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Original Article

Primary urinary tract infection in infants: Prophylaxis for uncomplicated pyelonephritis

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SUMMARY:

Background: Urinary tract infection (UTI) is one of the most common causes of unexplained fever in infants with a reported prevalence range of 5–11%. The clinical and laboratory findings were reviewed, and diagnosis and treatment for 95 infants with primary UTI were evaluated in this study.

Methods: All patients underwent renal ultrasonography, voiding cystourethrogram and 99mTc dimercaptosuccinic acid (DMSA) scan during hospitalization before treatment, with treatment consisting of 2- or 4-week appropriated antibiotic therapy for the patients associated upper UTI, followed by a second DMSA scan 6 months after therapy.

Results: In the present study the main symptom of UTI in infants was fever. High white blood cell count was not necessarily present, and urinalysis was also an imperfect diagnostic tool for discriminating UTI. In addition, colony count from urine culture and kidney ultrasonography was not efficacious in terms of predicting the occurrence of pyelonephritis. Intravenous antibiotic for 1 week followed by 3 weeks of the same oral antibiotic provided good prophylaxis for uncomplicated pyelonephritis.

Conclusion: Four weeks of antibiotic treatment resulted in good recovery from pyelonephritis in the present sample of infant primary UTI cases. voiding cystourethrogram, DMSA and ultrasonography scanning should be performed in primary infant UTI.

KEY WORDS: **infant, pyelonephritis, urinary tract infection.**

Urinary tract infections (UTI) are a common clinical problem and potentially serious source of morbidity in febrile infants, with reported prevalence ranging between 5% and 11%.[1] Pyelonephritis is detected in 20–40% of infants with upper tract infections. Importantly, early detection and prompt treatment of the associated structural defects protects the kidneys from reinfection and subsequent scarring.[2] Generally, however, medical practitioners order urine tests selectively, focusing on younger and frail infants and those without apparent fever sources.[3] Because of this practice and despite the prevalence of pyelonephritis, UTI are easily missed in a large proportion of cases, especially during infancy. Moreover, no test is available that can detect UTI in this age group rapidly and reliably, with urine culture remaining the standard method. It has been reported that haemocytometer white blood cell (WBC) count is a significantly better predictor of UTI in febrile infants.[4] In addition, it is very important to identify and differentiate between lower and upper UTI because this is the principle determinant of the duration of antibiotic treatment.[5,6] The standard therapy for upper UTI is appropriated antibiotics for 10–14 days.[7,8] It would be of interest, therefore, to establish whether the accepted regimen is adequate in terms of subsequent prevention of pyelonephritis.[9,10] The clinical and laboratory findings for a sample of 95 infants with primary UTI were analysed, and diagnosis and treatment were reviewed. Diagnoses were confirmed by urine culture reliability. Cases of antenatally diagnosed hydronephrosis and those with incomplete radiological investigations were excluded from the study.

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SUBJECTS AND METHODS

After informed consents had been obtained, 95 hospitalized paediatric cases of primary UTI (male, 54; female, 41; age range

Table 1 Personal and clinical characteristic data of patients

	Upper UTI (pyelonephritis) ($n = 52$) n (%)	Lower UTI ($n = 43$) n (%)	Total ($n = 95$)
Age (months)			
<1	20 (38.5)	4 (10)	24
2–5	15 (28.8)	27 (64)	42
6–12	17 (32.7)	12 (27)	29
Sex			
Male	30 (58)	24 (56)	54
Female	22 (42)	19 (44)	41
Fever (°C)			
38–38.5	15 (28)	10 (23)	25
38.6–39	17 (33)	12 (27)	29
39–40	15 (28)	19 (45)	34
>40	5 (11)	2 (5)	7
First DMSA			
Time since UTI diagnosis	52 (100)	0	52
Second DMSA (+6 months)			
Group 1	0	0	24
Group 2	16 (57.1)	0	28
VCUG			
Negative	48 (92.3)	41 (95.3)	89
Positive	4 (7.7)	2 (4.7)	6

DMSA, dimercaptosuccinic acid; UTI, urinary tract infection; VCUG, voiding cystoureterogram.

