

Original Research Article

Study of DMSA (99mTc-dimercaptosuccinic acid) scan disorders in children 1-12 years with first acute pyelonephritis and its association with vesicoureteral reflux

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ABSTRACT

Background: Acute pyelonephritis and vesicoureteral reflux are one of the main causes of renal scarring in children, which can lead to serious complications such as hypertension and chronic renal failure. The aim of this study was to evaluate the scan disorders in children aged 1-12 years with acute pyelonephritis and its relation with ureteral bladder reflux.

Methods: This retrospective cross-sectional descriptive study was conducted on all patients who had been diagnosed with febrile UTI for 4 years (2012-2015) in Ardebil's Children's Hospital. Information about 99mTc-DMSA scan and ultrasonography and cystourethrography of patients were extracted from the files and then analyzed by statistical methods in SPSS.19.

Results: 148 children (9 boys and 139 girls) with a range of 1 to 12 years old (mean age of 52.34 ± 4.34 months) were included in the study. Of these, 123 patients were subjected to cystourethrography after a negative urine culture. A 99mTc-DMSA scan report in the acute phase of the disease was abnormal in 80.4% of the children. VCUG and RNC tests were performed in 123 patients, in 70 (57%) normal cases, and in 53 cases (43%) of urinary reflux. The incidence of reflux with abnormal 99mTc-DMSA scan was 42%. There was no significant correlation between the prevalence of reflux in patients with abnormal 99mTc-DMSA scan in two groups of 1-4 years old and more than 4 years old. No significant difference was found in patients with abnormal scan in responding to treatment and comparing fever after admission in patients with normal 99mTc-DMSA.

Conclusions: The results indicate high prevalence of reflux in patients with acute pyelonephritis. Due to the high sensitivity of the scan to detect pyelonephritis and, Pyelonephritis.

Keywords: Acute pyelonephritis, Children, 99mTc-DMSA scan, Vesicoureteral reflux

INTRODUCTION

Vesicoureteral Reflux (VUR) is the return of the urine from the bladder to the ureter or the kidney, which can be due to obstruction of the lower bladder or other abnormalities of secondary urinary tract. In this case during urination, the kidneys are exposed to doubled

hydrodynamic pressure and the incomplete emptying of the ureter and bladder makes the patient susceptible to kidney infection.¹ Primary VUR occurs in less than 1% of the general population while more than 50% of children with urinary tract infection (UTI) had reflux.^{2,3} UTI is the most common genitourinary disorders in children which its important in diagnosis abnormalities of the urinary

tract and its association with bacteremia in infants.^{4,5} Infants and children with UTI due to kidney parenchyma are at risk of kidney scarring such as kidney growth disorder, hypertension, growth failure, proteinuria and chronic renal failure.^{6,7} The prevalence of UTI varies with age, and in girls were 1-3% and boys were 1%.⁸ The importance of reflux related to pyelonephritis which was associated with complications such as scarring of kidney tissue, high blood pressure, and chronic renal failure.^{9,10} Pyelonephritis is a common kidney acute bacterial infection be with symptoms such as fever, abdominal pain, irritation and frequency urination along with abnormal urine analysis.^{11,12} Clinical signs and symptoms of acute pyelonephritis in children was nonspecific and for its diagnosis we used dimercaptosuccinic acid (DMSA) scan.^{13,14} 99mTc-DMSA scan has sensitivity higher than ultrasound and intravenous pilography and currently the selective method of diagnosis of acute pyelonephritis.¹⁵⁻¹⁸ Urinary cystoidorography (VCUG) or radionuclide cystography (DRC) is used to diagnose of abnormalities in bladder, urethral or reflux.³ This method shows more anatomical details and its sensitivity is high but it is an invasive test with high radiation.¹⁹ Children with normal 99mTc-DMSA scan during acute pyelonephritis are rarely infected to VUR and so, failure to perform VCUG in these children can significantly reduce perform of this invasive test.^{20,21} The aim of this study was to evaluate 99mTc-DMSA scan disorders in children aged 1-12 years with the first acute pyelonephritis infection and its association with VUR.

METHODS

This retrospective cross-sectional descriptive study was performed on children aged 1 to 12 years old hospitalized in Ardabil city hospital during the years 2012-2016 by diagnosis of acute pyelonephritis. In this study, 148 children and 296 kidney units were studied. Information of 99mTc-DMSA scan, ultrasound and cystourethrography were extracted from patients file. Patients with fever above 38 degrees, presence of more than 5 white cells in urinalysis, positive urine culture with 100,000 colonies growth in a culture medium in a urine sampling method or urine sample with a sachet and detection of acute pyelonephritis in a 99mTc-DMSA scan of people whose urine culture was negative for receiving antibiotics before preparing the culture sample. Children with a history of UTI, congenital malformations, neurogenic bladder and structural disruption or urinary tract obstruction and history of surgery in the urinary system due to the possibility of chronic pyelonephritis or chronic renal failure and children under one year of age due to high prevalence of reflux and non performing 99mTc-DMSA routine scan excluded from the study. To study the status of renal parenchyma during 1-5 days after treatment, 99mTc-DMSA scan was performed. One or more areas with a reduced cortical absorption and reduced renal absorption were considered abnormal in the 99mTc-DMSA scan. Kidney involvement were classified in three groups mild (radiation therapy in the form of

