

Research Article

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Comparison of Two Diagnostic Methods of Vesicoureteral Reflux in Children with Urinary Tract Infection

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Ahmad Ali Nikibakhsh,^{1*}
Shams Vazirian,²
Abolhassan Seyedzadeh,²
Mahmood Jalili,²
Negare Hoseinzade¹

1 Urmia University School of Medicine, Iran.

2 Kermanshah University School of Medicine, Iran.

*** Corresponding Author**
Nikibakhsh Ahmad Ali, MD
Nephrology-Urology and Transplantation Research Center, Urmia University School of Medicine, Iran
Email: anikibakhsh@yahoo.com
Tel: +9891444113802

Introduction: Urinary tract infection is common in children and vesicoureteral reflux is one of its predisposing factors. Contrast cystography and radionuclide cystography are two common methods for the diagnosis of vesicoureteral reflux. This study compared two methods, indirect radionuclide cystography (IRC) with voiding cycling method and voiding cystoureterography with contrast (VCUG).

Materials & Methods: This analytical study was conducted on 55 children with urinary tract infection who were referred to our nephrology clinic in six months. In order to diagnose urinary reflux, 109 ureters (one child had a single kidney) were evaluated using IRC and VCUG methods with a one-month interval. Kappa coefficient was used to determine the agreement rate, and the McNemar's test was employed to compare the ability of two methods in the diagnosis of VUR.

Results: The mean age of the children was 5.4 years (range: 6 months to 13 years). A total of 38 children (69%) were female and 17 (30.9%) were male. Seventy percent of the children older than three years old had urinary control. From 109 ureters, 29 (26.4%) with urinary reflux were detected by the IRC method, whereas only 15 (13.6%) were diagnosed using VCUG.

Statistically, the two methods did not have agreement in the diagnosis of VUR (Kappa: 0.556, $p < 0.001$) and the IRC method had more power to diagnose VUR in comparison with VCUG.

Conclusions: Although we observed a significant difference in the diagnostic value of two methods, the choice of diagnostic method depends on specific technical conditions. However, in ideal conditions, the IRC method is suggested to be performed since it is more powerful in the diagnosis of urinary reflux.

Keywords: Vesico-Ureteral reflux; Urinary Tract Infections; Pediatrics; Diagnostic Imaging.

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Introduction

Vesicoureteral reflux (VUR) is an important anatomical abnormality which predisposes the person to urinary tract infection. Recurrent pyelonephritis can lead to kidney scars and hypertension [1-6]. Recent studies indicate that VUR is hereditary with a familial prevalence [4-7]. The prevalence of VUR is higher in younger children. It is about 25 percent in children

younger than four years with urinary tract infection, 12 percent in children between 4-12 years, and 5 percent in adults [4,7,8]. Despite early diagnosis and aggressive treatment of VUR, reflux nephropathy remains a significant cause of end stage renal disease in children [6,7]. Therefore, detection of VUR has an important role in pediatric medicine. The methods of the diagnosis of vesicoureteral reflux (VUR), considering the

risks of radiation exposure and invasive procedures, are challenging and have been questioned in the recent literature. Therefore, it is important for the pediatric nephrologists and urologists to reevaluate the diagnostic methods of VUR. An ideal method for the diagnosis of VUR would have some characteristics like no radiation, no bladder catheterization, no sedation, low cost, high sensitivity, and provision of complete anatomical details.

The common methods that are used to diagnose this disorder include cystography with contrast (VCUG) (with catheter and radiation), which is an invasive method, [8- 11] and direct radionuclide cystography (DRC), which is performed with less radiation but with a urinary catheter. Despite the use of digital and pulsed fluoroscopy in girls, the average ovarian radiation dose has been shown to be about 10 times greater in VCUG when compared to RNC [12].

In spite of the advantages of VCUG, it is influenced by specific conditions like the size and type of the catheter, the amount of bladder filling, the height of the contrast fluid to develop the necessary pressure for entering the bladder, hydration conditions, volume, temperature, and the density of the contrast fluid, and it is impossible to regard them all to create an ideal condition.

In the DRC method, radiopharmaceuticals diluted with normal saline are injected into that bladder with a catheter and then the kidney and bladder are scanned; in the IRC method, radiopharmaceuticals are intravenously injected and after the renogram period, entrance of the isotope into the bladder and reflux are evaluated [8, 11-19].

