Urinary tract infections in pregnancy

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ABSTRACT

QUESTION My pregnant patients often present with urinary tract infections. Are the medications commonly used for the management of urinary tract infections safe to use during pregnancy?

ANSWER Existing data indicate that exposure to penicillins, cephalosporins, fluoroquinolones, nitrofurantoin, or phenazopyridine during pregnancy is not associated with increased risk of fetal malformations. Trimethoprim-sulfamethoxazole should be avoided, if possible, during the first trimester of pregnancy because of the antifolate effect associated with neural tube defects.

RÉSUMÉ

QUESTION Il arrive souvent que mes patientes enceintes présentent une infection des voies urinaires. Les médicaments utilisés couramment pour la prise en charge des infections des voies urinaires sont-ils sans risque durant la grossesse?

RÉPONSE Les données les plus récentes indiquent que l’exposition à la pénicilline, à la céphalosporine, au fluoroquinolone, à la nitrofurantoin ou à la phénazopyridine durant la grossesse n’est pas associée à un risque accru de malformations fœtales. Il faudrait éviter dans la mesure du possible le triméthoprime-sulfaméthoxazole durant le premier trimestre en raison de son effet qui est de contrer l’acide folique, associé à des anomalies du tube neural.

Urinary tract infections (UTIs) are a common complication of pregnancy. Symptomatic UTI occurs in 1% to 2% of pregnancies, while asymptomatic bacteriuria has been reported in 2% to 13% of pregnant women. Several anatomical and hormonal changes in pregnant women lead to ureteral dilatation and urinary stasis, which contribute to the increased risk of developing UTIs. Untreated UTIs can lead to complications, such as pyelonephritis, low-birth-weight infants, premature delivery, and, occasionally, stillbirth; therefore, prompt treatment of symptomatic UTIs and asymptomatic bacteriuria is warranted in pregnant women.

Penicillins
Penicillins, such as amoxicillin, are commonly prescribed for the treatment of UTIs. The Collaborative Perinatal Project monitored 3546 mothers who were exposed to penicillin derivatives during their first trimesters, and 7171 mothers who were exposed at any time during their pregnancies. There was no increase noted in the rate of malformations. The Michigan Medicaid surveillance study found that among 8538 newborns exposed to amoxicillin during the first trimester, a total of 317 (3.7%) major birth defects were observed, which is within the population risk.

Cephalosporins
Cephalosporins are alternative antibiotics for treating UTIs. Cephalexin is among the most commonly prescribed oral cephalosporin for this indication. In the Michigan Medicaid surveillance study, a total of 176 (4.9%) major birth defects were observed (154 expected) among the 3613 newborns exposed to cephalexin during the first trimester. The results of a Hungarian case-control study did not indicate human teratogenic potential for oral cephalexin.

Fluoroquinolones
Fluoroquinolones are also commonly prescribed for the treatment of UTIs, and include norfloxacin and ciprofloxacin. Concerns regarding the safety of this class of drugs originated from reports of arthropathy in animal studies; such reports are rare in human cases. Nevertheless, the safety of these drugs in pregnancy has been explored in a number of studies. Based on existing data, fluoroquinolone exposure during human gestation is not associated with increased risk of major malformations, adverse effects in the fetal musculoskeletal system, spontaneous abortions, prematurity, intrauterine growth retardation, or postnatal disorders. However, because of the relatively higher cost of these agents and the concern about the emergence of antibiotic-resistant pathogens with frequent use, fluoroquinolones should not routinely be employed as first-line agents in uncomplicated UTIs.

Nitrofurantoin
Numerous studies have demonstrated the safety of nitrofurantoin in pregnancy. Case-control studies and case
series involving thousands of women who received nitrofurantoin in pregnancy reported no increase in major malformations among the newborns.\textsuperscript{5,16,17} In addition, a meta-analysis conducted by Motherisk failed to show teratogenic risk with first-trimester use of nitrofurantoin.\textsuperscript{18} The drug can theoretically induce hemolytic anemia in the fetus or newborn, particularly in those with glucose-6-phosphate dehydrogenase deficiency; however, cases of this toxicity are rare.\textsuperscript{19,20}

**Phenazopyridine**

Phenazopyridine is used to relieve UTI symptoms, such as burning, pain, urgency, and frequency, associated with irritation of the lower urinary tract caused by infection. The Collaborative Perinatal Project monitored 219 women with first-trimester exposure and 1109 women with exposure at any time during pregnancy. There was no increase in the rates of major malformations or any other adverse effects.\textsuperscript{4}

**Trimethoprim–sulfamethoxazole**

Trimethoprim-sulfamethoxazole (TMP-SMX) combination is widely used to treat UTIs. Sulfonamides as a group do not appear to pose a serious teratogenic risk;\textsuperscript{21} however, trimethoprim is a folic acid antagonist and its use during the first trimester has been associated with structural defects, such as neural tube and cardiovascular defects. A detailed review of this drug was published in a previous Motherisk Update.\textsuperscript{22} Whenever clinically feasible, trimethoprim alone or TMP-SMX combinations should be avoided during the first trimester of pregnancy. Also, sulfamethoxazole can persist in neonatal circulation for several days after delivery if taken near term. There is a theoretical risk of sulfonamides increasing unbound bilirubin owing to competitive protein binding;\textsuperscript{21} however, there have been no reports in the literature of this actually occurring. As other drugs are available and there is potential toxicity to the newborn, TMP-SMX should be avoided after 32 weeks of gestation.\textsuperscript{22}

**Conclusion**

Urinary tract infections during pregnancy can lead to serious consequences if left untreated. Antibiotics commonly used for this condition have not been found to be associated with an increased risk of birth defects when used during pregnancy. Using products containing trimethoprim is discouraged during the first trimester, and sulfonamides should be avoided in late pregnancy.

**Competing interests**

None declared.

**References**


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**Motherisk Update**

Motherisk questions are prepared by the Motherisk Team at the Hospital for Sick Children in Toronto, Ont. Ms Lee is a doctoral candidate in the Faculty of Pharmacy at the University of Toronto. Ms Bazzu is a member of the Motherisk Program. Ms Einarson is Assistant Director and Dr Koren is Director of the Motherisk Program. Dr Koren is supported by the Research Leadership for Better Pharmacotherapy during Pregnancy and Lactation. He holds the Ivey Chair in Molecular Toxicology at the University of Western Ontario in London.

Do you have questions about the effects of drugs, chemicals, radiation, or infections in women who are pregnant or breastfeeding? We invite you to submit them to the Motherisk Program by fax at 416 813-7582; they will be addressed in future Motherisk Updates.

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