Normal Dimercaptosuccinic Acid Scintigraphy Makes Voiding Cystourethrography Unnecessary after Urinary Tract Infection

Iulian Preda, MD, Ulf Jodal, MD, PhD, Rune Sixt, MD, PhD, Eira Stokland, MD, PhD, and Sverker Hansson, MD, PhD

Objective To test the hypothesis that infants with dilating vesicoureteral reflux (VUR) have abnormal acute dimercaptosuccinic acid (DMSA) scintigraphy results, as was suggested by an earlier retrospective study.

Study design We conducted a prospective study of infants <1 year old with first diagnosed symptomatic urinary tract infection at the Children's Hospital of Göteborg, Sweden. Two hundred ninety consecutive children (161 boys and 129 girls) with complete records were examined. Renal ultrasound scanning and DMSA scintigraphy were performed within a few days from diagnosis, and VCU was performed within 2 months.

Results VUR was found in 52 children, of which 27 had dilating VUR (grade III-V). DMSA scintigraphy results were abnormal in 149 infants (51%), 105 of 238 (44%) without VUR, 18 of 25 (72%) with VUR grade I to II, and 26 of 27 (96%) with VUR grade III to V ($P < .001$).

Conclusion DMSA scintigraphy results were abnormal in all 27 infants with dilating VUR except 1. This single false-negative finding should be compared with 140 unnecessary VCU investigations. This supports our hypothesis that DMSA scintigraphy results are abnormal when there is dilating VUR. Thus, a normal DMSA scan makes VCU unnecessary in the primary examination of infants with UTI. *(J Pediatr 2007;151:581-4)*

Urinary tract infection (UTI) occurs in about 2% of both infant boys and girls <1 year of age.[1] Some infants have congenital abnormalities, and permanent renal damage that potentially can cause long-term problems develops in some infants. It has therefore become clinical routine to perform imaging studies to identify abnormalities and renal damage. Various combinations of ultrasound scanning (US), voiding cystourethrography (VCU), and scintigraphy are used, and there is an ongoing discussion about the indications for imaging in infants and children with UTI.[2-5]

Traditionally, focus has been on the detection of vesicoureteral reflux (VUR) as a risk factor. Although the importance of VUR is being questioned,[6,7] there is a significant relation between dilating VUR (grades III-V) and permanent renal damage.[3] Non-dilating VUR (grades I-II) is of low clinical significance[8] and does not lead to further follow-up in our protocol for treatment of children with UTI. Long-term complications are primarily related to renal damage rather than to VUR. Furthermore, VCU is an unpleasant invasive procedure causing radiation and risk of catheter-induced UTI.

In an earlier retrospective study, we showed that a strategy to perform VCU only in patients with abnormalities on the dimercaptosuccinic acid (DMSA) scan to identify patients with dilating VUR would have reduced the number of VCUs by half.[3] This study was designed to test the hypothesis that dilating VUR rarely occurs when acute DMSA scintigraphy results are normal.

METHODS

During a 3-year period, we prospectively recorded all infants <1 year old with UTI at our hospital. Infants living within the catchment area of the hospital and diagnosed with a first symptomatic community acquired UTI at the emergency department were eligible for the study. Children with known urogenital or anorectal malformations or neurologic diseases were excluded.

Investigations, treatment, and further management followed hospital guidelines. Bacteriuria was defined as any growth of bacteria in urine from a suprapubic bladder

CRP	C-reactive protein	UTI	Urinary tract infection
DMSA	Dimercaptosuccinic acid	VCU	Voiding cystourethrography
MAG3	Mercaptoacetyltriglycine	VUR	Vesicoureteral reflux
US	Ultrasound scanning		

From the Departments of Pediatrics (I.P., U.J., S.H.), Pediatric Clinical Physiology (R.S.), and Pediatric Radiology (E.S.), The Queen Silvia Children's Hospital, Sahlgrenska Academy at Göteborg University, Göteborg, Sweden.

Submitted for publication Feb 8, 2007; last revision received Apr 10, 2007; accepted May 1, 2007.

Reprint requests: Sverker Hansson, The Queen Silvia Children's Hospital, SE-416 85 Göteborg, Sweden. E-mail: sverker.hansson@gu.se.

0022-3476/$ - see front matter

10.1016/j.jpeds.2007.05.008

Table I. Description of infants with incomplete imaging investigation

Eligible children	325
■ VCU not performed	11*
- Parent decision	7
- Protocol violation	3
- Catheter failure	1
■ DMSA scan not performed within 30 days	24
- Performed later	21†
- MAG3 scan instead	3‡
Total included	290

*DMSA scan performed in 10, all with normal findings.
†VCU performed in all; VUR grade IV and grade I performed in 1 infant each.
‡All 3 with uptake defects.

aspiration or ≥100,000 colony-forming units in urine from a midstream or bag sample. The acute infections were treated with co-trimoxazole or a cephalosporin.

