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Comparison of the Voiding Cystourethrogram Results One and Three weeks after the First Urinary Tract Infection in 1-Month to 15-Year-Old Children

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Introduction

Urinary tract infection (UTI) is one of the most common problems in infants and children and is one of the most important risk factors of vesicoureteral reflux (VUR). The retrograde flow of the urine from the bladder to the ureter and renal pelvis results in hypertension and chronic kidney disease if not treated in time or properly.

Introduction: To determine whether the timing of voiding cystoureterogram (VCUG) in the first or the third week after a diagnosis of urinary tract infection (UTI) is important in the diagnosis and severity of VUR.

Materials and Methods: In this case-control study, 72 children between 1 month and 15 years old diagnosed with their first episode of UTI were investigated over one year. The study population was divided into 2 groups of 36, early (VCUG in the first week after UTI) and late (VCUG 3 weeks after UTI), and compared the severity and incidence of reflux in both groups.

Results: The prevalence of VUR was 66.6%. Twenty-two cases in the first group (61%) and 26 cases in the second group (72.2%) presented with VUR. The peak age of the disease in both groups was 1-3 years with a female predominance. The most common germ detected was E-Coli and the most common presentations were fever (87.5%) and dysuria (26.3%).

Conclusions: As VUR following UTI is very common in children and is one of the most important risk factors of early hypertension and chronic renal failure, early diagnosis by VCUG seems to be useful in all UTI patients before discharge.

Keywords: Urinary Tract Infection; Vesico-Ureteral Reflux; VCUG; Child.

Running Title: VCUG Results One and Three weeks after the First UTI

The mean prevalence of UTI is 3-5% in girls and 1% in boys in spite of variations in different populations and the most common pathogen is E-Coli (75-90%) [1,2]. Although a renal/bladder ultrasound is recommended as the routine imaging after a diagnosis of UTI, a VCUG is the screening study of choice to detect VUR. In a study investigating the optimal timing of VCUG after UTI,

the authors suggested that it should be performed 3 to 6 weeks after the first UTI since there may be transient reflux immediately after a UTI secondary to inflammatory changes at the ureterovesical junction [1,3,4]; So, VUR should occur more commonly when the VCUG is performed earlier. Some studies have suggested that a VCUG should be immediately performed after a negative urine culture following proper UTI treatment. Some authors believe that early diagnosis of VUR is so important that a VCUG should be done before discharge in admitted patients and during treatment in outpatients since many patients do not return for further examination after discharge or treatment [1]. The objective of this study was to determine whether the timing of VCUG (in the first or the third week after a diagnosis of UTI) is important in the diagnosis and severity of VUR.

Materials and Methods

Study Design:

This case-control study was conducted on 72 children (1 month to 15 years old) with prove first UTI who were referred to nephrology ward and clinic of Mashhad Sheikh Hospital from July 2006 to 2008 in whom cystourethrography (VCUG) was indicated. Necessary parameters of the study and the general information of the patients were extracted from valid references.

Hospital admission criteria included age less than 1 year, bad or toxic general condition, fever (temperature equal or more than 39 °C), oral intake intolerance and vomiting, dehydration, uncooperative parents, or medication refusal by the patient, signs and symptoms in favor of UTI included fever of unknown origin, dysuria and frequency, abdominal or flank pain, sudden incontinency during the day or night, failure to thrive, hematuria, and signs of septicemia in infants younger than 3 months.

In order to prove UTI, urine analysis and urine culture were taken from all children and sent to the laboratory in less than 30 minutes. Urine samples were taken midstream in patients who had adequate urine continence and by the suprapubic method or catheterization in patients with urine incontinence.

Definitions:

UTI was defined as one of the below:

- a) A colony counts of more than 10^4 in a midstream sample along with active urine analysis and clinical symptoms

- b) A colony counts of more than 10^3 by catheterization along with active urine analysis and clinical symptoms
- c) The presence of at least one bacteria in a suprapubic sample along with active urine analysis and clinical symptoms

Active urine analysis was defined as pyuria (more than 5 WBC in each HPF), positive nitrite, or the presence of bacteria in a fresh urine sample.

