient, infliximab was detectable in breastmilk only on days 4 and 6 after the infusion, with values of about 100 mcg/L. After the second infusion, the highest milk concentration of about 130 mcg/L occurred after about 30 hours. Subsequent levels were lower over the next 5 days. In a second patient, infliximab was found in milk shortly after the infusion with the highest concentration of 300 mcg/L occurring at 3.3 days after the dose. A third patient had detectable infliximab in milk on days 2 and 4, with the highest level of about 100 mcg/L on day 4.[21]

In a multi-center study of women with inflammatory bowel disease in pregnancy (the PIANO registry), 29 women receiving infliximab provided milk samples at 1, 12, 24, and 48 hours after drug administration. Some also provided samples at 72, 96, 120, and 168 hours after drug administration. Nineteen of the women had detectable (>0.01 mg/L) infliximab levels in milk. Peak concentrations in breastmilk ranged from 0.15 to 0.74 mg/L and occurred at 24 to 48 hours after the dose. Seventeen women had detectable milk levels at 48 hours with a mean concentration of 0.2 mg/L and 5 of 8 women who submitted a 168 hour sample had detectable infliximab in milk.[22]

Infant Levels. A woman with Crohn's disease received infliximab during pregnancy, with the last of five 10 mg/kg doses 2 weeks before delivery. Doses were also given 2 and 10 weeks postpartum. She breastfed her infant from birth to 6 weeks, discontinued breastfeeding for 3 weeks and then restarted breastfeeding (extent not stated) at week 11 postpartum. Maternal and infant serum infliximab levels were equal when they were first measured at 6 weeks postpartum. The infant's serum infliximab steadily decreased over the next 7 weeks. The authors concluded that the initial high infant serum level was from transplacental passage of infliximab because the drug was undetectable in milk and the serum level dropped despite breastfeeding.[17]

Two infants were breastfed (extent not stated) by mothers who received 5 mg/kg doses of infliximab during pregnancy and breastfeeding. Infliximab was discontinued at or before 32 weeks of the pregnancy and restarted within 2 weeks postpartum. Infant serum samples were obtained 5 days after the mother's previous infliximab

dose in one when the infant was 15 days old and 43 days after the mother's dose at 57 days of age in the other infant. Infliximab was undetectable (<100 mcg/L) in both infants' serum.[19]

Two mothers received infliximab 300 mg intravenously for inflammatory bowel disease. The infant of the first woman had an undetectable serum infliximab level 3 weeks after the last dose of infliximab at 34 weeks postpartum. The second woman exclusively breastfed her infant for 3 months, then received a single intravenous dose of infliximab 300 mg and began partially breastfeeding her infant. Four weeks after beginning infliximab and 5 days after the second infliximab dose, her infant had a serum concentration of 1.7 mcg/L, which was 2.2% of the simultaneous maternal serum infliximab concentration.[20]

An infant was born at week 37 of gestation to a mother with ulcerative colitis was receiving long-term therapy with mesalamine 4 grams daily throughout pregnancy received inductions series of infliximab 5 mg/kg in weeks 20 and 31 of pregnancy for disease flares. She continued to receive infliximab infusions every 8 to 12 weeks, while the baby was breastfed (extent not stated) until 14 weeks of age. The infant's infliximab serum concentration at 16 weeks after birth was 0.6 mg/L, but was undetectable (<0.05mg/L) at 28 weeks of age. The serum concentration at 16 weeks was judged to have been a result of placental passage of the drug from mother to infant.[23]

A woman receiving infliximab (dosage not stated) every 7 weeks for Crohn's disease became pregnant and infliximab was continued until week 25 of pregnancy. Upon cesarean section delivery at week 37, her serum infliximab concentration was 1.41 mg/L. She partially breastfed her dizygotic twins for 6 weeks. Serial serum samples of the infants were taken at delivery and 3, 6, 9, 12, and 15 months of age. The male infant had serum infliximab levels of 3.06, 1.52, 0.2, 0.06, 0.03 mg/L, and undetectable at these times. The female infant had serum infliximab levels of 2.46, 0.52, 0.21, 0.11 and 0.03 mg/L, and undetectable at these times.[24]

A woman was treated for psoriatic arthritis with infliximab 6 mg/kg every 4 weeks from week 18 to week 26 of pregnancy when it was stopped. She delivered a healthy infant and resumed infliximab at 5 weeks postpartum at 6 mg/kg every 4 weeks initially, increasing to every 8 weeks over a year. The infant serum infliximab concentration was 4.46 mg/L at 24 days of age before infliximab was resumed, 0.19 mg/L at 155 days of age and undetectable (detection limit not stated) at 278 days of age. The extent of breastfeeding and exact days of drug administration relative to infant serum concentrations were not reported.[25]

A woman was treated for psoriasis with infliximab 6 mg/kg every 8 weeks until she was 26 weeks pregnant. Her infant was born at week 38 by cesarean section. She restarted infliximab at 5 weeks postpartum, and received it every 4 weeks for one year while breastfeeding her infant (extent not stated). The infant's serum infliximab concentration was 4.46 mg/L at 24 days of age, 0.19 mg/L at 155 days of age, and below the limit of detection (not stated) at 278 days of age.[26]

Effects in Breastfed Infants

A retrospective chart review of patients who received infliximab during pregnancy found that 5 mothers breastfed their infants during infliximab therapy at a dose of 5 mg/kg. No other patient details were reported and no adverse effects were reported in the infants, although observation during breastfeeding was not the purpose of the study.[27]

A woman with Crohn's disease received infliximab 5 mg/kg intravenously every 8 weeks throughout pregnancy and during lactation. The infant was reported to be good condition without any evidence of illnesses.[28]