The IRC method has some important advantages. For example, it is more similar to physiological conditions, no catheter is used, and the patient receives less radiation. In this method, it is possible to obtain some information on the kidneys function as well as ureteropelvic drainage. In comparison with VCUG, IRC is less biased by other conditions [1, 8, 11].

In recent years, especially in Europe, indirect radionuclide cystography (IRC) without using a urinary catheter (which is a noninvasive method) has been used [8, 11, 13].

In recent decade, through cycling voiding cystography (CVC), it has been possible to diagnose hidden cases of VUR. This method, which is performed by multiple bladder fillings, is of specific importance because of the low amount of radiation in comparison with cycling VCUG.

Most of the studies have indicated that DRC is highly accurate in the diagnosis of VUR, but there are different results regarding IRC. Some studies have reported acceptable constancy of the results of IRC in the diagnosis of VUR while some have not [8,11,19-24]. This study evaluated the constancy of two methods, IRC with VCUG, in the diagnosis of VUR.

Materials and Methods

This analytical study was done to determine the diagnostic value and constancy of two methods. Using convenience sampling, 55 children with UTI who referred to nephrology clinic in 6 months were enrolled in the study. The diagnosis of UTI was made according to the following criteria:

1. More than 5 white blood cells (WBC) per high-power field (HPF) in a urine specimen
2. Isolation of a bacterial strain in the quantitative count of $\geq 10(5)$ cfu/ml¹³ in the culture of a urine specimen
3. DMSA scan showing inflammation or scar in the kidney cortex

The DMSA scan was performed for patients who were clinically suspicious for UTI but did not have the first or the second criterion. By this way DMSA scan confirm the UTI.

Patients with hydronephrosis without ureteral dilatation on ultrasonography and radionuclide renogram were excluded.

VCUG and IRC were performed for the patients with a one-month interval.

IRC was performed in the Children's Hospital but VCUG was done in two other private centers, which were blind to the study.

After injection of the radioisotope intravenously (^{99m}Tc-diethylenetriamine penta-acetic acid) in the standard dose, renogram was performed. In order to evaluate VUR, scan was performed before and after voiding after about one to two hours. In this method, after the first voiding, enough time is given to the child to refill the bladder and then, the patient is evaluated for VUR before and after the second voiding.

Naturally, children who are cooperative are kept in a room and scan is performed immediately after the beginning of the voiding, which is considered as the after voiding phase.

Routinely, VCUG is performed for diagnosis of VUR in children with UTI, but because of performing IRC as an additional procedure, informed consent was obtained from the parents. Data were

analyzed by Kappa coefficient to determine the constancy rate and McNemar's test to compare the ability of two methods in the diagnosis of VUR.

Results

In this study, 55 children with UTI were evaluated and 109 ureters (one child had a single kidney) were investigated. The mean age of the children was 5.4 years (minimum 6 months and maximum 13 years). A total of 38 children (69%) were female and 17 (30.9%) were male. The age group 4-6 years with 22 patients (40%) had the highest frequency. Seventy percent of children older than three years had urinary control (Table 1). From 109 ureters, 29 (26.4%) with urinary reflux were detected with IRC whereas only 15 (13.6%) were diagnosed with VCUG (Table 2). The agreement rate of the two methods in the right kidney (Kappa: 0.48, $P < 0.05$), in the left kidney (Kappa: 0.62, $P < 0.01$), and in both kidneys (Kappa: 0.55, $P < 0.001$) was significant, and there was a significant difference in their diagnostic power (Table 3-5). Six right ureters were diagnosed with VUR using both methods; however, in eight other right ureters, VCUG was negative while IRC was positive for VUR (Table 3). VUR was detected in eight left ureters with both methods but IRC showed VUR in seven left ureters which were negative for VUR on VCUG (Table 4). In both sides, 14 ureters had VUR by both methods; there was only one ureter which had VUR on VCUG while IRC was negative. IRC detected 14 ureters jointly with VCUG, and 15 ureters were positive for VUR (despite negative VCUG results) (Table 5). According to the significant difference between the two method and the Kappa coefficient (Kappa: 0.556) and McNemar's test ($P = 0.001$), it could be concluded that these two method did not show agreement in the diagnosis of VUR in children with UTI and IRC was more powerful in diagnosing this disorder.

Discussion

VCUG with contrast is a standard and common method to detect VUR and other anatomical disorders in children with the first episode of UTI [8, 20, 25]. Direct radionuclide cystography (DRC) has the highest sensitivity in the diagnosis of VUR and because of the less radiation rate, was commonly employ this technique in the follow up of VUR [3, 4, 5, 26].

