UTIs Recur Despite Prophylactic Antibiotic Use

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Prophylactic antibiotics don't appear to protect children with a first febrile urinary tract infection from a recurrence, whether or not they have primary, nonsevere vesicoureteral reflux.

"Our study shows that prophylaxis does not reduce the rate of febrile urinary tract infection recurrence during the 12 months after the first episode," wrote Dr. Giovanni Montini of Padua (Italy) University, and his colleagues (Pediatrics 2008;122:1064-71).

The randomized controlled trial was conducted at 22 centers and included 338 patients (mean age 15 months); 69% were girls. All the children received antibiotic treatment for their initial urinary tract infection (UTI), and were placed on prophylactic treatment until a voiding cystourethrogram was conducted.

After the test, children were randomized to either no prophylaxis or to prophylaxis with either co-trimoxazole 15 mg/kg a day or co-amoxiclav 15 mg/kg a day, for 12 months. They underwent monthly urine cultures for the first 6 months, and then every other month during the study period. At the end of the study, they all underwent a 99-mTc dimercaptosuccinic acid scan to determine the extent of any renal scarring.

Recurrent febrile UTIs occurred in 12 (9%) of the control group patients and in 15 (7%) of the prophylaxis group patients—not a significant difference. The difference remained nonsignificant even when the two groups were stratified by degree of vesicoureteral reflux (VUR). Recurrence rates among those with VUR grade I were 9% in the control group vs. 5% in the prophylaxis group. The rates in those with VUR II were 9% in the control group and 8% in the prophylaxis group. Among those with VUR III, the rate of recurrence was 43% in the prophylaxis group and 23% in the control group, although the difference was not significant.

In a bivariate analysis, younger age and VUR grade were associated with recurrence. The mean age among patients with recurrence was 7 months, compared with 15 months among those without recurrence. The rate of recurrence increased with VUR grade, from 4% among patients without VUR to 7% in those with VUR I, 9% of those with VUR II, and 30% of those with VUR III.

Recurrent urinary tract infections occurred in 9% of patients in the control group and in 7% of those in the prophylaxis group, which is not a significant difference.

Most of the children (87%) underwent the renal scan at the end of the follow-up period. A new renal scar occurred in only four patients—just over 1%. Two scars were found in each treatment group.

During the study, 2,422 urinalyses were performed. Most of the 27 recurrences were from *Escherichia coli* infections (70%). Other infective agents included *Proteus mirabilis* and *Enterobacter* (7% each), and *Pseudomonas aeruginosa, Klebsiella pneumoniae,* and *Citrobacter* (4% each).

Antibiotic-resistant bacteria caused nine infections; eight of those occurred in the prophylaxis group, and the ninth in a child who was switched from the control to the prophylaxis group after developing two recurrences.

Ten percent more repeat positive urine cultures occurred in the control arm, but that finding doesn't necessarily indicate the need for antibiotics, the authors said. "This has been the driving force behind the use of prophylactic antibiotics; however, we believe that repeat positive urine cultures in the absence of fever or other symptoms of parenchymal localization of the infection are not clinically relevant and do not produce renal scars."

Adverse events—mostly gastrointestinal—occurred in 25 children, all of whom were taking prophylactic therapy.

Dr. Andrew Kirsch, a professor of urology at Emory University, Atlanta, said the study was well designed but did not go far enough in identifying VUR status and its possible impact on recurrent infection. "Voiding cystourethrograms were not cyclic, and they probably underestimated the incidence of VUR," he said in an interview. "Even in cases with VUR resolution, up to 20% may show VUR on a subsequent cystourethrogram, which was not done here. A second cycle may identify VUR in those not identified in the first cycle." ■