An infant was born to a mother who received infliximab 10 mg/kg 5 times during pregnancy at 6- to 8-week intervals. A maternal dose of 10 mg/kg was given at 2 weeks postpartum. The infant was breastfed for 6 weeks, discontinued for 3 weeks and then reinstated at 9 weeks of age (extent of nursing not stated). Another 10 mg/kg dose was given to the mother at 10 weeks postpartum. The infant underwent a formal evaluation of the immune

system and found to have normal immune markers and responses. The infant reportedly grew and developed normally throughout the first year of life.[17]

An infant was breastfed (extent not stated) for up to 4 months by a mother who was taking infliximab (dosage not stated) and azathioprine 150 mg daily for inflammatory bowel diseases. The infant was followed regularly for 22 months of age and found to have a normal growth rate, and no history of recurrent infections.[29]

A woman with severe Crohn's disease received infliximab 1000 mg (10 mg/kg) intravenously every 4 weeks during pregnancy and lactation. The extent and duration of breastfeeding were not reported. The child had no developmental abnormalities noted at 27 months of age.[18]

Three infants were breastfed (extent not stated) during maternal infliximab therapy at a dose of 5 mg/kg every 8 weeks. Infants were followed for almost 1 year and found to have no unusual number or types of infections and all seroconverted after their routine childhood immunizations.[19]

A 24-year-old woman with Crohn's disease received infliximab 5 mg/kg every 8 weeks during pregnancy until 33 weeks gestation. After delivering at term, she received her next infliximab dose at 1 week postpartum. The infant was breastfed (extent not stated) and received all vaccinations, except rotavirus, on schedule.[30]

A woman with severe psoriasis was treated during pregnancy and postpartum with infliximab 5 mg/kg intravenously every 8 weeks. Her last doses of infliximab before delivery were at weeks 20 and 29 of pregnancy. The drug was continued postpartum, although the timing of the first postpartum dose was not stated. Her infant was breastfed for 1 month and developed normally.[31]

A woman with Crohn's disease used infliximab 5 mg/kg every 8 weeks during pregnancy and postpartum. During breastfeeding (extent not stated) she also received sulfasalazine 4 g/day and prednisone 60 mg/day in a tapering schedule. At 6 months of age, the infant was asymptomatic with regular weight gain.[32]

Two women received infliximab 300 mg intravenously for treatment of inflammatory bowel disease. One woman nursed her infant (extent not stated) and the other began partial breastfeeding her infant at 3 months of age when infliximab was begun. She breastfed for approximately 5 weeks (2 doses) before discontinuing breastfeeding. At 22 and 18 months of age, respectively, neither infant had any signs of adverse drug reactions, allergic reactions or severe infections leading to hospitalization. The first infant had a low birth weight, but caught up and reached the 75th percentile at the age of 11 months. Developmental milestones were reached on time by both infants.[20]

A woman with ulcerative colitis was receiving long-term therapy with mesalamine 4 grams daily throughout pregnancy received inductions series of infliximab 5 mg/kg in weeks 20 and 31 of pregnancy for disease flares. She continued to receive infliximab infusions every 8 to 12 weeks, while the baby was breastfed (extent not stated) until 14 weeks of age. The infant received routine vaccinations (diphtheria, tetanus, pertussis, injectable polio, Haemophilus influenzae b, and pneumococcal vaccines) at 3, 5 and 12 months with no signs of adverse effects from them, or signs of allergic or infectious diseases. Development at 13 months of age was normal.[23]

A woman receiving infliximab (dosage not stated) every 7 weeks for Crohn's disease became pregnant and infliximab was continued until week 25 of pregnancy. She partially breastfed her dizygotic twins for 6 weeks. Her infants had detectable serum infliximab levels until 12 months of age. The boy developed normally. The girl was diagnosed with a non-significant atrial septal defect at the age of 6 weeks. At the age of 18 months, she was admitted to hospital due to asthmatic bronchitis. She was seen as an outpatient at the pediatric department due to late gross motor function development, but her monitoring was terminated at the age of 20 months due to normal development.[24]

Three women receiving infliximab for severe psoriasis breastfed 4 infants (2 pregnancies in 1 woman). No adverse effects were reported in the infants, although the dosage of infliximab and the extent of breastfeeding were not reported.[33]

In a multi-center study of women with inflammatory bowel disease in pregnancy (the PIANO registry), 168 women received infliximab while breastfeeding their infants. Among those who received infliximab or another biologic agent while breastfeeding, infant growth, development or infection rate was no different from infants whose mothers received no treatment. An additional 68 women received a biologic agent plus a thiopurine. Infant outcomes were similar in this group.[22]

A woman treated with psoriatic arthritis with infliximab 6 mg/kg every 4 weeks from week 18 to week 26 of pregnancy when it was stopped. She delivered a healthy infant and resumed infliximab at 5 weeks postpartum. Her infant was breastfed (extent not stated) and did not develop any sever infections over the first 278 days of life.[25]

Effects on Lactation and Breastmilk

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

Alternate Drugs to Consider

(Inflammatory Bowel Disease) Adalimumab, Certolizumab Pegol; (Psoriasis) Adalimumab, Etanercept, Phototherapy, Tretinoin; (Rheumatoid Arthritis) Adalimumab, Certolizumab Pegol, Etanercept, Tocilizumab

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Substance Identification

Substance Name

Infliximab

CAS Registry Number

170277-31-3

Drug Class

Breast Feeding

Lactation

Milk, Human

Antibodies, Monoclonal

Antirheumatic Agents

Dermatologic Agents

Gastrointestinal Agents

Tumor Necrosis Factor Inhibitors