Rise in *E. coli* Resistance In UTIs Starting to Slow

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WASHINGTON — The prevalence of urinary tract infections in women resistant to standard treatment has been increasing, but there are indications that the increase has begun to level off, Patricia D. Brown, M.D., said at an update on sexually transmitted infections.

Emerging uropathogenic *Escherichia coli* antimicrobial resistance—particularly to the front-line, first choice treatment of urinary tract infections (UTIs), trimethoprim-sulfamethoxazole (TMP-SMX)—has been documented worldwide. However, much of the data are based on passive surveillance, which can overestimate prevalence, because women with acute, uncomplicated UTIs often do not have cultures performed, so these cases are not reported, said Dr. Brown of Wayne State University, Detroit.

Women who do have a culture have complicated disease and fail treatment, leading to overestimates of true prevalence, she added. Still, passive surveillance can provide information on trends.

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In the United States, active surveillance has been conducted in specific geographic areas, where the true prevalence may not reflect that of other geographic areas, Dr. Brown said at the meeting, sponsored by OB.GYN. NEWS, FAMILY PRACTICE NEWS, and Boston University.

Recent studies indicate that TMP-SMX resistance "may be leveling off" after peaking at about 25%, which is probably because of the reduced use of this treatment, she said. But as the use of TMP-SMX for UTIs has decreased, resistance to other antimicrobial agents has been increasing.

In 890 isolates from women with UTIs in the United States who were a part of the North American Urinary Tract Infection Collaborative Alliance (NAUTICA) study, the prevalence of TMP-SMX resistance was about 23%. Resistance to ampicillin was 38%, and resistance to levofloxacin was nearly 7%.

As the use of TMP-SMX has dropped, the use of fluoroquinolones has increased, Dr. Brown said, noting that rates of resistance to β-lactams such as ampicillin have been high for some time.

In the NAUTICA study, resistance to nitrofurantoin was only 1.8%, which she said was "remarkable," considering that it has been available for about 50 years. But that rate has probably remained so low because the agent has several mechanisms of action and is indicated only for cystitis, she noted.

There are several clinical implications of these resistance trends: In treatment studies of pyelonephritis, antimicrobial resistance has clearly been shown to increase the risks of both clinical and microbiologic failure, she said. She cited a retrospective cohort study of women with acute uncomplicated cystitis, in which the risk of clinical failure was 45.4%, and a prospective study in Israel of empiric TMP-SMX in an area where the prevalence of resistance was high, in which the risk of clinical failure was 46%.

Identifying risk factors for resistance can help guide antibiotic choice, she said, referring to the difficulty facing clinicians, who usually do not have access to resistance trends and who likely will be given an overestimate of resistance if they call their local microbiology lab.

Results of retrospective case-control studies have identified potential risk factors for infection with a uropathogen resistant to TMP-SMX. Two risk factors found in every such study include recent antibiotic use and recent hospitalization, she said. Recent travel to underdeveloped countries has been identified as an independent risk factor in several studies.

The standard treatment of uncomplicated cystitis is 3 days of double-strength formulations of TMP-SMX twice a day. Avoid empiric treatment with TMP-SMX in patients who have recently been hospitalized or have taken antibiotics in the previous 3 months, she said.

Alternative treatments for those with risk factors for resistance are a 7-day course of nitrofurantoin or a 3-day course of a fluoroquinolone. The major drawback of the former is that a full-week course is necessary.

As for the fluoroquinolones, ciprofloxacin is available in generic formulations, so the drug is less expensive. The Food and Drug Administration has approved gatifloxacin as a single-dose treatment for uncomplicated cystitis. One fluoroquinolone that should not be used for UTI is moxifloxacin, which is indicated for respiratory infections, because treatment results in low levels of the drug in the urinary tract.

A single dose of fosfomycin is another alternative, but this is considered a second-line treatment because the efficacy is not that high and it is expensive. One benefit, however, is that resistance to this agent appears to be low, Dr. Brown said.

Short-course treatment is not appropriate for complicated cystitis, which should be treated with a 7-day course of therapy, she said. Avoid empiric TMP-SMX treatment in patients who have recently been treated with antibiotics or have recently been hospitalized, as you would for patients with uncomplicated cystitis. Culture all patients, and adjust treatment based on susceptibility data, she said.

As many as 25% of women with acute cystitis can develop frequent, recurrent UTIs, which are reinfections, not relapses. (Fewer than 5% of these women have a correctable structural or functional abnormality of the urinary tract.) ■

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