Water Loading Improves Specificity in Renal Imaging

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In previous renal imaging studies, we had the opportunity to study normal controls. We noted that the iodine-131 (^{131}I) orthoiodohippurate (OIH) renograms for this group had an abnormal configuration in one half of the subjects. The explanation for these abnormal [^{131}I]OIH scans was unclear, although the hydration status of the subjects was a suspected cause. The current studies were designed to compare 30-min [^{131}I]OIH and technetium-99m (^{99m}Tc) DTPA renal studies in water-deprived and water-loaded normal subjects. Each volunteer underwent two sets of OIH and DTPA scans under controlled conditions of hydration. In studies of subjects who were scanned after an overnight fast, only three of eighteen ^{99m}Tc-DTPA studies and twelve of eighteen [^{131}I]OIH studies were considered normal. After an oral water load of 10 ml/kg of body mass, all 30-min renal scans with DTPA and OIH were judged within normal limits. These results indicate that patients should receive oral water loading prior to renal scanning to avoid false-positive renal scans.

Both [^{131}I]OIH and ^{99m}Tc-DTPA have proven to be useful agents in renal function imaging (*1*), but the proper preparation of the patient in terms of hydration status is not often considered. In a review article on the clinical use of the renogram, Farmelant and Burrows (*2*) note that although radioisotopic renal function studies have proven diagnostically useful, controversy has surrounded the procedures since their inception. Informational content, interpretation of results, and patient preparation are areas of dispute. There is general agreement that patients should be "normally hydrated," although some authors suggest water loading be avoided (*3*) while others encourage water loading (*4,5*).

In our own studies of new imaging techniques for the evaluation of patients with renal artery stenosis (*6*), we had the opportunity to study normal controls. The three time-activity relationships evaluated in these studies included the computer-assisted 90-sec ^{99m}Tc-DTPA time-activity curve, the 30-min ^{99m}Tc-DTPA curve, and the [^{131}I]OIH renogram. Without special attention to hydration status, both the 30-min ^{99m}Tc-DTPA and [^{131}I]OIH studies in normal volunteers yielded abnormal time-activity curves in half of the subjects (*7*). The explanation for the high percent of false-positive scans was unclear, although the hydration status of the subjects was suspected. For this reason, the current studies were designed to address specifically the effect of the subjects' hydration status on the time-activity curves of both the 30-min ^{99m}Tc-DTPA and the 30-min [^{131}I]OIH scans in normal volunteers.

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MATERIALS AND METHODS

A total of 18 subjects (7 male and 11 female) between the ages of 21 and 65 were studied. These were normal volunteers, including students and employees of our institution, with no history of hypertension or kidney disease. All studies and procedures were approved by the Institutional Review Board. After determinations of blood pressure, serum creatinine, and urinalysis confirmed that the subjects had normal renal function and blood pressure, ^{99m}Tc-DTPA and [^{131}I]OIH studies were performed.

Eight of the eighteen subjects in the current study received only the hydration part of the protocol since they had previously been scanned without special attention to hydration status. The remaining 10 volunteers underwent two separate protocols of water deprivation and hydration. Each subject underwent sequential 30-min ^{99m}Tc-DTPA and 30-min [^{131}I] OIH scans on two separate occasions. The first set of scans was performed after 12 hours of overnight fasting. The second set, one month later, followed an oral water load based on body mass (10 ml/kg), 30-min prior to imaging. In order to eliminate curve distortions due to urinary bladder filling, the volunteers were asked to void after each study. A panel of clinicians and a nuclear medicine physician, uninformed about the state of hydration of the subjects, interpreted the scans using Gault's criteria (*8*).

The radionuclide administrations were performed by antecubital intravenous injection. Doses of 100 μCi of [^{131}I]OIH and 10 mCi of ^{99m}Tc-DTPA were each administered in a bolus of less than 1-ml volume. Patients were placed in the supine position with the anatomy viewed posteriorly by a LFOV gamma camera. Supine positioning is routinely employed in our department. It provides minimal kidney motion

from respiration and is less fatiguing to patients over the 60-min total imaging time. The detector has a 380-mm field of view and a medium energy parallel-hole collimator was utilized.

Data were acquired by computer using a predefined study routine. Data acquisition was in word mode and formulated into a 64 × 64 pixel matrix. For the [^{131}I]OIH study, a framing rate of 10 sec per frame was used. The dynamics for the ^{99m}Tc-DTPA study were specified by a rate of 1 sec per frame for 3 min followed by 10 sec per frame for 27 min. The iodine study was performed last, so that any remaining technetium activity from the first scan would not be seen in the higher energy ^{131}I window.