6 days–12 months) were recruited for this investigation. Diagnosis was confirmed by culture of urine samples obtained from suprapubic bladder puncture or transurethral catheterization. Imaging studies consisted of renal ultrasonography (US), voiding cystoureterogram (VCUG), and 99mTc dimercaptosuccinic acid (DMSA) scan. Renal parenchymal pathology was defined as mild, moderate or severe based on split renal uptake of >40%, 20–40% or <20%, respectively.[11] Blood culture was also performed. The upper UTI cases, diagnosed based on positive result of DMSA scan and urine culture ($n = 52$), were randomly assigned to two groups based on duration of treatment with appropriated antibiotics (intravenous first week, oral thereafter) selected based on the results of urine culture and sensitivity test as follows: group 1 ($n = 24$), 4 weeks; and, group 2 ($n = 28$), 2 weeks. All of the infants underwent repeat DMSA 6 months post-treatment.

Statistical analysis

Microsoft Excel and Statistical Package for the Social Sciences (SPSS, Chicago, IL, USA) software were used to store and process the data. Descriptive statistics, frequency values and percentages, *t*-test and one-way ANOVA were used for data comparison and statistical evaluation.

RESULTS

The study sample consisted of 54 male and 41 female infants with primary UTI. The patients' personal and clinical characteristics are summarized in Table 1. All children were 12 months of age or below, and none of the male infants had been circumcised. Urine specimens were collected either via bladder aspiration ($n = 44$) or transurethral catheterization ($n = 51$), with UTI diagnosed from positive urine culture of a single organism $\geq 10^3$ WBC/mm^3.[6,12] *Escherichia coli* (95%) was by far the most commonly isolated organism in urine culture, with *Klebsiella pneumoniae*, *Pseudomonas aeroginosa* and *Muganella morganii* also identified. The main clinical symptoms was fever; however, maximum temperature did not predict lower or upper tract infection. Other symptoms included poor feeding and reduced activity. When the laboratory parameters and results of imaging study were compared with the DMSA finding, haemocytometer WBC count, standard urinalysis and colony count of urine culture were not significantly correlated with pyelonephritis distribution (Figs 1,2). Further, kidney echo did not predict risk of pyelonephritis. Repeat DMSA scan was performed after treatment with appropriated antibiotics after 6 months in the pyelonephritis cases, with no evidence of photopenic defects or renal parenchyma scarring identified in group 1 ($n = 24$; 4 weeks). By contrast, however, only 12 of the pyelonephritis cases in group 2 ($n = 28$, 2 weeks) were improved ($P < 0.05$). Recurrent infection was only found in the cases involving vesicoureteral reflux (VUR) ($n = 6$), with VCUG very helpful in terms of detecting these UTI abnormalities. No bacterial growth was identified in the blood cultures of both groups.

DISCUSSION

Infants and children are among the specific subpopulations at increased risk of UTI, which elevates the incidence of pyelonephritis. Although most boys reportedly have primary, reflux-associated renal damage, most girls suffer scarring related to recurrence of febrile UTI.[13] The aim of the present investigation, therefore, was to determine the combination of initial diagnostic tests and follow-up management best suited to specific patient groupings in terms of minimization of such adverse outcomes. Moreover, UTI in

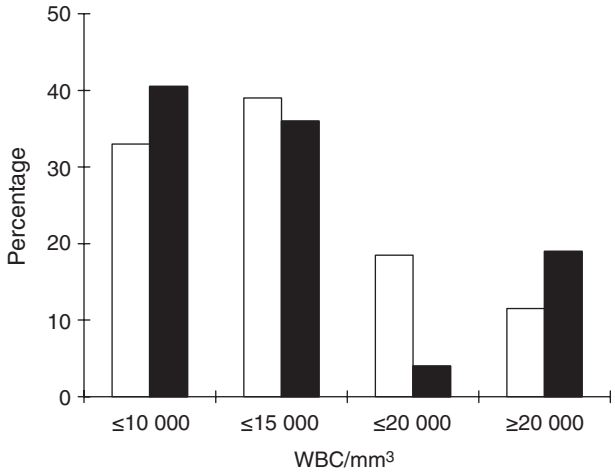

Fig. 1 Peripheral blood white blood cell (WBC) count in upper and lower urinary tract infections ($P < 0.05$). (□) Lower urinary tract infection; (■) pyelonephritis.

