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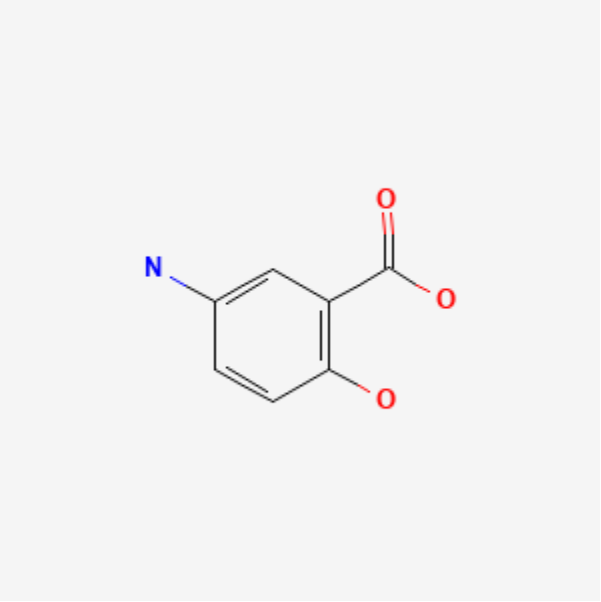
NLM Citation: Drugs and Lactation Database (LactMed®) [Internet]. Bethesda (MD): National Institute of Child Health and Human Development; 2006-. Mesalamine. [Updated 2024 Feb 15].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Mesalamine

Revised: February 15, 2024.

CASRN: 89-57-6



Drug Levels and Effects

Summary of Use during Lactation

Mesalamine is poorly excreted into breastmilk. However, rather high levels of the mesalamine metabolite N-acetyl-5-ASA appear in breastmilk and its effects on breastfed infants are unknown. A few cases of diarrhea have been reported in infants exposed to mesalamine, although the rate is not high. Most experts consider mesalamine derivatives to be safe during breastfeeding.[1-6] If mesalamine is required by the mother, it is not a reason to discontinue breastfeeding, but carefully observe breastfed infants for diarrhea during maternal use of mesalamine.

Drug Levels

Mesalamine (5-aminosalicylic acid; 5-ASA) is metabolized to N-acetyl-5-ASA, which is inactive in treating inflammatory bowel disease, but the metabolite's possible effects on the breastfed infant are unknown.

Maternal Levels. One woman with ulcerative colitis (time postpartum not stated) was taking delayed-release tablets of mesalamine (Claversal) 500 mg orally 3 times daily. A single milk sample taken 5.25 hours after a dose contained 0.11 mg/L of mesalamine and 12.4 mg/L of N-acetyl-5-ASA.[7]

A woman with inactive ulcerative colitis was taking mesalamine (product not specified) 1 gram orally 3 times daily. A milk sample taken 1 week postpartum at 5 hours after a dose contained mesalamine 0.1 mg/L and N-acetyl-5-ASA 18.1 mg/L. Another milk sample taken 4 days later at 5 hours after a dose contained mesalamine 0.1 mg/L and N-acetyl-5-ASA 12.3 mg/L. The authors also report another mother taking 1 g of mesalamine daily (product not specified) who had a milk level of mesalamine that was undetectable and N-acetyl-5-ASA level of 2.2 mg/L (time of sampling and assay method not reported). The authors estimated that a fully breastfed infant whose mother was taking 1.5 grams of mesalamine daily would receive 0.015 mg/kg of mesalamine and 2.3 mg/kg of N-acetyl-5-ASA daily.[8]

Twelve women taking mesalamine in various oral dosage forms and one taking olsalazine capsules collected 1 to 8 breastmilk samples over one day at 2 to 4 weeks postpartum. Mesalamine was undetectable (< 20 mcg/L) in most women, but detected in the milk of 3 women; one was taking Pentasa tablets 1 gram 3 times daily and one was taking Pentasa suppositories 1 gram at night and one was taking oral Asacol 400 mg twice daily plus Mesalal tablets 500 mg at night. Mesalamine milk levels ranged from 20 to 81 mcg/L. N-acetyl-5-ASA was detected in all milk samples, but there was no clear relationship between the dosages, times of the doses and the peak time in breastmilk. The individual average N-acetyl-5-ASA milk levels by product and dosage were Asacol tablets 800 mg daily, 0.24 mg/L (1 patient); Asacol tablets 800 mg daily plus Mesalal tablets 500 mg at night, 2.6 mg/L (1 patient); Mesalal tablets 500 mg daily, 0.75 mg/L (1 patient); Pentasa tablets 500 mg daily, 0.97 mg/L (1 patient); Pentasa tablets 1.5 grams daily, 2.8 to 6.5 mg/L (5 patients); Pentasa tablets 2 grams daily, 10.5 mg/L (1 patient); Pentasa tablets 3 grams daily, 10.2 mg/L (1 patient); Pentasa suppositories 1 gram daily, 1.9 mg/L (1 patient). Using the highest individual measured of 16.2 mg/L, the authors estimated that a fully breastfed infant would receive about 15 mg of N-acetyl-5-ASA daily, which is 1% of the usual daily dosage (not weight-adjusted) of mesalamine.[9]