Proper oral antibiotic was selected according to antibiogram results in outpatients. An intravenous third generation cephalosporin (ceftriaxone or cefotaxime) or ampicillin plus aminoglycoside were administered in admitted patients.

Renal and urinary tract ultrasonography was performed for all patients during the first week of diagnosis.

In this study, pyelocaliectasis was defined as pyelocaliceal system dilatation more than 5 mm, and a ureter diameter more than 5 mm was considered as ureter dilatation. A bladder wall thickness equal to or more than 4 mm was considered an abnormal finding. Any kind of bladder diverticulum was also considered pathologic.

After 48 hours of adequate treatment, urine analysis and urine culture were retaken to evaluate the response. In case of negative urine culture results, a standard VCUG was performed to diagnose vesicoureteral reflux (VUR). The patients then were categorized into two groups of "Early" and "Late" as below:

The first group (Early group) included patients who underwent VCUG during the first week of UTI diagnosis.

The second group (Late group) included patients who underwent VCUG after the third week of UTI diagnosis.

Diagnosis and Management:

The Early group patients underwent VCUG before hospital discharge and during UTI treatment but the Late group patients received proper prophylactic antibiotics in 1/3 to 1/5 of the therapeutic dose after UTI treatment was completed and then underwent VCUG after 3 weeks. A contrast VCUG was taken in a standard way for every patient by experienced radiology technologists in the pediatric radiology ward under the supervision of a radiologist. After appropriate cleansing and disinfecting of the perineal area, an 8-gauge feeding tube or a 5-gauge catheter was used considering the patients' age. The bladder was then filled with a contrast medium the volume of which was estimated according to the bladder capacity in milliliter (using the formula; $[7 \times \text{weight}]$

(kg)] in under 1 year infants and the formula [30 X (age(year)+2)] in older children). The parents were also educated to help by taking adequate care of the child and the catheter.

VUR was categorized into 5 grades according to international references:

Grade I: Reflux into nondilated ureter

Grade II: Reflux into renal pelvis and calyces without dilation

Grade III: Reflux with mild to moderate dilation and minimal blunting of fornices

Grade IV: Reflux with moderate ureteral tortuosity and dilation of pelvis and calyces

Grade V: Reflux with gross dilation of ureter, pelvis, and calyces, loss of papillary impressions, and ureteral tortuosity

The two mentioned groups were compared in terms of gender, fever or other infection signs, and ultrasound and VCUG reports. The severity and grade of VUR were also compared. All demographic, clinical, and paraclinical investigations were computerized and analyzed by SPSS version 22. Descriptive statistical methods included central tendency indexes, distribution indexes, and frequency distribution. Chi-2 was used to compare qualitative variables between groups. T-Test was used for quantitative variables if they had a normal distribution, nonparametric tests were employed if the parameters did not have a normal distribution, and other parametric or nonparametric tests were used if required. P values less than 0.05 were considered significant.

Results

The results of the data analysis of 72 patients are as follows:

In this study, the frequency UTI was 95.8% (69 patients) in girls and had a female preponderance in both groups. Thus, there was a significant difference between genders in each group (p=0.001) but the difference was not significant between the two groups (P>0.05).

VUR peaked in children aged 1 to 3 years in both groups. The minimum age of UTI was 45 and 90 days old and the maximums age was 11 and 13 years old in the Early and Late group, respectively; Chi-square showed no significant difference. The mean age of UTI was 26±13.8 months in the first group and 23±15.4 in the second which had no significant difference according to T-Test (P>0.05). No significant difference was found in external genitalia abnormalities between the two mentioned groups; only 3 girls (4%) had abnormal genitalia as labia minor adhesion.

As it was expected, the most common organisms was E-Coli (83.3%) followed by Klebsiella (15.7%). There was no significant difference in pathogens between the two groups (P>0.05) (Table 1).

