Resistance Increasing to Standard UTI Treatment

BY ELIZABETH MECHCATIE
Senior Writer

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.

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 fluoroquinolones, ciprofloxacin is available in generic formulations, so it 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 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. 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.) Management strategies include daily or postcoital prophylaxis and self-start therapy for women concerned about developing a UTI when they are away from home, she added.

Dr. Brown said that he considers topical estrogen for postmenopausal women who have recurrent UTIs. ■

Shorter Antibiotic Course For Childhood UTI Possible

BY LINDA LITTLE
Contributing Writer

SCOTTSDALE, ARIZ. — The treatment and diagnosis of urinary tract infections in young children are undergoing dramatic changes, Aaron L. Friedman, M.D., said at a pediatric update sponsored by Phoenix Children's Hospital.

Urinary tract infections affect 3%-4% of young girls and 1% of young boys—making the condition relatively common in children.

Dr. Friedman, chairman of the department of pediatrics at Brown University, Providence, R.I., said the standard treatment today is 7-14 days of antibiotics. However, there is now evidence that this could be shortened to 2-4 days for uncomplicated infections.

He pointed to a compilation of 10 studies of 652 children, aged 3 months to 18 years, comparing the conventional antibiotic course of 7-14 days with a 2- to 4-day treatment. The shorter course was found as effective as the longer course in eradicating lower urinary tract infections in children.

"There is increasing evidence that treatment as short as 2-4 days is sufficient for uncomplicated urinary tract infections in children who don't have bacteria floating in their blood and no kidney involvement," Dr. Friedman said.

Another change is the amount of work a physician should put into finding the cause of the urinary tract infection. Because of the fear of kidney damage due to ureterovesical reflux in young children, the dogma has been to order imaging studies, such as ultrasound and voiding cystourethrogram (VCUG), after the diagnosis.

Both imaging studies are conventionally done weeks after the diagnosis of urinary tract infection in young children, said Dr. Friedman.

Ultrasound is now considered of little value, and the utility of VCUG—especially in children older than 1 year—is under considerable review, he said.

This applies only to children aged 1 year and older, he said. "Infants should be examined aggressively, but for everyone else, there should be a more nuanced approach."

A U.S. study of more than 300 children with UTI aged 1-24 months showed that ultrasound was normal in 88% of children and that VCUG was positive for reflux in only 39%. Additionally, the nuclear medicine scan was positive for renal scarring in only 9.5% of patients.

"There is very little utility in ultrasound in urinary tract infections in children," he said. "It doesn't help in early treatment, and it doesn't give you any more information than what you had before."

There is increasing evidence about the use of VCUG with the first urinary tract infection, he said.

VCUG was thought to be useful in defining the population that needed prophylactic treatment. However, there is increasing skepticism such treatment is advantageous in these children.

"The problem is that we don't know that prophylactic treatment with low-dose antibiotics for an 18-month to 2-year period is useful," he said. "While it does reduce the recurrences, there is no evidence that it improves the long-term outcome."

"We are in a continuum here, where the conventional approach recommended a voiding study," Dr. Friedman said. ■