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Absolute Renal ^{99m}Tc-DMSA Uptake and Renal Scan in Children with Vesicoureteral Reflux

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═국문초록═

방광요관역류를 가진 소아의 DMSA 스캔과 절대 신섭취율의 평가

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^{99m}Tc-dimercaptosuccinic acid (DMSA) 주사후 일정시간에 측정한 절대적 신섭취량은 기능이 살아있는 신피질량과 관계있다. 소아의 신기능은 출생후 계속 성숙되어 생후 약 1~2년에 성인의 기능에 도달하는데 DMSA 섭취도 성인과는 다른 양상을 보일 것으로 기대되며 신질환에서 절대적 신섭취율의 평가는 연령을 고려해야 할 것이다.

저자들은 DMSA 스캔을 시행한 소아 환자를 대상으로 스캔상 피질 결손이 없으며 양측신의 섭취율이 비슷하고 혈중 크레아티닌치가 정상인 경우를 대조군으로 하여 연령별 DMSA의 절대적 신섭취율을 구하였고 방광요관역류를 가진 환아를 대상으로 DMSA 스캔을 시행하고 신섭취율을 조사하였다.

1) 대조군은 모두 65명으로 좌우측 신섭취율의 유의한 차이는 없었으며 연령에 따라 2세경에 플라토에 도달하였는데 한쪽 신장의 평균섭취율은 3개월 미만이 14.5±3.1%ID, 3개월에서 6개월 미만이 17.2±2.1%ID, 6개월에서 1년 미만이 18.4±1.3%ID, 1년에서 1년6개월 미만이 19.3±1.1% ID, 1년 6개월에서 2년 미만이 21.9±2.0%ID, 2세이상 15세이하가 20.1±0.6%ID였으며 전체 평균섭취율은 19.4±0.5%ID(injected dose, mean±S.E.)였다.

2) 방광요관역류를 가진 환아는 55명(일측성 26명, 양측성 29명)으로 109신장을 대상으로 하였다. 방광요관역류의 정도와 피질결손의 수와는 대체로 비례관계가 있었으나 방광요관역류가 없으면서 피질결손이 있는 경우가 25신장중 2예(8%)였으며, 방광요관역류가 있는 84신장중 27예(32.1%), 이중에서 방광요관역류가 3도 이상인 62신장중 13예(21%)에서는 피질결손이 없었다.

3) 이환신의 DMSA 섭취율을 연령에 따른 대조군의 섭취율에 대한 비(섭취율비)로 나타내면 한쪽에 역류가 있을 때 이환신의 경우 0.55±0.06, 정상신의 경우 1.34±0.05이었으며, 양쪽에 역류가 있을 때는 평균 0.82±0.08(mean±S.E.)이었다.

4) 피질결손이 있는 신장의 절대 DMSA신섭취율은 감소되어 있었고 상대측 신장의 섭취율은 피질

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결손이 있더라도 대상적인 증가의 경향을 보였다.

이상의 결과로 소아에서 DMSA절대적 신섭취율의 연령에 따른 변화를 알수 있었으며 방광요관역류의 정도와 피질결손의 정도가 반드시 비례하지만은 않아서 시간경과에 따른 추후 검사가 필요하리라 생각된다. 또한 방광요관역류가 있는 환아에서 DMSA 섭취율로 신기능을 평가할 때, 특히 영유아에서 연령에 따른 고려가 있어야 할 것으로 보인다.

INTRODUCTION

^{99m}Tc-DMSA renal scan gives not only anatomic images but also quantitative informations about renal function. Renal ^{99m}Tc-DMSA uptake has been shown to correlate well with the effective renal plasma flow (ERPF), glomerular filtration rate (GFR) and creatinine clearance[1].

The absolute renal DMSA uptake of children is expected different from that of adults because renal function differs among age groups. To evaluate the renal function using absolute renal DMSA uptake, the age of children at the time of DMSA scan should be considered.

We measured the absolute renal DMSA uptake of each kidney in young control patients and investigated the scan findings and absolute renal DMSA uptake of children with vesicoureteral reflux (VUR).

