Which UTI therapies are safe and effective during breastfeeding?

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Evidence-based answer

Trimethoprim/sulfamethoxazole (TMP/SMX) has a high success rate in eradicating bacteriuria for women with urinary tract infection and is compatible with breastfeeding (strength of recommendation: **C**, based on extrapolation from studies with nonlactating women and disease-oriented outcomes).

Quinolones (ciprofloxacin, ofloxacin) are effective and probably compatible with breastfeeding; however, their use has not been recommended by many investigators based on arthropathy in animal studies (SOR: **C**, based on extrapolation from case series and disease-oriented outcomes).

A 7-day course of nitrofurantoin has similar efficacy to TMP/SMX and is compatible with breastfeeding, but it should be avoided in populations at risk for glucose-6-phosphate dehydrogenase (G6PD) deficiency (also known as favism, most often found in patients of Mediterranean or African descent) (SOR: **C**, extrapolation from studies in nonlactating women and disease-oriented outcomes).

Clinical commentary

An antibiotic that's effective for mom and safe for baby is of paramount importance

Knowing the local resistance patterns can greatly aid in choosing a safe, effective antibiotic. Most local laboratories that do microbiology work either publish their antibiograms or make them available on a semiannual or annual basis. Keeping these readily available can be a time-saver when it comes to decision-making and writing a prescription.

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FAST TRACK

Safety data for quinolones in infants and children are mixed

Evidence summary

Urinary tract infections (UTIs) are common in reproductive-aged women. In lactating women, it's important to select a therapy that is not only effective, but also safe for the breastfeeding infant. No studies in the literature address the safety or efficacy of UTI treatments in lactating women and their infants. Therefore, recommendations are extrapolated from studies of efficacy in the general population, studies of antibiotic penetration into breast milk, and effects of antibiotics given to infants directly.

How the efficacy of UTI treatments stack up

The best evidence for efficacy of UTI treatments comes from a 1999 meta-analysis of uncomplicated UTI in nonpregnant, nonlactating women.[1] They found TMP/SMX to be the most widely

studied antibiotic and to have a 93% bacterial eradication rate; it was therefore used as a standard for comparison of other treatments. Nitrofurantoin and quinolones (ofloxacin, ciprofloxacin, and others) had comparable eradication rates to TMP/SMX in the same study; 7-day courses of nitrofurantoin were more efficacious than shorter ones. TMP/SMX is not recommended if the local resistance rate is more than 10% to 20%.[2]

Three-day therapy for uncomplicated UTI is more effective than single-dose therapy and equal to longer courses for most antibiotics.[1] A longer course (7 days) may be required for nitrofurantoin. Beta-lactams are associated with high levels of resistance and therefore not recommended in empiric treatment of UTI.[2]

A look at penetration into breast milk

Most of the data regarding antibiotic penetration into breast milk come from case series. One South African series measured breast milk levels of both trimethoprim and sulfamethoxazole among 50 Bantu women treated with TMP/SMX for various infections (including UTI).[3] The women received 160 mg TMP and 800 mg SMX 2 or 3 times daily for up to 5 days. The average level of TMP in breast milk was 2 mcg/mL, and the level of SMX was 4.7 mcg/mL. Researchers calculated that the average breastfeeding infant would ingest only 1 mg of TMP and 2.5 mg of SMX per day. TMP/SMX is generally considered safe for infants in the absence of G6PD deficiency.

In a case series, 9 lactating mothers were given nitrofurantoin 100 mg orally every 6 hours for 1 day.[4] On day 2, after a single 100 to 200 mg dose, drug levels in the breast milk 2 hours post-dose ranged from none (in 6 of the 9 women) to a maximum of 0.5 mcg/mL in one. Since even a very small amount of the drug may trigger a hemolytic reaction among G6PD-deficient individuals, the researchers called for caution when prescribing to mothers from high-risk populations.

A final case series administered ciprofloxacin 750 mg, pefloxacin 400 mg, or ofloxacin 400 mg twice daily to 3 groups of 10 women each.[5] Milk samples were obtained 6 times over 24 hours following the third dose of antibiotic. Maximum levels in breast milk occurred 2 hours after the dose, and were 3.79, 3.54, and 2.41 mcg/mL for ciprofloxacin, pefloxacin, and ofloxacin respectively. All 3 quinolones achieved higher concentrations in breast milk than in serum.

But are these drugs safe for children?

While TMP/SMX and nitrofurantoin are generally considered safe when given to infants and children (barring G6PD deficiency), data are mixed regarding the safety of quinolones. Ciprofloxacin's FDA indication for pediatric patients is limited to postexposure anthrax prophylaxis due to evidence of fluoroquinolone-induced joint toxicity in animal studies.[6] Despite this, they have been prescribed to tens of thousands of children for select scenarios such as chemotherapy-induced immunocompromise, cystic fibrosis, complicated UTIs, and salmonella infections.[7]

A report was published summarizing safety data from the Bayer database of compassionate use of ciprofloxacin.[8] The report indicates that 2030 treatment courses of ciprofloxacin were given to 1795 children up to age 17 for a variety of infections; only 3% were under age 5. Most patients received 21 to 40 mg/kg of ciprofloxacin per day; treatment duration was from 1 to 303 days. Arthralgia occurred in 1.5% of patients, most of whom had cystic fibrosis. Of the 31 patients affected, arthralgias resolved in 25, improved in 1, and remained unchanged in 1. (Data regarding resolution were unavailable for 4 patients.)

Recommendations from others

The American Academy of Pediatrics' Committee on Drugs considers the following antibiotics typically used for UTI to be compatible with breastfeeding:

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Three-day therapy for uncomplicated UTI is comparable with longer courses for most antibiotics

ciprofloxacin, ofloxacin, nitrofurantoin (caution for infants with G6PD deficiency), and TMP/SMX.[9]

Drugs in Pregnancy and Lactation considers trimethoprim and sulfamethoxazole to be compatible with breastfeeding but cautions against sulfamethoxazole use in infants with known G6PD deficiency. The authors categorize nitrofurantoin, ciprofloxacin, and ofloxacin as "probably compatible/limited human data," and advise caution with nitrofurantoin for infants with G6PD deficiency.[10] ■

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Avoid SMX in infants with known GSPD deficiency

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