Controversy Abounds Over UTI Management

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BOSTON — A recent study suggesting that prophylactic antibiotics for an initial urinary tract infection in children do not prevent recurrent infection and may, in fact, contribute to an increased risk of recurrent infection with a resistant bacteria has raised questions about the standard of care for these patients.

Dr. Ron Keren of the Children's Hospital of Philadelphia made this presentation at the annual meeting of the American Academy of Pediatrics.

The AAP 1999 practice parameter recommends that all children with a first urinary tract infection (UTI) undergo renal ultrasound to detect abnormalities such as hydronephrosis, bladder hypertrophy, and ureteroceles; and either a voiding cystourethrogram (VCUG) or direct radionuclide cystography (RNC) to evaluate the presence and degree of vesicoureteral reflux (VUR), Dr. Keren explained. Conventional wisdom has been that evidence of VUR, which is found in 30%-40% of children with UTI, warrants prophylactic antibiotic treatment to prevent recurrent infection and subsequent kidney damage, he said.

In an observational study, Dr. Keren and his colleagues reviewed the electronic health records of nearly 80,000 children with at least two pediatric care visits over a 5-year period and identified 611 children who had been diagnosed with a first UTI (JAMA 2007;298:179-86). "We then looked forward into the records to determine how many of these kids had recurrent [UTI], what the risk factors were, and whether the prescription of prophylactic antibiotics actually changed the risk," he said.

Of those 611 children who'd had a UTI, 83 (14%) had been diagnosed with a recurrent infection. With use of a time-to-event analysis, "white children, older children, and children with high-grade VUR had a statistically significant increased risk of recurrent UTI, while having been prescribed prophylactic antibiotics had no relationship to recurrent infection," he said,

Dysfunctional Voiding Often Causes UTIs

It's critical for general pediatricians to consider dysfunctional elimination as a cause of urinary tract infections in children, Dr. Keren said.

Dysfunctional elimination often goes undiagnosed and undertreated, despite the fact that approximately 40% of children with first UTI and 80% of children with recurrent UTI will have symptoms of the condition, Dr. Keren said. It is characterized by abnormal elimination patterns (frequent or infrequent voids, urgency, and constipation), bladder or bowel incontinence, and/or withholding maneuvers.

The possibility of dysfunctional elimination can be evaluated using the validated Dysfunctional Voiding Scoring System, which asks a series of simple questions about bowel and bladder practices (J. Urol. 2000;164:1011-5).

Once the condition has been diagnosed, parents should be encouraged to try some simple interventions, such as scheduling voiding times every 2 or 3 hours, treating constipation with laxatives and increased fluid intake, and avoiding bladder irritants such as caffeine, food coloring, chocolate, citrus, and carbonated beverages.

"If these interventions don't work, I would refer the child to a urologist for further evaluation. Often, some of the bigger academic hospitals will have dysfunctional voiding clinics, where a psychologist might work with the child using biofeedback to retrain the pelvic floor muscles. The urologist might also prescribe anticholinergics," Dr. Keren said.

Studies have shown treatment of dysfunctional elimination can decrease UTI recurrences and can speed the resolution of VUR, he said. As such, "screening for [dysfunctional elimination] is an important first step in the management of pediatric UTI," he said.

noting that children with low grade VUR, which is what the majority of kids have when there is evidence of VUR, were not at increased risk for reinfection. Additionally, "having been exposed to prophylactic antibiotics increased the odds of reinfection with a bug that was not pansensitive almost eightfold," he said.

Multiple clinical trials also have failed to show a benefit of prophylactic antibiotics for the prevention of recurrent UTIs, and the authors of a 2006 systematic review of the available literature reported that the evidence to support the widespread use of antibiotics to prevent recurrent, symptomatic UTI is weak but stressed the need for large randomized, double-blinded clinical trials (Cochrane Database Syst. Rev. 2006; doi:10.1002/14651858.CD001534).

Given the apparent contradiction between the evidence and the standard of care, what is a pediatrician or parent to do? "Remember the old saying: 'The absence of evidence is not evidence of absence of benefit,'" Dr. Keren advised. "Right now, the AAP says we should be screening these kids, and we should probably be doing something about what we find. It's perfectly fine to take the conservative approach and continue to screen all kids for VUR after the first UTI and continue to prescribe prophylactic antibiotics for kids with VUR until the VUR resolves, until we get better evidence."

But it's also okay to use clinical judgment with respect to individualizing care, Dr. Keren stressed. "There's a big difference between a 3-year-old girl with her first afebrile UTI concurrent with potty training vs. a 5-month-old girl with febrile UTI requiring hospitalization and a history of febrile illnesses that got better with antibiotics, and a sibling and mother with a history of dilating VUR," he said. "These are two very different creatures. I would seriously consider screening the latter child for VUR but waiting for recurrent UTI before screening the older child."

Interestingly, the AAP imaging recommendations as outlined in the practice parameter also have been the subject of controversy. "The guidelines were written for children from 2 to 24 months of age. There's no comment on what to do for older children, yet when you look at the epidemiology of UTI in kids, the majority of children are between 2 and 6 years old when they get their first UTI. Should we be doing the same for a 4-year-old as we do for a 2- to 24-month old?" asked Dr. Keren. And while the guidelines clearly spell out imaging recommendations, "they don't tell us what to do with the findings uncovered on imaging."

Because of this, the current management model for VUR comes from the American Urological Association (AUA) guidelines, which indicate that treatment should be decided based the age of the child and the grade of VUR based on the International Classification System for vesicoureteral reflux. "With the exception of kids between 1 and 5 years with bilateral grade V VUR and kids 6-10 years with bilateral grade III or IV reflux or unilateral grade V reflux, for whom surgery is recommended, the AUG recommends prophylactic antibiotics for initial management of kids who don't have renal scarring at the time of diagnosis," said Dr. Keren.

"Of course, a lot of sites are not doing DMSA [dimercaptosuccinic acid] renal flow scans up front, so they don't know whether there is scarring, but these recommendations stem from an empirical treatment model that's been in place for 20-30 years that suggests UTIs in the presence of reflux leads to scarring which can lead later in life to end-stage renal disease, hypertension, or preeclampsia in young women," he said. "The idea was that if you could knock out either one of these arms—UTI or VUR—either by surgically correcting the reflux or preventing UTI with prophylactic antibiotics, you could prevent the march down this path."

Multiple studies comparing the effectiveness of these interventions have failed to show that either approach is better than the other with respect to the development of new renal scars, "or whether any intervention does more good than harm for VUR," said Dr. Keren.

Because of this, "there is a lot of skepticism about that empirical model as the basis for our management, which has led to calls for a 'top down' management approach, starting with the kidneys vs. the bladder."

According to this approach, the kidneys of children with a UTI should be assessed by DMSA scan. "The absence of abnormalities on DMSA scan has a very good negative predictive value for high-grade VUR, which is most strongly associated with subsequent renal scarring and other effects of pyelonephritis," said Dr. Keren. "With normal DMSA scan, you can reassure parents that the kidneys are normal and that the child is unlikely to have dilating VUR, and you might want to consider skipping the VCUG." An abnormal scan warrants the VCUG and, depending on the degree of VUR, the consideration of antibiotics or surgery, he said.

Dr. Keren reported having no financial conflicts of interest with respect to his presentation. ■