

Urinary Tract Infection Treatment and Evaluation

Update

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In the 5 years since the last *Concise Reviews...* review of urinary tract infections (UTIs)¹ and the publication of the American Academy of Pediatrics practice parameter and technical report on the diagnosis, treatment and evaluation of the initial UTI in febrile infants and young children,^{2,3} new studies regarding treatment and radiographic evaluation have been published. This is a brief update.

TREATMENT

Which Route? Hoberman et al⁴ compared an all oral regimen to initial parenteral followed by oral medication in 306 febrile children 1–24 months old with UTI. There was no difference in fever duration, symptomatic improvement, sterility of urine at 24 hours, reinfection rate or rate of scarring but a marked difference in cost. Infants treated with oral cefixime initially received a double dose under direct supervision in the emergency department assuring that treatment was begun promptly and that the infant would tolerate the medication. The demonstrated effectiveness of oral therapy will not eliminate all hospitalizations for treatment of UTI in febrile children, particularly those with systemic toxicity, severe dehydration, vomiting or inability to tolerate the medication.

In a study conducted in pediatric practices, bacteremia occurred in 10% of febrile infants 0–3 months old with UTI, but these infants were indistinguishable

clinically from those without bacteremia.⁵ This rate of bacteremia has led some authors to recommend parenteral treatment of infants in this age group with UTI; studies to date have had too few infants with UTI-associated bacteremia to know whether this recommendation is warranted.^{4,5}

Which Antibiotic? In Hoberman's study,⁴ cefixime was selected because of its antibacterial spectrum, palatability, and convenient dosing schedule. Wyeth discontinued manufacturing it, but this year Lupon reintroduced cefixime, maintaining the trade name Suprax. Cefixime remains ideal, because resistance to amoxicillin and, in many areas, trimethoprim-sulfamethoxazole (TMP-SMX) have virtually eliminated the utility of these agents as first line drugs to treat UTI.

What Duration? Hoberman et al⁴ treated for 14 days in both arms of their study as the goal was to demonstrate whether an all-oral regimen was comparable with "standard" therapy. The researchers prudently used the duration recommended in most textbooks for the treatment of pyelonephritis. Studies comparing 7 or 10 days with 14 days suggest comparability, but this has not been definitively demonstrated. Shorter therapy is of interest, but studies agree that single dose or 1 day therapy is not comparable with 7–10 days, and results are conflicting regarding treatment of cystitis for 2–4 days.^{6–8} The majority of febrile infants with UTI have nuclear scan evidence of pyelonephritis,⁹ suggesting that infants should not receive short course treatment.

EVALUATION

Rationale. UTIs in healthy adults are generally considered acute infections with short term morbidity. Children's UTIs generate additional concern about possible

sequelae: renal scarring; and consequent renal impairment and hypertension. Radiographic studies in children have been recommended in the hope of preventing renal impairment and hypertension by revealing treatable conditions [eg, obstruction, vesicoureteral reflux (VUR)]. The high cost of treating hypertension in adults has been used to justify the performance of these tests on a cost-benefit basis.³ In the 1960s, it was presumed that asymptomatic childhood UTIs accounted for end stage renal disease in a large number of adults, but currently there is skepticism about the frequency of sequelae from uncomplicated UTIs. A prospective study from birth to age 40 with the number of patients sufficient to define the relationship between childhood UTI and adulthood renal impairment/hypertension is unlikely to be conducted. It may now be possible to follow a cohort of children who have had nuclear scans, relating the degree of UTI-associated scarring to outcome.

Ultrasonography (US). Both upper and lower tract imaging studies have been recommended. The rationale for the upper tract study, currently US, is to identify obstruction and major anomalies, such as duplication. The need for US, particularly in the age of prenatal US, has been questioned.^{9,10} US cannot be used in place of voiding cystourethrography (VCUG) to identify reflux, and the yield of conditions found that alter management is quite low. Were US as invasive and potentially toxic as intravenous pyelography, formerly used to assess the upper tracts, it is unlikely that its routine use would still be recommended. US does not involve radiation or much discomfort, but it adds expense

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and will undoubtedly be subjected to continued scrutiny regarding benefit.

Voiding Cystourethrography. Because reflux predisposes to pyelonephritis and is particularly dangerous when combined with infection, it follows that treatment should be beneficial, beginning with antimicrobial prophylaxis to control infection and extending to surgery for those with high grade reflux who fail prophylaxis. Clearly children with VUR are more likely to develop renal scars than those without VUR.^{3,9} That fact and face validity have perpetuated the stepwise reasoning for decades, but there are reasons to question current routines. For example, if antimicrobial prophylaxis prevents scarring no more than clinical surveillance and early treatment, then the value of imaging to identify reflux is questionable (see “Antimicrobial Prophylaxis”).

The VCUG warrants reconsideration. Considered the standard for identifying and grading reflux, a single study may not be as definitive as generally accepted¹¹ but may be similar to the upper gastrointestinal series used to identify gastroesophageal reflux: variable in the same patient. Although lower grades of reflux clearly improve with time in groups of children, individual children may have different grades at different times, including the “reappearance” of reflux after apparent resolution.

In addition to concerns about the validity and usefulness of VCUGs, there are other reasons to reduce the number of these procedures performed, including patient discomfort, catheterization, irradiation, and cost.

Nuclear Scans. ^{99m}Tc-Dimercaptosuccinic acid scanning has been an important research tool to: (1) identify pyelonephritis assuring that children assigned to one or another treatment group are comparably affected; and (2) assess scarring. It does not appear to contribute information that alters management acutely, however,⁹ and its routine use in

follow-up does not appear to confer additional benefit either.

ANTIMICROBIAL PROPHYLAXIS

Antimicrobial prophylaxis has been recommended for infants and children with VUR after a UTI to prevent recurrence, given that the combination of VUR and infection is more harmful to the kidney than VUR alone.^{2,3} In children with high grade reflux who experience breakthrough infections, studies have demonstrated a small additional long term benefit of surgery versus antimicrobials alone.¹² Notably such studies did not include a control group of children who received neither antimicrobial prophylaxis nor surgery. Data addressing placebo (or no prophylaxis) versus prophylaxis (generally TMP-SMX or nitrofurantoin) are inadequate.¹³ A recent study of 180 children did not demonstrate benefit from prophylaxis in children with or without reflux.¹⁴ A large, multicenter study is needed to answer this important question, the implications of which could determine whether expensive radiographic studies should continue to be recommended routinely for all infants and young children with UTI.

Many children with recurrent UTIs, including those with breakthrough infections, have a dysfunctional voiding syndrome.¹⁵ Attention to recognized causes of “nonneurogenic neurogenic bladder,” such as constipation, may improve bladder emptying and reduce or eliminate UTIs and the need for antimicrobial prophylaxis.

BOTTOM LINE IN 2004

Although there are a number of controversial issues regarding UTI in infants and children, the following remain true: (1) symptomatic UTI is a relatively common cause of fever with no obvious source in infants; (2) urine culture remains the diagnostic standard; (3) oral treatment is equivalent to a par-

enteral/oral regimen for patients who are able to tolerate oral medication and are not toxic-appearing or severely dehydrated; (4) the majority of febrile infants with UTI have pyelonephritis; short course treatment should not be prescribed in this group; (5) currently US and VCUG are still performed, although their use is increasingly being questioned; the answer is likely to depend on future studies demonstrating whether prophylactic antibiotics are beneficial or not; (6) evaluation of children with recurrent UTIs should include consideration of a dysfunctional voiding syndrome.

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