Ultrasonography with contrast is a method with less radiation that has showed acceptable

constancy with VCUG in the diagnosis of VUR in several studies [27, 28].

Cystography with multiple bladders fillings is a technique that improves the ability to diagnose VUR according to several studies [4, 8, 29].

Multiple studies have compared the diagnostic power of IRC with VCUG and DRC with different results; some of them have reported an acceptable agreement between these methods and some indicated that the power of IRC in comparison with VCUG and DRC was about fifty percent [12,19, 21, 26-32]. In a study by Pinthus JH et al, none of the patients who had normal IRC at the time of the acute illness had VUR in the long term. They found that early usage of IRC had a high sensitivity and accurate negative predictive value for detecting VUR [30]. Indirect RNC has some special characteristics including offering the possibility of detecting VUR without bladder catheterization, physiological setting with natural bladder filling, and the ability to assess the upper tract differential renal function and urinary tract system drainage with the injected radioisotope.

Magnetic resonance urography (MRU) was introduced in pediatric urology in 1999. This recent method is increasingly being advocated as a single imaging modality in UTI. MRU may provide information which can be obtained by using the combination of VCUG and DMSA scan in UTI. The unique advantage of MRU is its ability to distinguish between renal congenital cortical defects and acquired scarring.

MRU, like IRC, can provide information about renal perfusion, renal parenchymal and calyceal wash-out, and the differential renal function and can therefore serve as an important tool in prognosticating and following children with renal dysfunction. In infants and small children, MRU needs anesthesia. This is the most important disadvantage of MRU in comparison with IRC.

The results of this study showed that IRC was more powerful in detection and diagnosis of VUR in comparison with VCUG and these two methods did not have an acceptable constancy with each other. The high diagnostic power of IRC and VCUG could be justified in this way: we perform IRC using the CVC method, which could improve the diagnostic power of IRC [10, 19, 20, 21, 22]. The VCUG method is influenced by specific conditions like the size and type of the catheter, the amount of bladder filling, and volume, temperature, and the density of the contrast fluid, and it is impossible to regard them all to create an ideal condition. Therefore, one of the disadvantages of this method is that it depends on special technical

conditions. False positive cases could be another reason for the high power of IRC. In studies that compared IRC and DRC, false positive cases were reported in the IRC method [19]. In the studies in which IRC had a lower sensitivity in the diagnosis of VUR, diuretics were used but it was avoided in our study, which may be one of the reasons of the increase in the diagnostic power of IRC [22].

Conclusions

Considering the mentioned reasons in our study, the agreement between IRC and VCUG was not acceptable; moreover, the diagnosis of VUR could be improved using IRC with the CVC method. In order to evaluate the accuracy of IRC with the CVC method and compare it with other methods, further studies with larger sample sizes and standard methods are suggested. Because of the advantages of IRC in the diagnosis of VUR, especially in older people, and if other studies confirm its high sensitivity, it could be used an alternative noninvasive method in the diagnosis of VUR.

Table 1. Frequency of children with UTI according to age group

Age group	Frequency	Total	Percentage
Younger than 4	15		27.3
4-6 years old	22		40
7-9 years old	11		20
Older than 10	7		12.7
Total	55		100

Table 2. Frequency of VUR according to IRC and VCUG methods

Age group	Frequency	VCUG	IRC
Right	7 (12.72)		14 (25.45)
Left	8 (14.54)		15 (27.27)
Total	15 (13.63)		29 (26.36)
Total	15 (13.63)		29 (26.36)

Table 3. Constancy of VUR diagnosis in right kidney by IRC and VCUG methods
Kappa: 0.48 and P< 0.05

VCUG \ IRC	With VUR (+)	Without VUR (-)	total
With VUR(+)	6	1	7
Without VUR(-)	8	40	48
Total	14	41	55
Total	14	41	55

Table 4. Constancy of VUR diagnosis in left kidney by IRC and VCUG methods
Kappa: 0.62 and P< 0.01

VCUG \ IRC	With VUR (+)	Without VUR (-)	Total
With VUR(+)	8	0	8
Without VUR(-)	7	39	46
Total	15	39	54

Table 5. Constancy of VUR diagnosis in both kidneys by IRC and VCUG methods
Kappa: 0.55 and P< 0.001

VCUG \ IRC	With VUR (+)	Without VUR (-)	Total
With VUR(+)	14	1	15
Without VUR(-)	15	79	94
Total	29	80	109

Conflict of Interest

None declared

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None declared

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