METHODS

1. Patient Population

Sixty five children were chosen as disease control group (male 39, female 26, mean age±S.D., 4.7±4.1 years old) who had no evidence of VUR, obstruction and acute urinary tract infection, no cortical defect in DMSA scan and normal serum creatinine level. Fifty five children (male 33, female 22, mean age±S.D., 4.9±4.1 years old) who had VUR proven by radiologic voiding cystourethrography were included in this study, retrospectively. Twenty nine children had bilateral reflux and twenty six had unilateral reflux.

2. ^{99m}Tc-DMSA Renal Scan and Absolute DMSA Uptake

For measurement of the absolute renal DMSA uptake, we placed the syringe filled with ^{99m}Tc-DMSA 30 cm in front of gamma camera (Lem^{+}, Siemens) and counted the radioactivity using computer (MicroDelta, CDA. 64×64 matrix, word mode) (preinjected dose) for 1 minutes. After injection, we counted the remained radioactivity in the syringe by the same manner (postinjected dose). DMSA scans were performed three hours after the intravenous injection of 18.5−111 MBq(0.5−3.0 mCi) of ^{99m}Tc-DMSA. Images were acquired in the posterior, both posterior oblique projections, with the children laid prone and anterior projection with supine position for 500,000 counts using same camera with high-resolution collimator. We used the posterior planar images for renal DMSA uptake. Regions of interest were applied on each kidney and radioactivity in each kidney was counted. The C-shaped background region was placed laterally around each kidney and its radioactivity was counted for background correction. The renal depth was determined by using a calculation formula based on weight and height that was proposed by Tonnesen[2]. The absolute DMSA uptake of each kidney was expressd as %ID (injected dose=preinjected dose−postinjected dose) after subtrating the background activity and correcting for kidney depth and ^{99m}Tc decay by time.

Absolute ^{99m}Tc-DMSA renal uptake

$$=\frac{(\text{renal activity}-\text{background activity})}{e^{-\mu x}\cdot e^{-\lambda t}(\text{preID-postID})}\times 100(\%)$$

μ: 0.153(linear attenuation coefficient, cm^{-1})

x: depth of kidney (cm) t: time interval (hour)

λ: $0.693/T_p$(T_p: physical half-life of ^{99m}Tc)

We also used the DMSA uptake ratio (absolute DMSA uptake of patient/mean uptake of age-matched control) because the expected normal absolute uptake were not same among different age groups.

RESULTS

The changes of DMSA uptake of each kidney in control group is shown in Fig. 1. The DMSA uptake of children before 3 months old was 14.5±3.1% ID(mean±S.E.), then increased with the children's age and reached plateau which was adult level[3] at about 1-1.5 years old (21.9±2.0%ID).

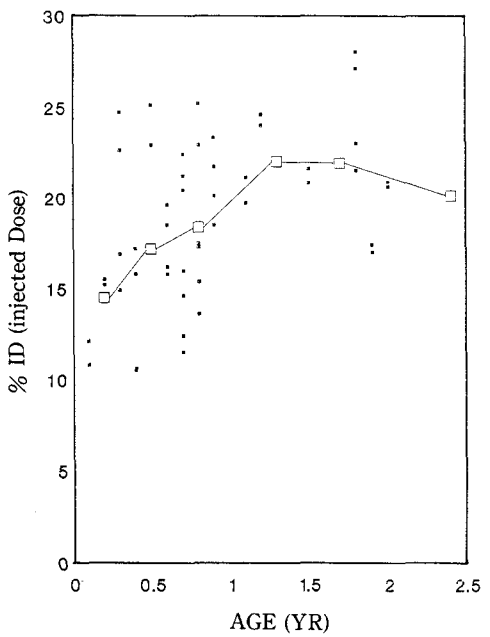

Fig. 1. The DMSA uptake of each kidney in control group.