Table 1. Organisms in urine culture results of the groups

Group	E-Coli	Klebsiella	Staph saprophyticus
Early	80.5%	16.6%	2.7%
Late	86%	13.8%	

According to statistics, the prevalence of right pyelocaliectasis was significant different between the groups (P=0.03) but this difference was not significant for the left kidney (P>0.05). Only one patient in the first group was diagnosed with ureteral dilatation on ultrasound and all the patients had normal ureters in the second group. The bladder wall thickness and the presence of diverticulum were also examined by sonography and the results showed 10 patients had increased wall thickness (27.7%) and one patient had diverticulum (2.7%) in first group. Ultrasound also showed that 19 patients (26.3%) had at least one of the mentioned abnormalities in the second group.

Table 2. Ultrasound Results in groups

Group	Normal ultrasound	Abnormal ultrasound
Early	66.6%	33.3%
Late	36.1%	63.8%

The prevalence of VUR was 61% (22 patients) in the first group and 72.2% (26 patients) in the second group. There was no significant difference neither in the prevalence of VUR nor in VUR severity and grade between the two groups (P>0.05). In addition, 33.3% of the patients in the first group and 63.8% of the patients in the second group had pathologic findings on ultrasonography and the most common reported abnormality was right pyelocaliectasis in both groups with a prevalence of 11% in the Early group and 33.3% in the Late group, which showed a significant different (p=0.03). However, no difference was found for the left side (P>0.05).

Other reported abnormalities were increased bladder wall thickness, bladder diverticulum, and

ureteral dilatation with no significant difference between the two groups ($P>0.05$).

As our main purpose in this study was to investigate the prevalence and severity of VUR in children with UTI, standard VCUG was performed for both the Early and Late groups and the results were compared with other previous studies.

Fisher's exact test showed a significant difference in the frequency of VUR between the two groups ($P=0.028$) but no difference was found between left and right VUR ($P>0.05$) or in VUR prevalence of the two groups.

As for UTI signs, the most and least frequent sign was fever and urine incontinency, respectively. The prevalence of fever was significantly different between the two groups ($p=0.04$) as it was seen in 86% of the first and 61% of the second group.

Our analysis showed VUR grade 2 and 3 were the most prevalent grades in both groups. There was no patient with grade 4 VUR of the right kidney in the first group; moreover, the lowest VUR grades in the left kidney were grade 4 and 5. There was no grade 5 VUR in neither kidneys of patients in the second group.

There was no significant difference in the VUR grade between the two groups according to Chi-square test ($P>0.05$).

Discussion

UTI secondary to VUR is one of the childhood bacterial infections which can result in multiple complications such as hypertension, kidney scar, and eventually chronic kidney disease. It can be prevented by the early diagnosis and prompt treatment [1].

The purpose of this study was to investigate the impact of the timing of VCUG after the first UTI.

In a similar study, McDonald et al investigated 352 UTI patients aged less than 10 years old. There was no significant difference in this parameter between these groups which is compatible with our results [5]. The prevalence of UTI was higher in younger children.

Caggiani et al studied 63 patients with UTI and reported 88.8% of them were below 2 years of age [6].

We noticed a female predominance in all the reviewed studies [5,6,7,8].

Similar to previous studies, UTI was much more prevalent in girls than boys in our study since girls have a shorter urethra and its opening is closer to the anus.

We found no significant difference between fever and the other UTI signs [6]. Therefore, as fever is

one of the most frequent UTI signs in children, urine analysis and culture are necessary in every child with fever of unknown origin.

Similar to previous studies, we found that E-Coli was the most common pathogen [5,6,7]. This point should be kept in mind for antibiotic prescription.

Although no difference was found in the prevalence of VUR between the two groups in the previous studies [5,6,9], it has to be noted that, VCUG was performed for all the UTI patients in the first group and for 48% of the second group, since many of the patients did not return for follow up after discharge [5].

Since the prevalence of VUR was higher in our study than previous studies and VUR is inherited in an autosomal dominant fashion, the prevalence must be higher in some specific populations and therefore VCUG is suggested in patients with indication.

Similar to previous studies, we found no significant difference in VUR severity between the two groups [5].

Conclusions

As a result, it seems that a delay in VCUG has no impact on the VUR grade.

According to the results of this study and considering the high prevalence of VUR in some specific populations like Iran, it is suggested to perform VCUG before discharge in patients with negative second urine culture.

Conflict of Interest

Authors declare that they have no conflicts of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in this study.

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