Analysis

A color display monitor was used for reviewing each dynamic study. To produce the [^{131}I]OIH renograms, regions of interest (ROIs) were selected which outlined each kidney, the bladder, and a common tissue background area, situated inferior to the right kidney. For the ^{99m}Tc-DTPA study, ROIs included the aorta, left and right kidneys, bladder, and corresponding background areas. For the kidney background, separate crescent-shaped background regions were established inferior and lateral to each kidney ROI. The dynamic curve data which were generated served as input for our analysis programs.

A number of data manipulation and output options have been developed in an attempt to optimize the information which is displayed. Typically, the ^{99m}Tc-DTPA data are processed as follows: frame-by-frame background subtraction is performed for each ROI and the dynamic curves are then passed twice through a 1-2-1 temporal smoothing filter. This level of processing has been found to moderate the statistical fluctuations present at the 1 per sec framing rate, while preserving the desired temporal features of the time-activity curves. The renal curves are both plotted on the same set of axes with the activity scale normalized to the higher peak activity. This display format facilitates direct bilateral comparison. A separate dynamic curve for the aorta region is plotted in order to assess the quality of the bolus at the main renal arteries.

The pairs of time-activity curves derived from the 30-min ^{99m}Tc-DTPA renal flow studies on normal volunteers, prior to and after water loading, were analyzed visually as well as quantitatively. Curves were subjectively judged normal or abnormal by comparing their configuration, slope, and symmetry to the curve of the contralateral kidney. The [^{131}I]OIH curves were analyzed in the same manner.

In order to more objectively assess differences in curve configurations under the two conditions of hydration, several curve parameters were defined. These parameters included: (1) ratio of left and right kidney maximum value counts, (2) ratio of area under the left and right kidney curves, measured for the first 5 min, (3) time to maximum value (min), and (4) time from maximum value to 50% of the maximum during washout (min).

Curves were described as normal if both kidney curves were subjectively similar by visual analysis and had no significant differences in curve parameters.

RESULTS

A comparison of 30-min scans in the 18 study subjects is presented in Table 1. Results for those who were scanned with no special preparation or in a water deprived state are combined and compared to results of scans performed after water hydration. This grouping of results was used since a paired t-test showed no significant difference ($p > 0.2$) when comparing the scans of subjects studied without preparation to scans of those who were water deprived.

Scans were judged to be normal or abnormal by conventional criteria (*8*) including time to peak (T_{max}), time from maximum to return to 50% of maximum ($T_{½}$), and symmetry between right and left kidney. Limits of normality were $T_{max} \leq 5$ min and $T_{½} \leq 10$ min with left and right maximum kidney counts differing by less than 30%. Only twelve of eighteen [^{131}I]OIH scans and three of eighteen ^{99m}Tc-DTPA scans were considered normal by these criteria. In comparison, after the oral water loading, all 30-min [^{131}I]OIH scans as well as all 30-min ^{99m}Tc-DTPA scans were considered normal using the same criteria.

Figures 1A, 1B, 2A, and 2B demonstrate representative 30-min [^{131}I]OIH and 30-min ^{99m}Tc-DTPA scans under water-deprived and water-loaded conditions in one subject. Without water loading, abnormalities associated with time from maximum to return to 50% of maximum and symmetry of the left/right kidneys are demonstrated. After hydration in the same subject, all study parameters are quite consistent and clinically within normal limits.

The quantitative analysis of the 30-min ^{99m}Tc-DTPA radionuclide study and the comparison of right versus left kidney curves in each group of subjects is shown in Table 2. The curve parameters are expressed as mean values ± s.e.m. Statistical analysis was accomplished by the use of a paired Student's t-test.

