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ORIGINAL ARTICLE

Renogram in Children with Nephrotic Syndrome*

by

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Abstract

Fifty children with nephrotic syndrome, aged 3 to 13 years, were studied for renogram patterns. Twenty-one cases had normal renograms; one case with bilateral and one with unilateral renal function. Seven cases showed bilateral renal impairment in both secretion and excretion phases. Impairment of excretion phase was found in 12 cases bilaterally and 8 unilaterally. None of them showed abnormality in the secretion phase alone. Eighteen out of 29 cases with abnormal renograms were studied further in remission states. The second renogram of these cases showed improvement to normal in 13 cases, two other cases still had impairment in the secretion and excretion phases, and the remaining 3 cases showed only impairment in the excretion phase. Ten healthy children as control had normal renograms. The correlation of clinical/laboratory findings and abnormal renograms patterns was discussed. Further studies on the use and limitation of the renograms in nephrotic syndrome in children are needed.

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Introduction

Since Taplin et al. in 1956 introduced the radio-isotope renogram, this test has come to be accepted as a reliable external method for assessing individual renal function. In 1960 Nordyke et al. published a paper on the use of I^{131} Hippuran for individual kidney function test, and it was concluded that I^{131} Hippuran has become the most widely used compound for obtaining renograms. The clinical application, physiological and technical problems have been widely reviewed by Britton and Brown (1971). Clinically, renograms are mainly used as a screening test in hypertensive patients, obstructive nephropathy, and some miscellaneous conditions to detect cases of unilateral renal disease. However, the report of the application of this test in children with nephrotic syndrome is very rare. Swyngedow and Sulman (1967) only noted unspecific results in cases with nephrotic syndrome. Since the procedure is easily done and puts no strain to the patient even in a bad condition, this study was made in an effort to apply renogram as a guide to know the renal function in patients with nephrotic syndrome.

Material and methods

The renogram analysis has been divided into 3 groups :

Group 1. consisting of 10 healthy children aged 1 - 12 years, 5 males and 5 females, who attended the outpatient clinic for general check-up or for immunization purposes. All these children had neither previous history of renal disease nor hypertension. Physical examinations and laboratory investigations including IVP gave normal results.

Group 2. comprising 50 cases of fullblown first attack of nephrotic syndrome, aged 1 - 13 years, 28 males and 22 females. A renogram was made on the first day of admission; none of them got any medical treatment before. Laboratory investigations including urea and creatinine clearance tests were done on the day of renography. Renal biopsies were done in 46 cases. Histopathological examination were also done including ordinary light microscopy, immunofluorescence, and some of them electron microscopy.

Group 3. consisted of 18 out of 29 cases, 9 males and 9 females which showed abnormal renograms on the first examination (Group 2). It was made soon after remission was achieved.

Renography was done with a dual probe renogram, comprising dual channel measuring system and a dual channel flat bed recorder. A standard dose of 0.5 U ci./kg. body weight of I^{131} Hippuran has been employed. Scintillation detector of 1.75 inches diameter, which had been calibrated with standardized sodium radioiodide (I^{131}), was connected to a dual ratemeters set at a time-constant of 10 seconds; the total tracer activity set on 1×10^2 count per second (c.p.s.). The recording was done

with the patient in a sitting position. The detector was placed over the expected renal landmarks. Hippuran was injected into an antecubital vein as rapidly as possible.

The recording was continued up to 30 minutes or until the renal activity became less than 50% of maximum count rate. All tracings were interpreted by 2 experienced personnel from the Division of Nuclear Medicine by measuring T max. and T ½ according to Steward and Hayne (1962). The normal renogram pattern is divided into 3 phases for the purpose of discussion:

1) a rapid, rising first phase related to the inflow of blood carrying the radioactive tracer;
2) a less rapidly rising second phase related to the accumulation of tracers within the kidney by glomerular filtration and mainly by tubular secretion; and
3) the third decreasing segment which predominantly represents the urine outplow carrying the excreted tracer to the bladder.

The time from the first appearance to the maximum renal activity is called T max., and the time from maximum activity falling to half maximum is called T ½. Impairment of the first phase was assessed based on the renal tracer activity noted by a less rapidly initial rise or sometimes almost flat, nearly similar to the blood background tracer activity. Impairment of the second and third phases could be detected from the results of T max. and T ½ respectively.