topical), medium (radiotherapy removal between 20-40%) and severe (atrophic kidney or radiotherapy less than 20%). The normal rate of radiotracer withdrawal was reported to be between 45% -55%. In the acute stage of disease, sonography of the urinary system was performed by pediatric radiologist and intravenous antibiotic therapy was performed for 14 days. In order to match the degree of reflux in an isotope type radiographic method, mild reflux in the cyst graph isotope is equivalent to grade II, I, medium grade type III and severe type IV reflux disease in the VCUG standard cyst gram. Data from 99mTc-DMSA scan and sonography and bladder reflux degree were recorded in a checklist and analyzed using statistical tests such as T and chi-square in SPSS.19. The p<0.05 was set as significant.

RESULTS

In this study, 148 children aged 1-12 years with a mean age of 52.34±34.34 months and 296 kidney units were entered. The mean age of the girls was 51.67±51.52 and the boys were 62.66±31.62 months. In this study, 80.4% of children and 47.6% of kidneys had an abnormal 99mTc-DMSA scan. 49 (33.1%) of the right renal unit and 92 (62.2%) of the left renal unit had acute pyelonephritis (Table 1).

Table 1: Results of scan by sex and kidney units.

Scan DMSA	Sex				Kidney units	
	Girl		Boy		N	%
	N	%	N	%		
Normal	28	20.1	1	11.1	155	52.3
Abnormal	111	79.9	8	88.9	141	47.7
Total	139	100	9	100	296	100

Out of 198 lesion locations, 48% were in the upper part, 23.2% in the middle third and the rest were lower and prevalence of scarring was 11.5%. Urinary tract reflux was detected with VCUG or RNC tests in 43% of patients and 26.4% of kidneys. Of all kidneys with urinary tract reflux, 2% were in grade I, 5.3% in grade II, 10.1% in grade III, 7% in grade IV and 2% in grade V. Of the 53 patients with reflux, 3 patients had normal 99mTc-DMSA scan and the rest were abnormal. 94% of all patients with low grade reflux (I, II), and 94.6% of patients with high grade reflux (V, IV III) had a lesion in their 99mTc-DMSA scan. The prevalence of reflux with abnormal 99mTc- DMSA scan was 42% (Table 2).

In ultrasonography, of 119 patients with abnormal 99mTc-DMSA scan and 29 patients with normal scan, 17 cases of pyelonephritis and 3 cases of renal lesion were observed and of all patients with a scan disorder, 71 (59.7%) had normal ultrasonography. In ultrasonography, acute pyelonephritis and renal lesions were 11.5% and 34.5%, respectively. Increased Cortical ecchymosis of the kidneys (Pyelonephritis) was 11.5% and mild to severe hydronephrosis was 17.6% and mild to severe hypertrophic was 3.4% and renal scar was 2% and cystitis

as bladder infection about 27%)Table 3). Out of 9 male patients, 7 cases (77.8%) had reflux. Comparison of the incidence of reflux in patients with abnormal 99mTc-

DMSA scan was not found in two age groups 1-4 and over 4 years.

Table 2: Results of cystourethrography and scan in patients and kidney units.

Urine cystourethrography		Patient		DMSA scan				Units of kidney	
		N	%	Normal		Abnormal		N	%
				N	%	N	%		
Reflux	-	70	57	1	25	69	58	181	61.1
	+	53	43	53	43	3	5.7	50	94.3
Type of reflux	One way	41	77.3	-	-	-	-	-	-
	Two way	12	22.7	-	-	-	-	-	-
Degree of reflux	I, II	16	30.1	1	33.3	15	30	18	7.3
	III, V, IV	37	69.9	2	66.3	35	70	47	19.1

Table 3: Results of sonography-ultrasonography and scan.

