Use of ciprofloxacin during breastfeeding

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Abstract

Question My patient has a urinary tract infection and is currently breastfeeding her 9-week-old son. I would like to prescribe her ciprofloxacin. Should I be concerned about osteoarticular toxicity in the infant?

Answer Although there are concerns about the possible risk of osteoarticular toxicity with ciprofloxacin, the amounts excreted into breast milk are low and studies report no substantial increase in osteoarticular toxicity even with the systemic use of ciprofloxacin in neonates and children. Therefore, interrupting breastfeeding during ciprofloxacin treatment appears unnecessary.

La ciprofloxacine durant l'allaitement

Résumé

Question Ma patiente a une infection urinaire et elle allaite actuellement son fils de 9 semaines. J'aimerais lui prescrire de la ciprofloxacine. Devrais-je m'inquiéter au sujet de la toxicité ostéoarticulaire chez le nouveau-né?

Réponse Même s'il existe des préoccupations entourant le risque possible de toxicité ostéoarticulaire avec la ciprofloxacine, les quantités excrétées dans le lait maternel sont faibles et les études ne signalent aucune augmentation substantielle de la toxicité ostéoarticulaire même avec l'utilisation systémique de la ciprofloxacine chez les nouveau-nés et les enfants. Par conséquent, il ne semble pas nécessaire d'interrompre l'allaitement durant un traitement avec de la ciprofloxacine.

Urinary tract infections (UTIs) occur in 3% of women in the postpartum period.[1,2] Ciprofloxacin is a second-generation, broad-spectrum fluoroquinolone antibiotic with bactericidal activity against Gram-positive and Gram-negative organisms, including those resistant to penicillins, cephalosporins, and aminoglycosides.[3] Fluoroquinolones interfere with supercoiling of DNA and, therefore, with transcription, by inhibiting the bacterial enzyme DNA gyrase.[4]

The bioavailability of ciprofloxacin is approximately 70%. It is widely distributed to tissues after oral administration, where it often reaches higher concentrations than in plasma. It is partly metabolized in the liver and excreted as the unchanged drug in the urine to an extent of 40% to 50%, where active tubular secretion also has an important role.[5] The spectrum of activity and its high urine-to-plasma concentration ratio make it a useful agent for treating UTI.[3]

Relative infant dose (RID) is the key parameter when considering the safety of taking medications during breastfeeding. It is calculated by dividing the dose supplied to the infant via milk by the mother's weight-adjusted dose. An RID of less than 10% of the mother's weight-adjusted dose is generally considered safe for breastfeeding.[6]

Animal and human studies on osteoarticular toxicity

The demonstration of toxic effects from fluoroquinolones on diarthrodial joints of immature beagles in the late 1970s suggested that they could pose a risk to the growing cartilage in the human skeletal system and raised concerns about their use in children.[7,8] However, several studies have demonstrated the safe use of ciprofloxacin in the pediatric population since then.[9-13] A systematic review evaluating the efficacy and safety of ciprofloxacin in neonates found no evidence of osteoarticular toxicity.[14] Another systematic review assessing the safety of ciprofloxacin use in more than 16000 pediatric patients demonstrated an increased but relatively low and reversible risk of arthropathy and concluded that the risk of ciprofloxacin-induced arthropathy should be weighed against the benefits of using ciprofloxacin in children with appropriate indications.[15]

Ciprofloxacin levels in human breast milk

Ciprofloxacin is excreted in breast milk in both animals and humans.[16-19] A study by Giamarellou et al included 10 postpartum women who received 3 oral 750-mg doses of ciprofloxacin every 12 hours.[17] The highest average ciprofloxacin level reported in the breast milk of these women was 3.79 mg/L at the second hour. The 12- and 24-hour levels were measured as 0.20 mg/L and 0.02 mg/L, respectively.[17] Infants were estimated to receive an average maximum dose of 0.57 mg/kg per day, with an RID of 2.7% if the weight of the mother is assumed to be 70 kg.

Gardner et al detected a breast-milk ciprofloxacin level of 0.98 mg/L at about 11 hours after the last dose in a mother who had been taking 500 mg of oral ciprofloxacin per day for 10 days. The 4-month-old infant (6.1 kg) had no detectable levels of ciprofloxacin in her serum 2.7 hours after nursing, which occurred 1 time 8 hours after the dose.[18] No adverse effects were observed. The maximum dose that the infant would receive was estimated at 0.15 mg/kg per day, which would be equal to an RID of 2.1%.

Cover and Mueller reported on a mother with acute renal failure who received a single 500-mg dose of oral ciprofloxacin.[19] The 4-hour ciprofloxacin level in her breast milk was 3.02 mg/L. However, the level could have been elevated because of her renal dysfunction. This study estimated the infant would receive a maximum dose of 0.45 mg/kg per day, which is equivalent to an RID of 6.3%, assuming the weight of the mother was 70 kg.

Effects reported in breastfed infants

Clostridium difficile toxin–positive pseudomembranous colitis treated surgically was reported in a 2-month-old infant whose mother used ciprofloxacin during breastfeeding.[20] Pseudomembranous colitis in children is also commonly associated with the previous use of other antibiotics.[21] Ampicillin, penicillin, amoxicillin, cephalosporins, and clindamycin are frequent causes of pseudomembranous colitis in childhood.[22]

In long-term follow-up of 3 children who were exposed to ciprofloxacin in utero and during breastfeeding owing to their mothers' multidrug-resistant tuberculosis treatment, no adverse effects were detected at the ages of 1.25, 1.8, and 3.9 years. One of these children, who had also been diagnosed with multidrug-resistant tuberculosis, presented with poor weight gain and failure to thrive (below the third percentile for his age).[23]

Greenish discoloration of the teeth was reported in 2 of 5 infants who received intravenous ciprofloxacin for the treatment of severe nosocomial *Klebsiella pneumoniae* infection.[24]

Conclusion

Limited evidence suggests that ciprofloxacin is excreted in breast milk; however, the amount of infant exposure is low and the estimated RIDs are between 2.1% and 6.3%. Although the manufacturer and some authorities advise against ciprofloxacin use during breastfeeding, clinical data show no substantial evidence of osteoarticular toxicity in neonates and children who received ciprofloxacin for various indications, including neonatal sepsis, nosocomial *Klebsiella pneumoniae* infection, and cystic fibrosis with acute pulmonary exacerbations.[9-15] Further, it is worth mentioning that neonates and children with these clinical conditions were exposed to much higher doses (5-60 mg/kg/d[14] and 3.1-93.8 mg/kg/d[15]) than the infants who were exposed via breastfeeding (0.15 mg/kg/d[18] to 0.57 mg/kg/d[17]).

Therefore, based on the existing data, interrupting breastfeeding during the treatment of a maternal infection that necessitates ciprofloxacin therapy is highly unjustifiable. Nevertheless, monitoring the breastfed infant for gastrointestinal symptoms such as diarrhea is necessary, as it is with any other antibiotic use during breastfeeding.

Competing interests
None declared

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MOTHERISK

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