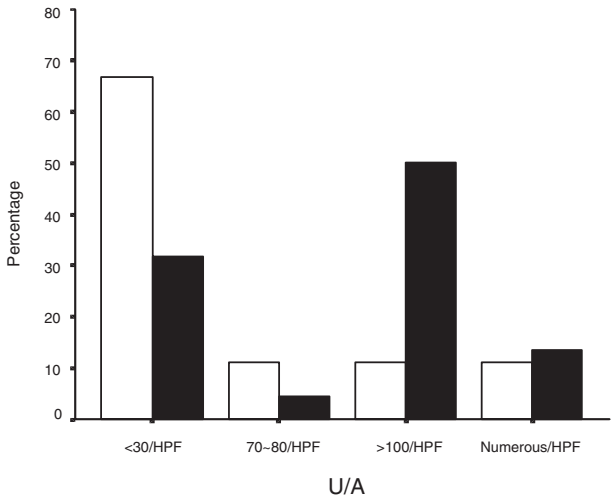

Fig. 2 Urine white blood cell count in upper and lower urinary tract infections ($P < 0.05$). (□) DMSA-1-negative; (■) DMSA-1-positive. DMSA, dimercaptosuccinic acid; HPF, high-power field; U/A, urinalysis.

infants may present a range of severity from lower to upper tract infection and pyelonephritis, and the respective presentations may be vague and have non-specific symptoms. Thus, early diagnosis of acute pyelonephritis is a challenge, and UTI should be considered in all infants with fever where other sources have been excluded.[14,15] In our study of 41 female and 54 male infants with confirmed diagnoses of primary UTI, 55% had pyelonephritis (42% and 58%, respectively) (Table 1) and fever was the predictive symptom identified, although some instances were associated with poor appetite and reduced activity. Maximum fever was associated with urine testing, particularly in uncircumcised male infants, and WBC; however, it was not correlated with the incidence of pyelonephritis (Fig. 1). Physicians should send urine samples, which obtained by suprapubic bladder puncture or transurethral catheterization for culture in all infant cases suggestive of UTI, despite the reported contamination rate of 36.8%; although second urine culture reduces the overall rate to 12.6%.[16] This contamination rate suggests that the proper urine collection procedure is transurethral catheterization or superpubic aspiration. In another study, WBC counts provided a more valid and precise prediction of UTI in febrile infants than standard urinalysis; however, this finding contrasted with the results of the present study (Fig. 2). *E. coli* was the pathogen in 90–95% of cultures, with organism colony count not predictive of the site of infection. Doppler sonography was neither highly specific for pyelonephritis nor correlated with positive DMSA renal scan in any age group.[17] Further, correlation was not demonstrated between the clinical symptoms of UTI, urinalysis results, urine culture and the type of the microorganism, WBC count in peripheral blood, US findings, or clinical presentation of pyelonephritis.

Accurate diagnosis of acute pyelonephritis from clinical and laboratory parameters is often difficult in children and infants. In the present study, 17, 24 and 7 of the sample had mild, moderate and severe renal parenchymal pathology, respectively. VUR may result from inadequate length of the intravesical ureteric tunnel or from urodynamic dysfunction.[18] Voiding cystourethrogram detected VUR in 6.3% of the patients, with this accuracy possible due to the exclusion of prenatally diagnosed hydronephrosis cases. In the present study, all six patients with reflux grade 2–3 had suffered reinfection by *E. coli* despite 2 or 4 weeks of antibiotic treatment. In another study, it was suggested that most recurrent UTI are endogenous relapses rather than reinfections caused by new organisms.[19] In the present study, parenteral antibiotics were given to the patients for the first week, followed by oral antimicrobial therapy. Split renal uptakes were resolved in group 1 patients (4-week treatment), with no renal scarring identified at the follow-up DMSA scan after 6 months and no recurrent infections found. In group 2, however, 16 (57%) pyelonephritis cases were refractory after 2 weeks of appropriated antibiotic treatment ($P < 0.05$). Another unresolved issue was the overestimation of pyelonephritis from DMSA scan.[20]

In conclusion, based on the results of the present study, it appears reasonable to recommend 4 weeks antibiotic treatment for primary infant UTI with uncomplicated pyelonephritis to reduce the risk of recurrence upper UTI and subsequent scarring. Moreover, VCUG, DMSA and US scanning should be routine for infants with primary UTI to prevent pyelonephritis.

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