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Q / How best to treat UTIs in women who breastfeed?

EVIDENCE-BASED ANSWER

A / It's **UNCLEAR**, as no studies have specifically evaluated therapies for uncomplicated urinary tract infections (UTIs) in breastfeeding women. However, trimethoprim/sulfamethoxazole (TMP/SMX), β -lactam antibiotics, nitrofurantoin, and fluoroquinolones all produce cure rates of 78% to 95% for uncomplicated UTIs in women who aren't breastfeeding, and all appear to be equivalent (strength of recommendation [SOR]: **A**, a systematic review).

Women who take TMP/SMX develop drug concentrations in breast milk that are below recommended maximum safe levels for infants who don't have glucose-6-phosphate dehydrogenase (G6PD) deficiency (SOR: **B**, a small observational

study and expert opinion); treatment with nitrofurantoin and ciprofloxacin also produces low levels in breast milk (SOR: **C**, extrapolations from small observational studies and expert opinion). (Though in the case of nitrofurantoin, this does not include patients with G6PD deficiency.)

Some antibiotics taken by breastfeeding mothers may occasionally be associated with adverse effects in their infants: TMP/SMX may cause poor feeding; amoxicillin and cephalexin may cause diarrhea; nitrofurantoin may cause diarrhea or, in infants with G6PD deficiency, hemolytic anemia; and ciprofloxacin may cause pseudomembranous colitis in infants and green teeth in neonates (SOR: **C**, case reports and expert opinion).

Evidence summary

Because no randomized controlled trials have evaluated the efficacy of UTI treatment in lactating women, recommendations are extrapolated from studies in other populations and case reports.

Antibiotics: Comparable and effective

A 2010 Cochrane review examined 21 good-quality randomized trials that compared the effectiveness of TMP-SMX, β -lactam antibiotics, nitrofurantoin, and fluoroquinolones for uncomplicated UTIs in 6016 women.¹ The authors found no significant differences in short-term symptom cure rates: all antibiotics were very effective. Seven studies reported mixed (clinical and bacteriologic) cure rates.

Symptom cure rates for patients followed for as long as 2 weeks ranged from 78% to 95%; longer-term (as long as 8 weeks)

symptom cure rates ranged from 82% to 91%. The review suggested that TMP-SMX may be slightly more likely to cause a rash than other antibiotics.¹

Antibiotic concentrations in breast milk

In a case series, TMP/SMX, 160/800 mg, given to 50 lactating women 2 times (40 women) or 3 times (10 women) daily resulted in an average breast milk concentration of 2 μ g/mL of TMP and 4.6 μ g/mL of SMX, corresponding to respective doses of 0.3 and 0.7 mg/kg/d for infants taking 150 mL breast milk/kg/d.² The authors state that this dose is safe for infants without G6PD deficiency. The study included only women with UTIs or other infections requiring antibiotic treatment.

A case series of 4 lactating mothers who received a single 100-mg oral dose of nitrofurantoin found that peak breast milk concentration

occurred 4 hours later and averaged 2.4 µg/mL (standard deviation=1.7-3.2 µg/mL).³ The authors calculated a mean concentration over 12 hours of 1.3 µg nitrofurantoin/mL breast milk. This level would correspond to an estimated dose of 0.2 mg/kg/d for an infant consuming 150 mL/kg/d of breast milk whose mother takes 100 mg nitrofurantoin twice daily, much lower than the recommended pediatric dose of 5 to 7 mg/kg/d.

Data from a case series and a case report suggest the amount of ciprofloxacin transferred to breastfed infants is low. In the case series, researchers gave 10 lactating women 3 oral doses of ciprofloxacin, 750 mg, at 12-hour intervals and then measured ciprofloxacin levels in breast milk.⁴ The highest levels occurred 2 hours after the third dose and averaged 3.79 µg/mL. Average levels fell gradually to 0.02 µg/mL 24 hours after the third dose. Assuming a milk intake of 150 mL/kg/d, a breastfed infant would consume approximately 0.3 mg/kg/d, much lower than the 10 to 40 mg/kg/d dose recommended for treating sick infants.

A case report of a woman who took oral ciprofloxacin 500 mg/d for 10 days noted a breast milk ciprofloxacin concentration of 0.98 mg/L at 10.7 hours after the last dose.⁵ Ofloxacin, norfloxacin, and levofloxacin have been associated with lower milk concentrations than ciprofloxacin.⁶

Adverse effects

In a cohort study of 838 women from a program for pregnant and lactating women exposed to drugs and other substances, 2 of

12 mothers taking TMP/SMX reported poor feeding in their infants.⁷

The same program received reports of infants with diarrhea from mothers taking amoxicillin (3 of 25 infants), nitrofurantoin (2 of 6 infants), and cephalexin (2 of 7 infants), but no reports of other adverse effects. Another study demonstrated that nitrofurantoin is actively transported into the mother's milk, making hemolytic anemia a possibility in G6PD-deficient infants.³

Studies indicate that adverse effects of fluoroquinolones in children are similar to those in adults despite a contraindication in children because of reports of arthropathy in young animals. One case of pseudomembranous colitis in a breastfeeding infant and 2 cases of green teeth in neonates have been reported with ciprofloxacin use.^{6,8,9}

Recommendations

The Infectious Disease Society of America recommends nitrofurantoin, TMP/SMX, or fosfomycin for first-line treatment of uncomplicated UTIs in women, although fosfomycin appears to be inferior to other standard short-course antibiotics based on FDA data. Fluoroquinolones and β-lactams are recommended alternative treatments.¹⁰

The American Academy of Pediatrics' Committee on Drugs says that TMP/SMX (unless G6PD deficiency is present), amoxicillin, nitrofurantoin, ciprofloxacin, and ofloxacin usually are compatible with breastfeeding.¹¹

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