Overall and Single-Kidney Clearance in Children with Urinary Tract Infection and Damaged Kidneys

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The overall and single-kidney clearance in children with acute urinary tract infection was investigated retrospectively using the combination of the relative ^{99m}Tc-dimercaptosuccinic acid (DMSA) uptake and the ^{51}Cr-ethylenediaminetetraacetic acid clearance. **Methods:** There were 180 patients with both normal kidneys, 56 with clear unilateral abnormalities on DMSA scintigraphy and 11 with two abnormal kidneys. Half of the patients were younger than 2 y, and because of the progressive maturation of the renal function, they were not considered in the analysis of the absolute overall and single-kidney clearance; nevertheless, they were included in the analysis of the relative DMSA percentage uptake. **Results:** When only one kidney was affected on DMSA scintigraphy, the clearance of the affected kidney was lower than on the normal side and often abnormally low. In these unilaterally affected kidneys, contralateral compensation mechanisms tended to occur, resulting in preservation of overall clearance. This compensation was probably not present only on the contralateral side. On the abnormal side, the clearance was normal in about half of the cases, probably because of intrarenal compensation occurring in regions not damaged by the infection. In addition to these compensation mechanisms, hyperfiltration was probably present in many cases of acute urinary tract infection with intact or unilaterally damaged kidneys.

Key Words: clearance; ^{99m}Tc-dimercaptosuccinic acid; ^{51}Cr-ethylenediaminetetraacetic acid; urinary tract infection; children

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During recent years, many reports have been devoted to the detection of acute renal lesions in children with urinary tract infection (UTI). ^{99m}Tc-dimercaptosuccinic acid (DMSA) scintigraphy is generally considered as the most sensitive tool for that purpose.

However, not much is known about the functional impairment associated with this acute condition. Few data are available concerning the overall renal function, and as far as we know, no data at all are related to single-kidney function, although the final aim in the management of these patients, in addition to the prevention of renal scars, is the preservation of renal function.

The aim of this paper is to evaluate the functional changes occurring during the acute phase of UTI.

MATERIALS AND METHODS

Patients

From a retrospective database, we reviewed all of the patients sent to the department of radioisotopes for evaluation of UTI between 1991 and 1996. These patients were admitted to the hospital on the basis of their clinical symptoms. No attempt was made to separate, on a clinical and biological basis, the patients with complicated UTI (acute pyelonephritis) from those with uncomplicated UTI (cystitis). Only patients having had both DMSA scintigraphy and ^{51}Cr-ethylenediaminetetraacetic acid (EDTA) clearance simultaneously within the first days of admission were considered. The DMSA reports were reviewed, and those with equivocal DMSA findings were rejected. Therefore, the data of 247 patients with either normal or clearly abnormal DMSA scintigraphy constitute the material analyzed in this study.

Radioisotopic Techniques

DMSA scintigraphy was performed 2–4 h after injection of a dose calculated according to body size (*1*). A posterior view was acquired in supine position using zoom facilities whenever necessary; oblique posterior views were performed systematically and pinhole views only occasionally.

Kidneys were classified as normal, abnormal and equivocal. A normal kidney shows regular, well-delineated contours and has a more active outer part (cortex) and less active inner part (medulla and calyces). Contour flattening or concavity is often observed at the superolateral level of the left kidney (spleen).

Abnormal kidneys include all types of abnormalities: hypoactive pole with indistinct margins, single or multiple cortical defects, normal- or small-sized kidney with deformed contours and diffuse hypoactive kidney without regional defects.

The result of the scintigraphy was considered as equivocal when it was not possible to decide whether or not the kidney was abnormal. These patients were deleted from the study. Therefore, the patients could be divided in three groups, according to the results of DMSA scintigraphy: those with two normal kidneys, those with clear unilateral abnormalities and those with clear bilateral abnormalities.

Quadrangular regions of interest were drawn over the two kidneys, and a small background above and below each kidney was

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subtracted. The contribution of each kidney was calculated and expressed in percentage of the total function. No correction was introduced for kidney depth.

^{51}Cr-EDTA was injected together with DMSA at a dose of 0.37–1.85 MBq in function of body size (*1*). A blood sample was taken at 120 min on a site different from the injection point. The dose, a standard of the dose and the residue of the dose after injection were measured twice on the gamma camera. The standard was diluted in 1000 mL, and an aliquot of this dilution, together with 1 mL of the serum sample, was measured twice in a well counter; a background was measured before and after the samples. The one blood sample clearance was calculated according to Ham and Piepsz (*2*), and the result was corrected for body surface and was expressed in milliliters per minute per 1.73 m^2.