Results

Analysis of T max. and T ½ of each group of this study is shown in Tables 1 and 2 respectively. The mean T max. of the control group was 2.95 minutes on the right kidney and 3.10 minutes on the left side with a standard deviation of 0.89 and 0.29 respectively. The first renogram done in nephrotic syndrome patients revealed a mean of 4.38 and 4.60 minutes in the right and left kidney respectively with a standard deviation of 1.67 and 1.81. The second renogram done on remission revealed a mean of 3.86 minutes on the right kidney and 4.19 minutes on the left side with a standard deviation of 1.21 and 1.43 respectively.

The results of T max. of the renogram done in nephrotic syndrome at the time of admission and on remission were not statistically different from each other ($p > 0.05$), but they were highly significant compared to the control group ($p < 0.01$) both in the right and left kidney. Analysis of the T ½ of the control group revealed a mean of 7.0 and 6.7 minutes with a standard deviation of 3.26 and 2.49 on the right and left kidney respectively. The mean T ½ measured in nephrotic syndrome patients on admission was 12.17 and 14.09 minutes with a standard deviation of 4.49 and 5.98 in the right and left kidney respectively. After excluding those with the T ½ more than 30 minutes on re-

TABLE 1.

STATISTICAL ANALYSIS OF T max.

Groups of investigations	RIGHT					LEFT				
	% EXCL	N	$\bar{X}$	SD	P	% EXCL	N	$\bar{X}$	SD	P
I NORMAL	-	10	2.95	0.85	I & II P < 0.01 Significant	-	10	3.1	0.29	I & II P < 0.01 (S)
II Nephrotic syndrome (on admission)	4%	48	4.38	1.67	II & III P = 16.65% (N.S)	6%	47	4.6	1.81	II & III P = 33.2% (N.S)
III Nephrotic syndrome (on remission)	-	18	3.86	1.21	I & III P < 0.05 (S)	-	18	4.19	1.43	I & III P < 0.01 (S)

TABLE 2.

STATISTICAL ANALYSIS OF T. Y2.

Groups of Investigations	RIGHT					LEFT				
	% Excl.	N	$\bar{X}$	SD	P	% Excl.	N	$\bar{X}$	SD	P
I NORMAL	-	10	7.0	3.26	I & II p<0.01 (S)	-	10	6.7	2.49	I & II p<0.01 (S)
II Nephrotic syndrome (on admission)	34 %	33	12.17	4.94	II & III P=67.45% (N.S)	36%	32	14.09	5.98	II & III P=32.22% (N.S)
III Nephrotic Syndrome (on remission)	11 %	16	11.56	4.6	I & III P<0.01 (S)	11%	16	12.5	4.81	I & III P<0.01 (S)

cording (34% from the right and 36% from the left kidney), the result of T ½ was still statistically different from the control group ($p < 0.01$). The mean of T ½ measured on remission after excluding those with the recording of T ½ more than 30 minutes (11% on both sides) was also statistically different from the control ($p < 0.01$).

The renogram patterns of 50 cases of nephrotic syndrome on admission are shown in Table 3. Twenty-nine cases (58%) showed abnormal renograms, namely 2 cases with renal afunction or impairment of all phases of renograms, 7 cases with impairment of the second and third phases, and 20 cases with impairment of the third phase only. The remaining 21 cases showed normal renograms. There was no sex preponderance found in the distribution of the renogram pattern except in cases of renal afunction. Both of them were males. Edema of the anasarca type (elevation of more than 20% of the actual body weight) was found in 10 out of 29 cases of the abnormal renogram group and in 10 out of 21 cases of the normal renogram pattern. Statistically speaking there was no correlation between the gradation of edema and the renogram pattern ($p > 0.05$).

Urea and creatinine clearance tests (Table 4) were measured in 46 cases. Normal clearance was detected in 19 out of 20 cases of the normal renogram group, while in the abnormal renogram group 21 out of 26 cases showed abnormal clearance (urea clearance less than 60% and creatinine clearance below 72%). The correlation between renogram patterns and histopathological findings is shown in Table 5. Minimal changes were found in 16 out of 21 cases of normal renogram pattern. The remaining 5 cases were mesangial proliferative glomerulonephritis. Renal biopsies done in 25 out of 29 cases from the abnormal renogram group, revealed 17 cases with minimal changes, 3 cases with focal sclerosing glomerulonephritis, 2 cases with mesangial-proliferative, 2 with membrano-proliferative, and 1 with chronic glomerulonephritis. Efforts have been made to divide the histopathological changes into 2 groups, namely minimal changes and non-minimal changes. Related to the renogram patterns, there was no correlation between these 2 proportions ($p > 0.05$).