Table 1. The Relation Between the Grade of VUR and the Number of Defects in the Patients with Bilateral VUR

Grade of VUR	No. of Defects					Small contracted
	0	1	2	3	Multiple	
I	1	0	1	0	2	0
II	9	0	1	0	0	1
III	5	6	3	2	0	1
IV	4	2	4	5	2	1
V	0	0	1	0	4	2

Table 2. The Relation Between the Grade of VUR and the Number of Defects in the Patients with Unilateral VUR

Grade of VUR	No. of Defects					Small contracted
	0	1	2	3	Multiple	
0	23	2	0	0	0	0
I	0	0	1	0	0	0
II	4	1	1	0	0	0
III	2	3	5	0	0	1
IV	1	1	1	1	1	2
V	1	0	0	0	0	1

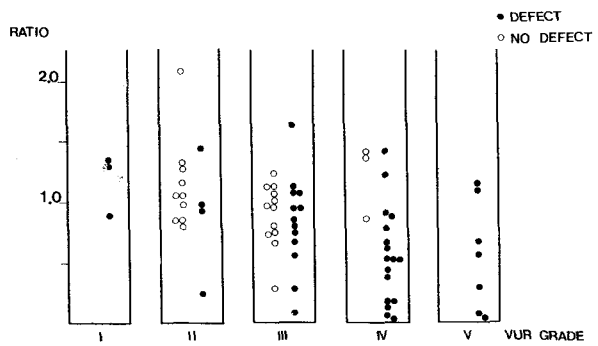

Fig. 2. The relation between renal DMSA uptake ratio and the grade of VUR.

The relation between the grade of VUR and the number of cortical defect is shown in Table 1, 2. In general, the more severe the grade of VUR, the more the number of cortical defect(s). But there were some exceptional cases. Two among 25 kidneys (8%) which had no demonstrable VUR showed cortical defect. 27 of 84 kidneys (32.1%) which had VUR, among these 13 of 62 kidneys (21%) which has VUR of grade 3 or more showed no cortical defect.

Fig. 2 shows the relation between renal DMSA uptake ratio and the grade of VUR. As the grade of VUR was severe, the renal DMSA uptake ratio was decreased, especially in the kidney which had cortical defect (s).

Fig. 3 shows renal DMSA uptake ratio pattern in children with unilateral VUR. In the left column which represents the uptake ratio of kidney which has no cortical defect, the uptake ratio pattern of normal and diseased kidney is not so different. But in the kidney which has cortical defect (s), as shown in the right column, the uptake ratio of diseased kidney is likely to be below 1.0 and that of normal (contralateral) kidney is usually above 1.0. There is a trend that the lesser the uptake ratio of diseased kidney, the greater that of normal (contralateral) kidney.

The uptake ratio in children with bilateral VUR is shown in fig. 4. The more seriously injured kidney, that has more cortical defects, is shown in the left column. The uptake ratio of more injured kidney is lesser than that of contralateral kidney. Usually, the lesser the uptake ratio of one kidney, the greater that of contralateral kidney.

DISCUSSION

Technetium-99m DMSA is an excellent renal cortical imaging agent that provides high resolution images of renal anatomy as well as individual function[4~8]. Many studies have shown that renal cortical scintigraphy is more sensitive than IVP and renal sonography in the detection of renal parenchymal injury[9~12]. Also, the relative uptake of ^{99m}Tc-DMSA by the kidneys has been shown to correlate closely with relative renal function[1,13,14].

The renal function of infant matures and reaches adult level at about 1~2 years old. In our study, the renal DMSA uptake increased with children's age after birth and reached plateau at about 1~1.5 years

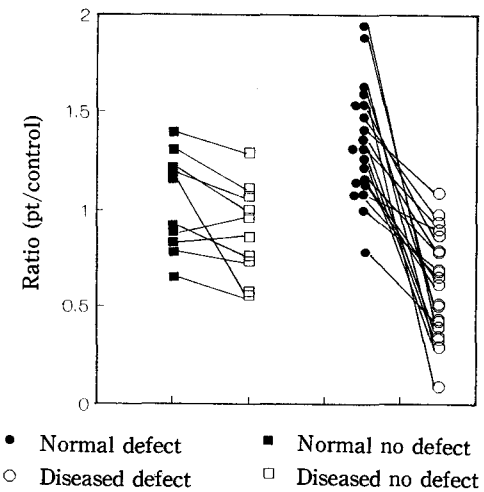

Fig. 3. Renal DMSA uptake ratio pattern in children with unilateral VUR.