Four women with inflammatory bowel disease who were breastfeeding during mesalamine use had breastmilk samples taken. Specific dosages and mesalamine products were not reported nor were sampling times with respect to the doses. Mesalamine milk levels ranged from 4 to 40 mcg/L and N-acetyl-5-ASA milk levels ranged from 5 to 14.9 mg/L. The authors calculated a daily dosage of mesalamine of 0.6 to 6 mcg/kg daily in an exclusively breastfed infant. However, the N-acetyl-5-ASA dosage would be about 1000 times greater. The authors speculated that mesalamine might be metabolized in the breast to N-acetyl-5-ASA in the breast tissue, but provided no direct evidence of this happening.[10]

Ten exclusively nursing mothers who were receiving long-term treatment for inflammatory bowel disease with a delayed-release form of mesalamine (2 Asacol HD, 8 Lialda) provided milk samples at 0, 1, 2, 4, 8, 12, and 24 hours after a dose. The women were 35 to 251 days postpartum and their once-daily doses ranged from 1.2 to 4.8 grams. Milk mesalamine levels were highly variable among the participants and the N-acetyl-5-ASA metabolite was not measured. The average infant dosage was 15.7 mcg/kg daily (range 1.8 to 76.8 mcg/kg daily) and the mean percentage of weight-adjusted maternal dose was 0.02% (range 0.01 to 0.085%).[11]

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

Effects in Breastfed Infants

A 6-week-old breastfed infant developed watery diarrhea 12 hours after the first maternal dose of mesalamine rectal suppositories 500 mg twice daily. The drug was stopped and reintroduced 4 times and each time the infant's diarrhea began 8 to 12 hours after the drug was started and ceased 8 to 12 hours after the drug was stopped. The infant's diarrhea was probably caused by mesalamine or it metabolite in breastmilk.[12]

A 4-month-old breastfed infant developed thrombosis of the superior sagittal sinus following severe thrombocytosis. The infant's mother was receiving oral mesalamine in dosages averaging 1 to 1.5 grams daily throughout pregnancy and lactation. Breastfeeding had been stopped abruptly 1 week prior to the thrombotic event. The authors ruled out other causes of thrombosis and hypothesized that the abrupt discontinuation of long-term mesalamine exposure caused the thrombocytosis and thrombosis in the infant. They rated the reaction as possibly caused by the drug.[13]

In a prospective telephone follow-up study, 8 nursing mothers reported taking mesalamine (dosage and route unspecified). One mother reported diarrhea in her infant. No other adverse reactions were reported in the infants by their mothers.[14]

A case-control study compared the infants of mothers taking mesalamine (n = 117; average dose, 2065 mg daily), olsalazine (n = 2) or sulfasalazine (n = 2) to infants of matched control mothers (n = 121) who were exposed to no treatment known to be harmful to a breastfed infant. Infants were exposed to mesalamine through milk for a mean of 5.3 months (range: 3 days-24 months). Infants were breastfed for an average of about 7.4 months and were followed up at an average age of about 22 months. No difference in the frequency or characteristics of maternally reported adverse events were found between exposed and control infants.[15,16]

Two women who developed inflammatory bowel disease were treated with mesalamine during pregnancy and postpartum. They breastfed their infants (extent not stated), one for 2 months and one for 10 months. Their breastfed infants had normal growth and development after 1 year of follow-up.[17]

Effects on Lactation and Breastmilk

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

Alternate Drugs to Consider

(Inflammatory Bowel Disease) Adalimumab, Azathioprine, Budesonide, Certolizumab Pegol, Infliximab, Mesalamine, Olsalazine, Prednisone, Sulfasalazine

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Substance Identification

Substance Name

Mesalamine

CAS Registry Number

89-57-6

Drug Class

Breast Feeding

Lactation

Milk, Human

Gastrointestinal Agents

Anti-Inflammatory Agents, Non-Steroidal