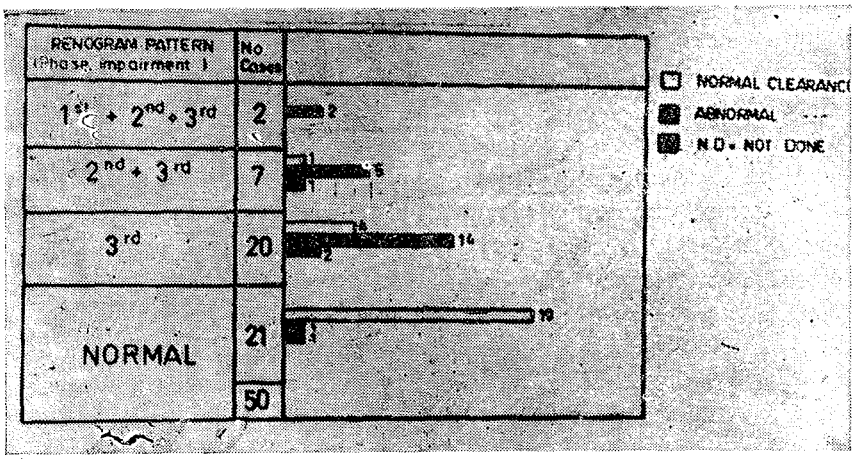
Evaluation of the renogram on remission is shown in Table 6. Eighteen out of 29 abnormal renograms were evaluated. Thirteen cases recovered to normal patterns, consisting of 9 cases with minimal changes, 2 cases with glomerulosclerosis, 1 with mesangial proliferative, and 1 with membrano-proliferative glomerulonephritis. The remaining 5 cases still had renogram impairment. As mentioned before, based on the calculation of T max. and T ½, statistically speaking the renogram done on remission was still different from normal control groups; in other words they had not fully recovered to the normal pattern. It was also important to point out that

TABLE 3.

RENOGRAM PATTERN IN 50 CASES OF NEPHROTIC SYNDROME ON ADMISSION

Renogram pattern (phase impairment)	Bilateral	Unilateral	Total
1st + 2nd + 3rd	1	1	2
2nd + 3rd	7	0	7
2nd	0	0	0
3rd	13	7	20
NORMAL	21		21

TABLE 4.



the improvement of the renogram pattern did not fully depend on the histological changes. The picture other than minimal changes could also return to a normal pattern.

Discussion

The basis of renogram is the external scanning of the kidneys following the injection of radioactive isotope I ^{131} Hippuran. There are several methods to assess renogram patterns such as measuring height and angle of the initial rise of the curve, but we preferred to use the method suggested by Steward and Hayne (1962) by measuring T max. and T ½ due to its simplicity and maximum diagnostic accuracy which can be obtained by measuring these parameters only. Other parameters do not increase the percentage of diagnostic tracings and actually they gave a higher percentage of false positive renograms. T max. represents mainly the formation of the second phase of renograms, while T ½ reflects the formation of the third phase. Impairment of the previous phase practically is followed by impairment of the next phase, in other words impairment of the first phase is always followed by impairment of the second and third phase.

This study shows that 58% of the cases of nephrotic syndrome had renogram impairment on admission. The presence of 2 cases with renal function impairment in this study is not clearly understood. Other factors rather than nephrotic syndrome per se can play a role in giving this impairment. Analysis of T max. and T ½ of the renogram pattern in nephrotic syndrome reveals that there are significant impairments of the second and third phases of renograms compared to the normal control. Swyngedow and Sulman (1967) related these abnormalities to the "renal parenchymal stasis". Analysis of the T max. and T ½ on remission reveals that the renogram patterns are still abnormal in both the second and third phases even though the urine flow has returned to a normal range. We conclude that the renogram abnormality found on remission is still caused by the parenchymal stasis and not only by the oliguria which can also cause the third phase impairment. This conclusion is also supported by the fact that the gradation of edema found in nephrotic syndrome, which is usually reflecting the severity of oliguria, has no relation to the renogram impairment.