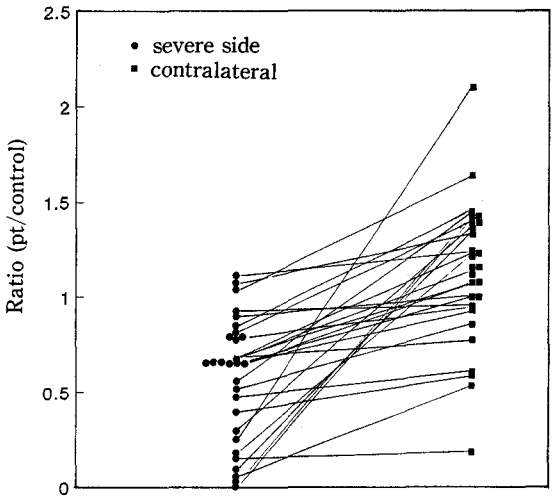

Fig. 4. Renal DMSA uptake ratio pattern in children with bilateral VUR.

old. It represents that the renal DMSA uptake correlates with renal function and was different among age groups especially early childhood. Also, our data showed that affected kidneys with defects or reflux could compensate the partner kidney with more ailments. For follow-up study in children with cortical defect(s), using the simple left-to-right ratio(R/L ratio) is not accurate because of the various factors such as increasing DMSA uptake along the growing age, the variable degree of compensation and functional recovery. Therefore the age of patients should be considered to evaluate the renal function by renal DMSA uptake, especially in young children. So we measured the DMSA uptake ratio, that is the ratio of the absolute renal DMSA uptake of patient to mean uptake of age-matched control to compare the DMSA uptake pattern in children with VUR.

There is many contradictory reports about the relation between the degree of VUR and number of cortical defects. One study have reported that the positive detection rate for renal defects depended on the severity of VUR[10]. Some other studies have reported that changes in the appearance of defects were independent of the presence or degree of reflux at presentation and symptomatic recurrence of infection[15] and new scarring in kidneys without reflux was as common as in those with reflux[16]. Our study also shows that the number of cortical defects is partly dependent on the degree of VUR but 32% of kidney with VUR had no cortical defect and 8% of kidney without VUR had cortical defect. These findings suggest that some other factors such as the children's age, disease duration and reponse to therapy should be considered.

The role of vesicoureteral reflux in the pathogenesis of renal scarring is controversial. The common assumption was that vesicoureteral reflux is a prerequisite for renal scarring[17,18]. In our study there is 2 kidneys (8%) which has cortical defect in the absence of VUR. We also noted that the kidney has cortical defect(s) not always in proportionate to the severity of VUR. 13 among 62 kidneys (21%) which had VUR grade 3 or more had no cortical defect. Recent reports have demonstrated the role of bacterial virulence and other host defense factors besides vesicoureteral reflux in the pathogenesis of renal scarring[19,20,21]. Other studies report that acute pyelonephritis in the absence of reflux is more common than previously thought, and that acquired renal scarring following urinary tract infection also occurs in the absence of demonstrable vesicoureteral reflux is more common than previously thought, and that acquired renal scarring following urinary tract infection also occurs in the absence of demonstrable vesicoureteral reflux[22,23]. Subsequent progressive renal scarring can be successfully prevented by keeping the patients free of infection.

In conclusion, because the severity of VUR does not always tell the degree of renal injury, we should evaluate the renal injury using renal DMSA scan and its absolute uptake. And we should consider the patient's age to evaluate the renal function using renal DMSA uptake, especially in young children. The relation between the degree of VUR and severity of renal injury may be followed by further study.