Statistically significant differences are seen between the curves obtained from the water-loaded subjects and those obtained from the same subjects without water loading. In particular, the times to maximum activity and from maximum to 50% activity during the clearance phase are within normal limits only under conditions of the prescribed oral hydration. Moreover, the subject-to-subject variance in these volunteers is much less for the time-activity curves obtained under the hydration protocol. The parameters comparing left to right kidney variations were not significantly different in

TABLE 1. Comparison of 30-Min [^{131}I]OIH and ^{99m}Tc-DTPA Scans According to Hydration Status

	Without water loading		Water loaded	
	^{99m}Tc-DTPA	[^{131}I]OIH	^{99m}Tc-DTPA	[^{131}I]OIH
Normal	3	12	18	18
Abnormal	15	6	0	0

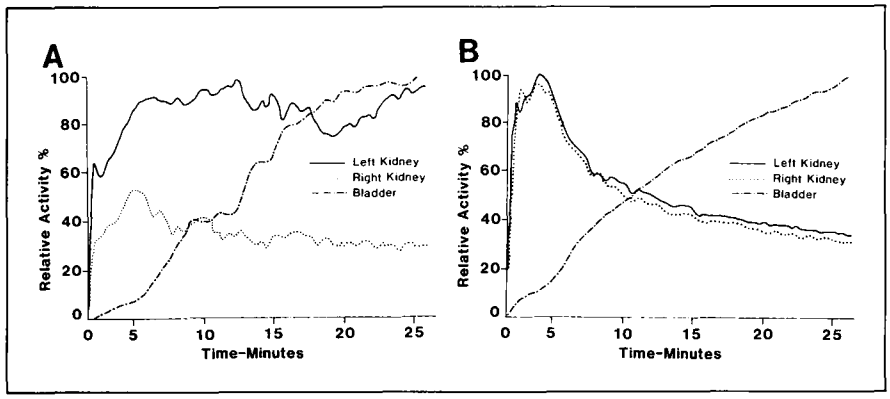

FIG. 1. (A) Thirty-min ^{99m}Tc-DTPA time-activity curves under conditions of water deprivation. The kidney curves are asymmetric. The left kidney curve shows greater activity than the right but with no excretion component suggesting obstruction on the left side. (B) Thirty-min ^{99m}Tc-DTPA time-activity curves under conditions of oral water hydration. Kidney curves are nearly identical with normal accumulation and excretion components.

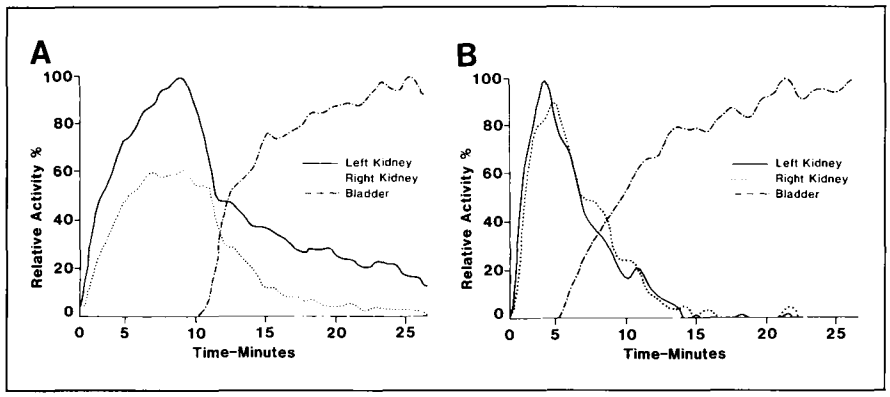

FIG. 2. (A) Thirty-min [^{131}I]OIH time-activity curves under conditions of water deprivation. The kidney curves are asymmetric. The left kidney curve shows greater activity than the right, although both curves demonstrate accumulation and excretion components. (B) Thirty-min [^{131}I]OIH time-activity curves under conditions of oral water hydration. The left and right kidney curves are nearly superimposed with normal accumulation and excretion components.

TABLE 2. Thirty-Min ^{99m}Tc-DTPA Time-Activity Curve Parameters

	Ratio of max value counts	Ratio of area under the curves	Maximum value time (min)		Time from max to 50% of max (min)	
	L/R Kidney	L/R Kidney	Left	Right	Left	Right
Non water loaded						
Mean	1.128	1.146	8.80	8.16	14.02	15.87
(±s.e.m.)	(±0.052)	(±0.052)	(±1.86)	(±1.42)	(±1.96)	(±1.83)
Water loaded	NSD	NSD	$p<0.01$	$p<0.01$	$p<0.03$	$p<0.01$
Mean	1.067	1.052	3.33	3.75	8.28	8.17
(±s.e.m.)	(±0.042)	(±0.041)	(±0.14)	(±0.27)	(±0.71)	(±0.79)

NSD: No significant difference, $p > 0.2$.

the scans obtained with and without water loading. However, visual differences in the time-activity patterns of the right and left kidneys for the non water-loaded subjects suggest abnormal differences in radionuclide perfusion and distribution. These abnormal signs were totally eliminated with prior water loading.