Single-kidney glomular filtration rate (GFR) was estimated on the basis of the combination of ^{51}Cr-EDTA overall GFR and the left and right relative uptake obtained by means of the DMSA counts.

RESULTS

The characteristics of the DMSA findings are reported in Table 1. Half of the patients were younger than 2 y. There were 180 patients with both normal kidneys, 56 with unilateral abnormal kidneys and 11 with both abnormal kidneys. These proportions were almost the same younger and older than 2 y.

Overall Clearance (GFR)

Only patients older than 2 y were considered, because GFR corrected for body surface reaches the adult values only after 18 mo (*3*). There was a significant difference between patients with bilateral normal kidneys and those with bilateral abnormal kidneys ($P = 0.03$, unpaired t test) (Table 2). No significant difference could be found between patients with bilateral normal kidneys and those with unilateral abnormal kidney ($P > 0.2$, unpaired t test).

High clearance values (>140 mL/min/1.73 m^2) were found in 20% of the patients with either bilateral normal kidneys or unilateral abnormal kidney. In patients with bilateral abnormal kidneys, there were still 9% with high clearance values.

Low clearance values (<80 mL/min/1.73 m^2) were found in 2% of patients with bilateral normal kidneys, 8% of patients with unilateral normal kidney and 27% of patients with bilateral abnormal kidneys.

Single-Kidney Clearance

For the same reason as for the overall clearance, only patients older than 2 y were analyzed (Table 3).

TABLE 1
Patients and ^{99m}Tc-DMSA Scintigraphy

Patients	Kidneys on DMSA scintigraphy: Both normal	Unilateral abnormal	Both abnormal	Total
Younger than 2 y	82	31	0	113
Older than 2 y	98	25	11	134
Total	180	56	11	247

TABLE 2
Overall ^{51}Cr-EDTA Clearance in Children Older than 2 Years

Patients' condition	n	Mean (mL/min/1.73 m^2)	SD (mL/min/1.73 m^2)
Both normal kidneys	98	120	30
Unilateral abnormalities	25	112	33
Bilateral abnormalities	11	98	29

Single-kidney GFR in patients with bilateral normal kidneys was not significantly different from that of the normal patients with unilateral abnormal kidneys ($P = 0.18$, unpaired t test). In this last group of patients, the clearance of the abnormal kidney was significantly lower than on the contralateral side ($P < 0.0001$, paired t test). The single-kidney GFR in patients with two abnormal kidneys was significantly lower than in patients with bilateral normal kidneys ($P = 0.004$, unpaired t test).

In patients with bilateral normal kidneys, 17% of the kidneys had high single-kidney GFR values (>70 mL/min/1.73 m^2). In the abnormal kidney of patients with unilateral renal abnormalities, high clearance was found in 16% of the cases. On the contralateral side, such high values were encountered in 36% of the cases. In patients with bilateral lesions, only 9% of kidneys had high clearance values.

Low clearance values (<40 mL/min/1.73 m^2) were found in 4% of bilateral normal kidneys and in 27% of bilateral abnormal kidneys. In patients with unilateral renal lesions, low clearance values were found in 4% of the kidneys on the normal side and in 44% on the abnormal side.

Relative Percentage Uptake

For this parameter, all patients were considered regardless of age.

The percentage uptake of the left kidney of patients with bilateral normal kidneys was 51.2% (SD, 2.7%) (Fig. 1). In the abnormal kidneys of patients with unilateral abnormal kidney, the percentage uptake was 43.6% (range, 16%–59%; SD, 7.9%). In all patients except one, the percentage uptake was <51%. One abnormal kidney was enlarged (duplex) and had a relative uptake of 59%. The percentage uptake of the unilateral abnormal kidneys was significantly lower than

TABLE 3
Single-Kidney ^{51}Cr-EDTA Clearance in Children Older than 2 Years

Patients' condition	n	Mean (mL/min/1.73 m^2)		SD (mL/min/1.73 m^2)
Two normal kidneys	196	60		15
Unilateral abnormalities				
Normal side	25	65	*	19
Abnormal side	25	46		20
Two abnormal kidneys	22	49		18

*$P < 0.0001$.

