Early treatment of acute pyelonephritis in children fails to reduce renal scarring: data from the Italian Renal Infection Study Trials


Nephrology, Dialysis, and Transplant Unit, Pediatric Department, Azienda Ospedaliera di Padova, Padova, Italy

Objectives: The American Academy of Pediatrics recommendation for febrile infants and young children suspected of having a urinary tract infection is early antibiotic treatment, given parenterally if necessary. In support of this recommendation, data suggesting that delay in treatment of acute pyelonephritis increases the risk of kidney damage are cited. Because the risk was not well defined, we investigated renal scarring associated with delayed versus early treatment of acute pyelonephritis in children. Methods: The research findings are derived from 2 multicenter, prospective, randomized, controlled studies, Italian Renal Infection Study 1 and 2, whose primary outcomes dealt with initial antibiotic treatment and subsequent prophylaxis, respectively. From the 2 studies, we selected the 287 children with confirmed pyelonephritis on acute technetium-99m-dimercaptosuccinic acid scans who underwent repeat scanning to detect scarring 12 months later. The children were 1 month to < 7 years of age when they presented with their first recognized episode of acute pyelonephritis in northeast Italy.

Results: Progressive delay in antibiotic treatment of acute pyelonephritis from < 1 to >/= 5 days after the onset of fever was not associated with any significant increase in the risk of scarring on technetium-99m-dimercaptosuccinic acid scans obtained 1 year later. The risk of scarring remained relatively constant at 30.7 +/- 7%. Clinical and laboratory indices of inflammation were comparable in all groups, as was the incidence of vesicoureteric reflux.

Conclusions: Early treatment of acute pyelonephritis in infants and young children had no significant effect on the incidence of subsequent renal scarring. Furthermore, there was no significant difference in the rate of scarring after acute pyelonephritis when infants and young children were compared with older children.

Editorial Comment

Because of the long-term effects of pyelonephritis in children, including hypertension, proteinuria, and chronic renal failure, these authors studied whether early treatment of acute pyelonephritis diminishes renal scars in 287 children in a multicenter open-label parallel-group trial in Italian children, presenting with their first documented episode of acute pyelonephritis.

Initially the children were randomized to receive in one group either co-amoxiclav, or parenterally administered ceftriaxone. The second group was randomized to treat with antibiotic prophylaxis versus no treatment in a follow up study. Children were one month to seven years of age and acute pyelonephritis was the diagnosis when WBC > 25 cells/microliter in the urine, and a growth of a single organism of > 100,000 colonies in two consecutive tests as well as two or more of the following criteria: fever > 38°C, increased erythrocyte sedimentation rate or C-reactive protein level or neutrophil levels above normal for the age. Children are only included in the study with acute positive technetium DMSA scans performed within ten days of beginning antibiotic treatment and follow up scans 12 months later, and ultrasounds were also done.

There was no significant difference in the incidence of scarring with progressive delay and the initiation of antibiotic therapy from 1 to > 5 days after the onset of the fever. This was true for the subgroup of patients under two years of age. The scarring changes were found to be independent of early resolution of fever.
This article is discouraging in some respects since it has been long-held that prompt aggressive antibiotic treatment will diminish renal scarring in the setting of acute pyelonephritis. It would encourage the use of prophylactic antibiotics to prevent pyelonephritis except recent studies have cast a long shadow on the efficacy of prophylactic antibiotics to do this. Data also shows that the overall risk of scarring was independent of age between one month and seven years in this large study population. This would also suggest that early stoppage of prophylactic antibiotics and follow up in vesicoureteral refluxing patients may not be a wise choice also.

This is very good data in spite of the results confusing clinicians with older studies, it sheds light on the fact that this topic is one to be watched carefully in the future to guide further management.

Dr. Brent W. Snow
Division of Urology
University of Utah Health Sci Ctr
Salt Lake City, Utah, USA
E-mail: brent.snow@hsc.utah.edu

Undescended testis in older boys: further evidence that ascending testes are common
Guven A, Kogan BA
Department of Pediatric Surgery, Gulhane Military Medical Academy, Etlik, Ankara, Turkey

Introduction: We recommend orchiopexy between 9 and 18 months of age for surgical, testicular, and psychological reasons. However, in practice, we observed many patients coming to orchiopexy at a later age. To understand this difference better, we reviewed our experience with patients undergoing late orchiopexy.

Methods: We reviewed retrospectively the office medical records of all boys who had undergone an orchiopexy between July 1997 and April 2006. We defined a “late” orchiopexy as that performed at 4 years of age or later. Each boy was examined carefully by a pediatric urologist, and preoperative, intraoperative, and postoperative findings were reviewed.

Results: There were 191 late orchiopexies in 177 patients (from a total of 587 orchiopexies in 552 patients). Median age at the operation was 7.2 years (range, 4.0-16.2). Preoperatively, the testes were palpable in 140 (72%) and nonpalpable in 51 (28%). The apparent reason for the late orchiopexy was an ascending testis (previously descended) in 85 (45%), parental delay in 41 (22%), late referral in 39 (20%), and iatrogenic cryptorchidism in 18 (9%). Ascended testes were more likely to have a history of being retractile (85% vs. 30%), to have a patent processus vaginalis (78% vs. 54%), and to be localized to the superficial inguinal area (87% vs. 50%).

Conclusions: Primary care provider and parent education on the benefits of early orchiopexy is important, but in addition, ascending testes are much more common than previously thought. Patients with retractile testes should be followed regularly.

Editorial Comment
This manuscript explores orchiopexies in boys over four and compares them to patients who were under four years of age. 552 had 587 orchiopexies. 177 of these boys had 191 orchiopexies over the age of four. The stated reasons were ascending testicles in 45%, parental delay in 22%, referral or insurance problems in 20%, entrapped testes in 9%, with the remaining cases uncertain. 85% of the ascending testis group and 30% of the others had a history of retractile testes. Palpable testes were found in 93% of the ascending testes and only 58% of the other patients. The ascending testes were more likely to be found in the superficial inguinal pouch (87%) while only 50% of the other categories had the testicles in the superficial inguinal pouch with a statistical difference of $p < 0.001$. The processus vaginalis was more likely to be patent in the ascending testis.
group (78%) than the other group (54%) with a p-value of < 0.001. Excluding the iatrogenic group where the testes were stuck with scar tissue, the p-values were still significant.

It is becoming better understood that some testes that were found in the scrotum ascend and become fixed in a non-scrotal position. It is interesting to note that the ascending testes are more likely to be in the superficial inguinal pouch and more likely to have a patent processus vaginalis than the other delayed orchiopexy patients. It is still important for urologists to recognize that early orchiopexy before the second year of life has significant benefit. Educating primary care physicians and referring physicians about early referral is still the best policy.

Dr. Brent W. Snow  
Division of Urology  
University of Utah Health Sci Ctr  
Salt Lake City, Utah, USA  
E-mail: brent.snow@hsc.utah.edu