The presence of unilateral renogram impairment in this study cannot be explained clearly. Further investigations are needed to evaluate whether this phenomenon is due to the pre-existing unilateral renal disease such as pyelonephritis which is aggravated by the impairment of renal function in nephrotic syndrome, or whether this disparity apparently is due to normal functional and anatomic variation, as well as errors in the positioning of the detectors as stated by Wedeen et al. (1963). The possibility

TABLE 5.

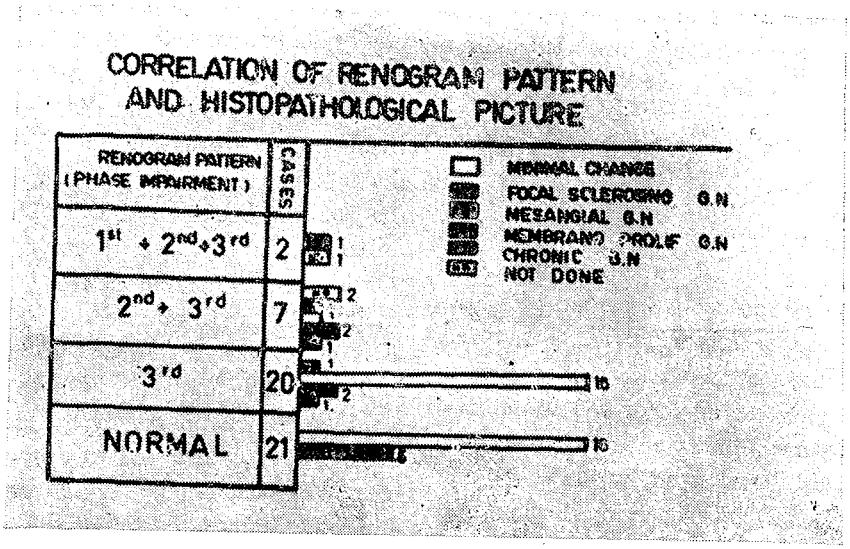
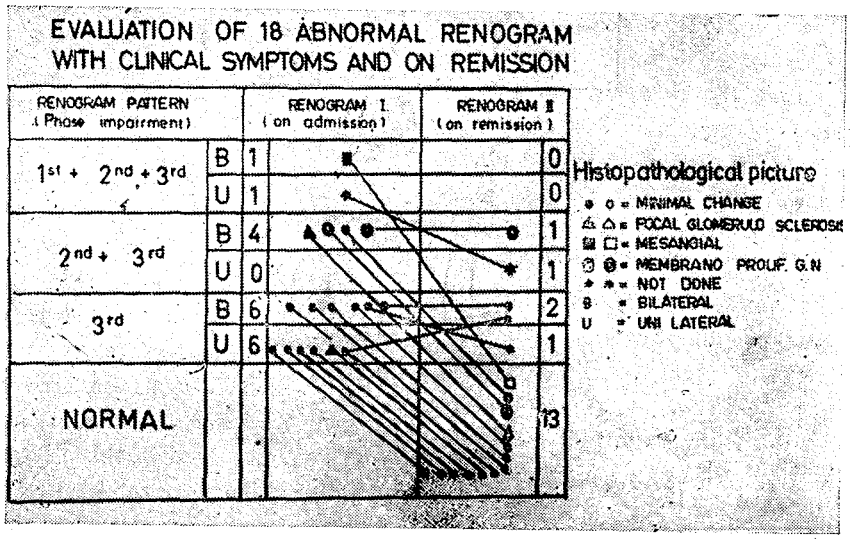


TABLE 6.



of obstructive nephropathy as a cause of unilateral renogram impairment can be excluded since most of this renogram abnormality disappeared on remission. Urea and creatinine clearance are closely related to the renogram impairment even though this correlation is not fully understood. Urea and creatinine clearance mainly reflect glomerular filtration rate. On the other hand, the majority of hippuran is excreted by the renal tubules, only 5.7% are filtered by the glomeruli (Britton and Brown, 1971). The correlation of renogram impairment and histopathological changes of the kidney is not proved in this study. It is believed that the renal function in nephrotic syndrome does not depend on the type of histopathological changes.

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