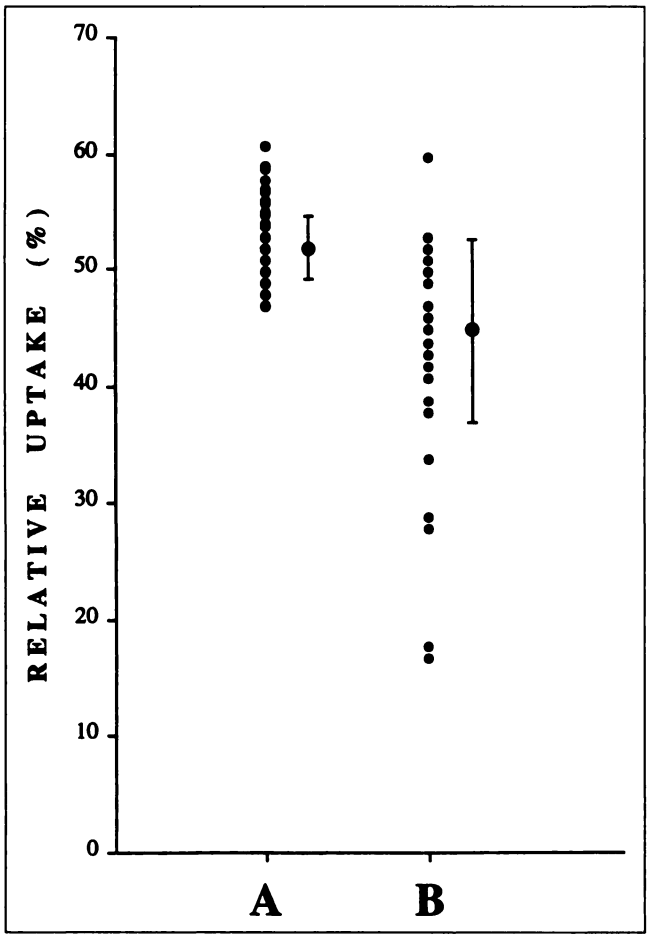

FIGURE 1. Relative DMSA percentage uptake in patients with two normal kidneys and with unilateral abnormalities (all ages included). Patients with bilateral lesions are excluded. (A) Percentage uptake on left side in patients with two normal kidneys (n = 180). (B) Percentage uptake in abnormal kidneys of patients with unilateral lesions (n = 56).

the kidney uptake in those patients with bilateral normal kidneys ($P < 0.0001$, unpaired t test). Similar values were found in patients younger and older than 2 y.

DISCUSSION

Methodology

In this study, we have used the DMSA images to classify the kidneys as normal and abnormal. It is now well admitted that DMSA scintigraphy is a sensitive and specific tool for renal lesions in acute UTI (*4*). The relative low number of abnormal scintigraphies observed in the present series may have several explanations. To get rid of the borderline cases that are difficult to classify, we have rejected all of the equivocal cases from this study and, therefore, probably several patients who, in other circumstances, would have been considered to have "small" renal lesions. Moreover, not all patients had severe kidney damage, and some patients with low UTI may well be included in the study.

As far as overall clearance is concerned, ^{51}Cr-EDTA clearance is presently well accepted as a good marker of GFR, closely correlated to inulin clearance (*5–7*). Simplified methods using one or two blood samples have been shown to be closely correlated to the reference method using multiple blood samples and biexponential analysis (*5,6,8*), and the reproducibility of these simplified methods is as good as the reference method (*9*). Ham's method, based on a single blood sample at 2 h, allows for an accurate estimation of overall GFR in children (*2,10*), as long as the clearance is >30 mL/min/1.73 m^2.

For the estimation of single-kidney GFR, we made the assumption that the relative DMSA uptake, reflecting a tubular function, is closely correlated to a relative uptake obtained by means of a glomerular tracer. Comparing ^{99m}Tc-diethylenetriamine pentaacetic acid and DMSA relative uptake, Taylor et al. (*11*) found a close correlation between these two parameters. Moreover, the DMSA relative uptake is a robust and reproducible parameter because of the high signal/noise ratio (*12*).

We estimated therefore that the combined use of DMSA relative uptake and ^{51}Cr-EDTA simplified clearance was an accurate measurement of the single-kidney GFR.

It was necessary to separate children younger and older than 2 y and to present the results of both the overall and single-kidney clearance only for children older than 2 y. In fact, despite the correction for body surface, it takes approximately 18 mo for GFR to reach the adult values (*3*). It was therefore difficult to compare normal and abnormal kidneys before the age of 2 y. On the contrary, the age factor is unimportant for the relative DMSA uptake, and the analyses have been performed on the whole population.