DISCUSSION

The results of our study suggest that in patients undergoing renal isotopic imaging, oral water hydration is necessary to prevent false-positive scan results using either [^{131}I]OIH or ^{99m}Tc-DTPA as renal function imaging agents. Our study was carried out in normal control subjects where the percentage of abnormalities on renal scanning should be minimal. Our results demonstrate 33% abnormal scans for [^{131}I]OIH and 84% abnormal scans for ^{99m}Tc-DTPA. The "abnormalities" were totally corrected with an oral water load 30-min prior to scanning.

A particularly interesting result of this study is that the same types and degree of abnormal curve shapes were demonstrated both for the water deprived group and those scanned without special attention to hydration status. The volunteer subjects were healthy individuals who underwent their studies during a day of typical activity. Those who were not water deprived were thus "normally hydrated." It is clear that une-

quivocal scans for these normal volunteers resulted only when a significant oral water load was included in the procedure.

The clinical utility of water loading was demonstrated by Mogensen et al. (*5,9*) in normal patients and patients with essential and renovascular hypertension. For normal patients, he found a decrease in the time to peak and a decrease in the percent of maximal activity at 20 min (A_{20}) when tested under conditions of hydration. He did not describe any changes in fractional share of the renal function to the right kidney or ratio of peak time (L/R kidney). Although no figures accompanied the articles, these descriptions suggest no alteration in curve configuration between the left and right kidneys even under conditions of dehydration.

Besides changes in time to peak and time to return to 50% maximum, a significant number of the subjects in our study also demonstrated discrepancies in L/R kidney configuration. Although the Mogensen data were published in 1975, other articles published at that time (*10*) and even more recently do not address the importance of water loading patients for renal imaging (*3,11*).

The quantitative changes exhibited in the time-activity curve parameters induced by water loading correlate well with the visual interpretation of these curves.

Several acceptable radiopharmaceutical agents are available for anatomical and functional studies of the kidneys (*1*). Evaluation of ^{99m}Tc-DTPA for measurements of glomerular filtration rate (GFR) has been reported in animal studies and in a number of patient studies (*12–20*). It has been demonstrated that differential GFR can be determined from the counts accumulated by each kidney during the first few minutes of the study (*14–21*). During this interval, the glomerular filtrate is in transit through the tubules and none has left the kidney, so that its activity is directly proportional to the GFR (*25*).

In our study, time-activity curves were derived from 30-min ^{99m}Tc-DTPA renal flow studies performed on normal subjects. The parameters of counts at maximum value and area under the curves during the first 5 min were used to represent the uptake of radionuclide and its relative activity in kidneys. Integrating over the first 5 min was used not as a functional marker, but as a means to quantitate asymmetry in curve shapes. There was no correction for kidney depth and tissue attenuation because no absolute values of GFR or blood flow were calculated using these parameters. The relative activity of ^{99m}Tc-DTPA between normal right and left kidneys was observed prior to and after water loading.

The discrepancy in configuration and symmetry of time-activity curves of the right and left kidney and the statistically significant differences in curve parameters suggest relative asymmetrical perfusion, uptake, and excretion of radionuclide even in subjects without any renal disease. Remarkable changes in configuration of these curves, such that right and left kidneys appear symmetrical with nonsignificant differences in curve parameters after oral water loading, suggest almost equal radionuclide distribution in both normal kidneys and hence eliminates false-positive detection of renal disease.

Although this study was performed in normal controls, it was done in conjunction with studies in patients with renal artery stenosis (*6*). It is hoped that newer noninvasive renal imaging techniques will discriminate patients with essential hypertension or obstruction from those with renal artery stenosis.

Mogensen (*5*) has already demonstrated abnormalities in L/R kidney configuration in patients with essential hypertension, which improve somewhat with oral hydration. In patients with essential hypertension, documented by a negative renal arteriogram, Giese (*9*) observed false-positive [^{131}I]OIH or ^{99m}Tc-DTPA after water loading. The current studies suggest that in patients undergoing renal imaging for any putative pathologic condition, either oral or intravenous hydration should be performed prior to imaging to ensure adequate renal perfusion during the scans and guard against false-positive time-activity curves.

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