The imaging protocol included renal and bladder US and ^{99m}technetium DMSA scintigraphy as acute investigations and VCU within 2 months after the diagnosis. Dilatation at US examination was defined as an anterior-posterior diameter of ≥7 mm or a dilatation of calyces or ureters. Patients in whom DMSA scan was delayed >30 days were not included in the analysis. Static renal scintigraphy was performed 3 to 4 hours after injection of DMSA in a dose of 1 MBq/kg body weight (minimum, 15 MBq). Images were obtained in 1 posterior and 2 oblique projections, with 300,000 counts in the posterior view. A focal reduction or absence of uptake in ≥1 areas in the kidney was considered abnormal. A kidney with relative function ≤44% was also classified as abnormal. The radiological examinations were performed according to standard procedures of the pediatric radiology department. VUR was graded I to V according to the recommendation of the International Reflux Study in Children.[9] Additional examinations, such as intravenous urography, dynamic renal scintigraphy, or computerized tomography were performed on an individual basis according to findings at the primary investigation.

From June 2002 to June 2005, 325 infants were eligible and prospectively recorded. All were investigated with US, but 35 were not studied with VCU or DMSA scan according to the protocol (Table I). Thus VCU was not performed in 11 infants, acute DMSA scintigraphy was delayed >30 days in 21 infants, and a mercaptotriacetyltriglycine (MAG3) instead of DMSA scan was performed in 3 children. Ten of the 11 children without VCU had normal DMSA scan results; in 1 child, no scan was performed. Of 21 children with a delayed DMSA scan, 14 had normal results and 7 had abnormal results. Of the children with abnormal results, 1 had VUR grade IV and 1 had VUR grade I. Three children with pronounced dilatation of the upper urinary tract were investigated with MAG3 instead of DMSA scan, and all 3 had abnormal renal imaging but none of them had VUR. The investigation protocol was hence fulfilled in 290 infants, 161 boys with a median age of 2.7 months and 129 girls with a median age of 7.4 months.

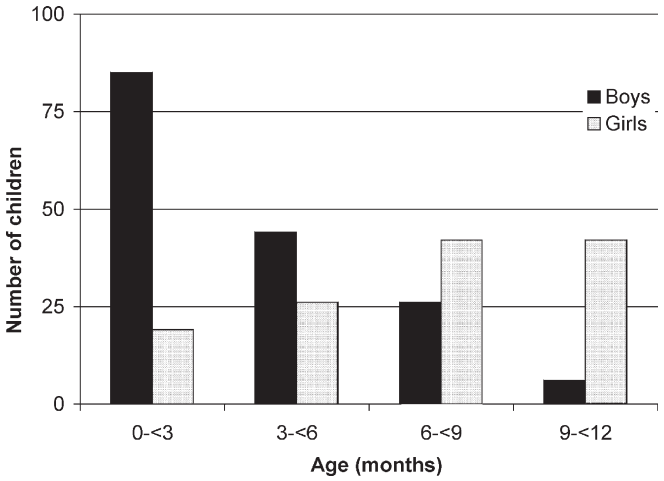

Figure 1. Age distribution of 161 boys and 129 girls with first known UTI.

The median temperature was 39.3°C (range, 36.5-41.1°C); ≥38.5°C was seen in 229 infants (79%). The median C-reactive protein (CRP) level was 72 mg/L (range, 0-360 mg/L); 231 infants (80%) had CRP levels ≥20 mg/L. The bacteriuria was caused by *Escheerichia coli* in 265 cases (91%), *Klebsiella/Enterobacter* in 11 cases, Enterococci in 4, Proteus in 3, and 1 case each of coagulase negative staphylococci, *Staphylococcus aureus*, *Citrobacter*, *Haemophilus parainfluensae*, *Serratia*, *Pseudomonas,* and beta-hemolytic streptococci.

DMSA scintigraphy was performed a median of 5 days after admission (range, 0-22 days), in 74% of cases within 1 week and in 97% of cases within 2 weeks. Analysis of the DMSA scans were performed by a clinical physiologist (R.S.), and the VCUs were performed by a radiologist (E.S.) without knowledge of other data.

Statistical Analyses

The statistical analyses were performed by using SAS software version 8.2. For comparisons between dichotomous values, the Fisher exact test was used, and for ordered values, the Mantel–Haenszel χ^2 test was used. The capacity of DMSA scintigraphy to detect children with VUR ≥3 was determined by calculating sensitivity, specificity, negative and positive predictive values, and likelihood ratios with 95% CIs. Likelihood ratio positive was defined as Sensitivity/(1-Specificity), and likelihood ratio negative was defined as (1-Sensitivity)/Specificity.

The study was approved by the research ethics committee of Göteborg University (Ö118-02).

RESULTS

As illustrated in Figure 1, the boys in this study were significantly younger than the girls ($P < .001$).

US showed dilatation in 48 patients (17%), 14 of whom (5%) had an anterior-posterior diameter >10 mm. Renal duplication was observed in 10 patients (3%), and unilateral