Results

Overall ^{51}Cr-EDTA clearance was found to be lower in patients with both abnormal kidneys than in those with two normal kidneys. This confirms the results observed by Berg (*13*) and Berg and Johansson (*14*) using inulin clearance and intravenous urography.

Despite the presence of acute infection, no abnormally low clearance values were observed in patients with bilateral normal kidneys. One could argue about the real existence of acute pyelonephritis in these patients with normal DMSA scintigraphy. However, even in those patients with unilaterally affected kidneys, the overall clearances were not significantly lower. It is obvious that in many cases, acute pyelonephritis is not associated with a low overall clearance.

A better understanding of this phenomenon comes from the analysis of single-kidney GFR. The clearance of the abnormal kidney (and also the relative percentage uptake) was significantly lower than the contralateral one. It is the contralateral kidney that maintained the overall clearance in the normal limits. The clearance of this "normal" kidney tended to be higher than the single kidney clearance of patients with two normal kidneys, and high clearance values (>70 mL/min/1.73 m^2) were more often observed on the contralateral side of the unilaterally affected kidney than in patients with two normal kidneys. The difference however was not significant, because of the wide range of values. It

should be underlined that, although the abnormal kidney was often associated with low clearance values (in 44% of cases), in more than half of the cases, despite obvious renal lesions, the clearance of the abnormal kidney remained normal, and the relative percentage uptake was comparable to the contralateral side (Fig. 2). This suggests that, in the abnormal kidney, an intrarenal mechanism of compensation exists in the region that has not been damaged by infection.

Is there any reason to believe that hyperfiltration is present in this series of acutely infected kidneys, as it was previously described by Berg (*15*)? For evident ethical reasons, no strictly normal values are available in children. In a previous retrospective study (*3*), the normal ^{51}Cr-EDTA clearance values have been estimated in children without renal abnormalities on DMSA scintigraphy. In this group of patients, as in this study, high clearance values of >140 mL/min/1.73 m^2 were often found. However, most of the clearance determinations in this so-called normal population were performed because of present or past UTI, and the high clearance values observed might not reflect what can be found in a strictly normal population. Moreover, inulin clearance, which is almost identical to ^{51}Cr-EDTA clearance, is <140 mL/min/1.73 m^2 in most of the normal patients. This suggests that the clearance values that are >140 mL/min/1.73 m^2 observed in this study in patients with two normal kidneys as well as in patients with one abnormal kidney corresponded to abnormal high clearance values.

Similarly, if one accepts that single-kidney clearance of >70 mL/min/1.73 m^2 is abnormally high, then a high percentage of elevated single-kidney clearance was indeed obvious in the patients with two normal kidneys as well as on the normal side of patients with unilateral renal abnormalities. This phenomenon of hyperfiltration was shown by Berg (*15*) for the overall clearance in a study comparing acute and remission phases of infection.

CONCLUSION

In acute UTI when only one kidney is affected on DMSA scintigraphy, the clearance of the affected kidney is lower than on the normal side and often abnormally low. In these unilaterally affected kidneys, contralateral compensation mechanisms tend to occur, resulting in preservation of overall clearance. This compensation is probably not only present on the contralateral side. On the abnormal side, the clearance is normal in about half of the cases, probably because of intrarenal compensation occurring in regions not damaged by the infection. Finally, in addition to these compensation mechanisms, hyperfiltration is probably present in many cases of acute UTI with intact or unilaterally damaged kidneys. Follow-up studies of the single-kidney clearance, with comparisons between acute and remission phases of infection, would allow a better delineation of this phenomenon of hyperfiltration.

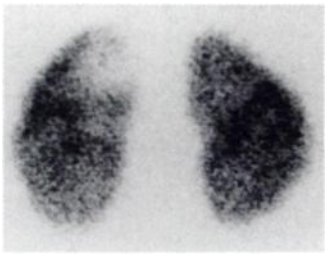

FIGURE 2. DMSA scintigraphy (posterior view) in child with acute pyelonephritis. Large hypoactive area in the upper pole of left kidney. Percentage of ^{99m}Tc-DMSA uptake is 48% left and 52% right. Overall clearance with ^{51}Cr-EDTA is 153 mL/min/1.73 m^2.

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