Scan disorder	Pyelonephritis in sonography			Ultrasonography				
	Yes		No	Normal		Abnormal		
	N	%	N	%	N	%	N	%
Yes	17	100	102	77.9	71	59.7	48	40.3
No	0	0	29	22.1	26	89.7	3	10.3

DISCUSSION

The aim of the treatment of pyelonephritis in children is to prevent and reduce the prevalence and long term complications of renal scarring. 99mTc- DMSA is currently the standard for the detection of acute parenchymal lesions and renal scarring in patients with pyelonephritis. Rushtan and Majd reported sensitivity and specificity of 99mTc DMSA scan in detecting pyelonephritis about 87% and 100%, respectively.²² Rickwood and Jacobson SH and Risdon RA reported DMSA scan sensitivity about 80-91% and specificity about 99-100%.²³⁻²⁵ In the study of Tseng et al, parenchymal pylonfrit lesions were observed in 70% of patients in 99mTc-DMSA scan.²⁰ In two study, the evidence of acute pyelonephritis in 99mTc-DMSA scans were seen in 79% and 78.8%, respectively.^{26,27}

In Hashemian et al study the prevalence of pyelonephritis in children aged 1 month to 11 years with UTI was 74.8%.²⁸ In the present study, in 80.4% of children with 99mTc-DMSA scan the pyelonephritis was observed which was consistent with the findings of the Hashemian study.²⁸ In this study, the prevalence of scarring was about 11.5% which was observed as irregular margin of kidneys in 99mTc-DMSA scan. In the study of Hoberman and MH Tseng and Mohkam et al, the prevalence of scarring in patients with pyelonephritis was 10%, 9.5% and 1.4%, respectively which was lower than the present study, while in the study of Lin KY et al, high percentage of scarring (57%) was observed.^{20,27,29,30} The

reason for this difference may be due to the difference in the number of samples and the heterogeneity in the patients such as the difference in age, sex, diagnostic Criteria for UTI, urinary tract reflux, urinary tract and genital anomalies, and genetic. VUR known as a risk factor for renal scarring in the present study, the prevalence of reflux was 43%, of which 42% were associated with an abnormal scan and in a study, VUR in children with acute pyelonephritis was 24% -39%.³¹

In the study of Hashemian and Tseng and et al, the rate of urinary tract reflux was 36.3% and 29.6%, respectively.^{20,28} Lin KY et al reported the prevalence of reflux in patients with abnormal 99mTc-DMSA scan about 31% that was 39% in Ditchfield and et al, and 37% in Majd et al and 34.6% in Ataei et al which all of them lower than the present study.^{30,32-34} Ajdinovic B et al in their study showed that the incidence of abnormal 99mTc-DMSA after kidney infection in cases with reflux was more than other cases. In patients with grade I and II reflux, the incidence of scarring is less than that of degree IV, V, and the probability of scarring in UTI cases with VUR is approximately 3 times that of a non VUR.¹⁹

Stokland and et al in a study showed that kidney damage increases significantly in children with high VUR in 99mTc-DMSA scan.³⁵ In this study, urinary reflux was found in 43% of patients who underwent VCUG, which was high compared to previous studies. 42% of refluxes were associated with an abnormal 99mTc-DMSA scan. Since the possibility of scarring in patients with acute

pyelonephritis and reflux is high, so timely diagnosis of VUR and performing 99mTc-DMSA scan to detect scarring and side-effects are effective.^{8,36-39} Sheu et al in a study, showed that performing of 99mTc-DMSA scan after acute pyelonephritis is a strong predictor of high grade reflux (III, IV, V) and Performing VCUG is recommended when the 99mTc-DMSA scan or ultrasound was abnormal because high grade reflux is associated with high probability of kidney scarring.⁴⁰

The present study showed that acute pyelonephritis can occur without VUR, but severe reflux can be major risk factor for acute pyelonephritis. In the present study, the majority of patients with low grade reflux showed lesion in 99mTc-DMSA scan and only 1 case had normal 99mTc-DMSA scan and of the 37 patients with high grade reflux (III, IV, V), only 2 cases had normal 99mTc-DMSA scan but there was no statistically significant relationship. In the present study, ultrasonography of 29 patients with normal 99mTc-DMSA scan only 3 renal lesion and in 119 patients with abnormal scan, 71 was normal and 17 cases as increased cortical echymosis. In Ataei et al study, in sonography of 41 patients with acute pyelonephritis renal lesions was observed in 16 patients.²⁶ As it is seen, the results of the present study emphasize the uncertainty of ultrasound as a method of imaging in evaluating patients with acute pyelonephritis.

The results showed that in boys aged 1 to 12 years, the number of boys with acute pyelonephritis is high compared with girls but the incidence of reflux is high and upside down the prevalence of infection in girls is high compared to boys, which is consistent with the findings of other studies.^{36,6} It seems that, severe urinary reflux can be a major risk factor for acute pyelonephritis in boys over one year.

There was no statistically significant difference in the response to treatment and the period of discontinuation of fever after admission of children with normal and abnormal DMSA 99mTc scan. In this study, the use of antibiotic by the parents up to few days before admission was an important factor in reducing the fever rate and the partial recovery rate of children with abnormal 99mTc-DMSA scan.

CONCLUSION

In the study of UTI with pyelonephritis symptoms, due to the high sensitivity of 99mTc-DMSA scan to detect pyelonephritis, invasiveness and high levels of VCUG radiation, it is possible to minimize the number of VCUG in patients by doing scan before VCUG and perform VCUG only in patients with abnormal scans.

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