REFERENCES

1) Kawamura J, Hosokawa S, Yoshida O: *Renal function studies using ^{99m}Tc-dimercaptosuccinic acid. Clin Nucl Med 4:39-47, 1979*
2) Tonnesen KH, Munck O, Hald T, et al: *Influence on the radiorenogram of variation in the skin to kidney distance and the clinical importance hereof. In: Winkel K, Blaufox MD, Funck-Bretano J-L, eds, Proceedings of the international symposium on redionuclides in nephrology. Stuttgart, Thieme, April 1974, pp79-86*
3) Kim SE, DH Moon, DS Lee, et al: *Quantitation of renal function using absolute kidney uptake of ^{99m}Tc-DMSA. J Korean Med Ass 33:1345-1358, 1990*
4) Handmaker H, Young BW, Lowenstein JM: *Clini-*

cal experience with ^{99m}Tc-DMSA(dimercaptosuccinic acid), a new renal imaging agent. J Nucl Med 16:28-32, 1975

5) Kawamura J, Hosokawa S, Yoshida O, et al: *Validity of ^{99m}Tc-dimercaptosuccinic acid renal uptake for an assessment of individual kidney function. J Urol 119:305-309, 1978*

6) Taylor A Jr: *Quantitation of renal function with static imaging agents. Semin Nucl Med 12:330-344, 1982*

7) Gordon I, Evans K, Peters AM, et al: *The quantitation of ^{99m}Tc-DMSA in paediatrics. Nucl Med Comm 8:661-670, 1987*

8) Bingham JB, Maisey MN: *An evaluation of the use of ^{99m}Tc-dimercaptosuccinic acid (DMSA) as a static renal imaging agent.*

9) Björgivinsson E, Majd M, Eggli KD: *Diagnosis of acute pyelonephritis in children: Comparison of sonography and ^{99m}Tc-DMSA scintigraphy. Am J Roentgenol 157:539-543, 1991*

10) Itoh K, Yoshihumi A, Tsukamoto E, et al: *Single photon emission computed tomography with Tc-99m-dimercaptosuccinic acid in patients with upper urinary tract infection and/or vesicoureteral reflux. Ann Nucl Med 5:29-34, 1991*

11) Monsour M, Azmy AF, MacKenzie JR: *Renal scarring secondary to vesicoureteric reflux. Critical assessment and new grading. Brit J Urol 60:320-324, 1987*

12) Goldraich NP, Ramos OL, Goldraich IM: *Urography versus DMSA scans in children with vesicoureteric reflux. Ped Nephrol 3:1, 1989*

13) Daly MJ, Jones W, Rudd TG, et al: *Differential renal function using technetium-99m dimercaptosuccinic acid (DMSA): in vitro correlation. J Nucl Med 20:63, 1979*

14) Daly MJ, Henry RE: *Defining renal antomy and function with ^{99m}Technetium dimercaptosuccinic acid: Clinical and renographic correlation. J Urol 126:5-9, 1981*

15) Verber IG, Meller ST: *Serial ^{99m}Tc-dimercaptosuccinic acid (DMSA) scans after urinary infections presenting before the age of 5 years. Arch Dis Children 64:1533-1537, 1989*

16) Rushton HG, Majd M, Jantausch B, et al: *Renal scarring following reflux and nonreflux pyelonephritis in children: Evaluation with ^{99m}Technetium-dimercaptosuccinic acid scintigraphy. J Urol 147: 1327-1331, 1992*

17) Bailey RR: *The relationship of vesico-ureteric reflux to urinary tract infection and chronic pyelonephritis-Reflux nephropathy. Clin Nephrol 1: 132-141, 1973*

18) Smellie J, Edwards D, Hunter N, et al: *Vesicoureteric reflux and renal scarring. Kidney Int 8:S65-S72, 1975(suppl)*

19) Lombereg H, Hanson LA, Jacobsson B, et al: *Correlation of P blood group, vesicoureteral reflux, and bacterial attachment in patients with recurrent pyelonephritis. N Engl J Med 308:1189-1192, 1983*

20) Svanborg Edén C, Hanson CA, Jodal U, et al: *Variable adherence to normal human urinary tract epithelial cells of Escherichia coli strains associated with various forms of urinary infection. Lancet 2: 490-492, 1976*

21) Källenius G, Svenson SB, Hultberg H, et al: *Occurence of P-fimbriated Escherichia coli in urinary tract infections. Lancet 2:1369-1372, 1981*

22) Smellie JM, Normand ICS: *Bacteriuria, reflux, and renal scarring. Arch Dis Child 50:581-585, 1975*

23) Majd M, Rushton HG: *Renal cortical scintigraphy in the diagnosis of acute pyelonephritis. Semin Nucl Med 22:98-111, 1992*