The Significance of Radiopharmaceutical Choice on the Estimation of the Absolute Renal Function in Different Stages of Renal Failure

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Key Words

^{99m}Tc -DTPA · ^{131}I -OIH · Renal failure

Abstract

Objective: An abnormal filtration fraction due to divergence between glomerular filtration rate (GFR) and effective renal plasma flow (ERPF) may lead to different estimations of absolute renal function, depending on the radiopharmaceutical administered. The purpose of this study was to estimate GFR and ERPF by measuring the clearances of technetium-99m diethylenetriamine pentaacetic acid (^{99m}Tc -DTPA) and iodine-131 sodium *o*-iodohippurate (^{131}I -OIH) in patients with renal failure and evaluate the significance of these radiopharmaceuticals in the prognosis of the disease. **Methods:** This study included 25 patients who were followed up during different phases of acute renal failure (ARF) as well as 46 patients with incipient and advanced chronic renal failure (CRF). Results were compared with those obtained in 20 healthy volunteers. Clearance of ^{99m}Tc -DTPA and ^{131}I -OIH was measured by the technique of a single blood sample taken 180 and 44 min after administration of the radiotracer, respectively. **Results:** In the patients with ARF, absolute values of GFR and ERPF decreased during oligoanuric and diuretic phases, but the lower filtration fraction suggested a greater reduction of GFR. In the recovery phase of ARF, both GFR and ERPF improved

and an almost normal filtration fraction suggested a more prominent GFR increase. The recovery of ARF patients was in accordance with ^{131}I -OIH clearance values recorded in the oligoanuric phase. The GFR and ERPF decreased concordantly in patients in the incipient stage while in advanced CRF, a slightly greater decrease in GFR was recorded. **Conclusions:** In ARF, the degree of the initial fall in GFR does not serve as a prognostic indicator whereas the degree of the initial fall of ERPF does have prognostic significance. The decrease in GFR parallels the decrease in ERPF in CRF and a measurement of either parameter should give a comparable estimate of renal function.

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Introduction

Renal radionuclide studies are noninvasive techniques suitable for routine clinical examinations in nephrourology [1, 2]. The use of various renal localizing radiopharmaceuticals reflects different functional parameters that allow quantitative measurements of absolute and relative kidney functions. Considering radiopharmaceutical elimination, technetium-99m diethylenetriamine pentaacetic acid (^{99m}Tc -DTPA) is used as the primary indicator of glomerular filtration rate (GFR), while iodine-131 sodium *o*-iodohippurate (^{131}I -OIH) is used to evaluate effec-

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Table 1. Underlying diseases of patients with renal failure

Underlying diseases	Patients
ARF	
Gastrointestinal diseases (gastroenteritis, enterocolitis)	4
Postabortal and postpartal	4
Postrenal (stone disease, bladder carcinoma)	4
Parenchymal kidney diseases (glomerulonephritis, pyelonephritis)	3
Liver and pancreas diseases (cholecystitis, pancreatitis)	4
Major surgery	2
Toxicosis (acetic acid, mushrooms)	2
Posttraumatic	2
Total	25
CRF	
Glomerulonephritis	14
Diabetic nephropathy	6
Pyelonephritis	5
Obstructive nephropathy	6
Endemic nephropathy	3
Polycystic kidney disease	3
Nephroangiosclerosis	6
Unknown etiology	3
Total	46

tive renal plasma flow (ERPF) and tubular function due to its predominant excretion of ^{131}I -OIH by tubular secretion [3, 4].

In kidney diseases where renal functions deteriorate concordantly, values of separate renal function are independent of the radiopharmaceutical chosen. However, there are occasions where a significant divergence between GFR and ERPF exists, resulting in a different estimation of absolute renal function by $^{99\text{m}}\text{Tc}$ -DTPA and ^{131}I -OIH [5, 6].

Renal failure evolution may take either an acute or a chronic course. Acute renal failure (ARF) is a mostly reversible process, rapid in its onset, while chronic renal failure (CRF) is a progressively irreversible state. In both forms there is a severe impairment of global kidney function as well as the GFR or tubular function [7, 8].

The aim of this study was to estimate GFR and ERPF, measuring $^{99\text{m}}\text{Tc}$ -DTPA and ^{131}I -OIH clearance in different phases of ARF and CRF, and to evaluate the significance of these radiopharmaceuticals in the prognosis of renal failure.

Subjects and Methods

Twenty-five patients with differing etiologies of ARF and 46 patients with CRF were examined (table 1). Patients with renal failure were of both sexes, 17 males and 8 females with ARF, while 21 males and 25 females had CRF. The average age of ARF patients was 36.4 ± 9.2 years. The ARF patients were followed up by radionuclide methods during three phases within 6 months from the beginning of the disease: (1) oligoanuric ARF = urine output 340 ± 140 ml/24 h, serum creatinine 676 ± 242 $\mu\text{mol/l}$; (2) diuretic ARF = urine output $1,430 \pm 440$ ml/24 h, serum creatinine 316 ± 234 $\mu\text{mol/l}$; (3) recovery ARF = urine output $1,720 \pm 430$ ml/24 h serum, creatinine 101 ± 19 $\mu\text{mol/l}$.

Additionally, 5–10 days and 6 months after ARF onset, patients with recovered kidney function were analyzed separately as groups with complete (8 patients) and partial (17 patients) recovery compared with 6 irreversible renal failure patients.

According to the residual kidney function, 46 patients with CRF were divided into two groups: (1) incipient CRF = 26 patients, serum creatinine less than 250 $\mu\text{mol/l}$; (2) advanced CRF = 20 patients, serum creatinine 250–500 $\mu\text{mol/l}$.

All results obtained in the patients studied were compared with those of 20 healthy volunteers, aged 32.3 ± 6.1 years, 11 males and 9 females. The patients were investigated on 2 successive days following intravenous injection of 74 MBq $^{99\text{m}}\text{Tc}$ -DTPA and 18.5 MBq ^{131}I -OIH. The $^{99\text{m}}\text{Tc}$ -DTPA and ^{131}I -OIH clearances were measured by the technique of a single blood sample taken at 180 min [9] and 44 min [10] after radiotracer administration, respectively. Filtration fraction was calculated as a ratio between $^{99\text{m}}\text{Tc}$ -DTPA and ^{131}I -OIH clearance values.

The data are presented as means $\pm$ standard deviation. Statistical analysis was done using one-way analysis of variance (ANOVA). The paired-sample t test was used to compare the means of two variables for a single group.

Results

The results obtained by clearance studies in all three ARF phases are shown in table 2. Clearance values of both $^{99\text{m}}\text{Tc}$ -DTPA and ^{131}I -OIH indicated a significant reduction of both GFR and ERPF in all the groups compared to the control. In patients in the oligoanuric phase, $^{99\text{m}}\text{Tc}$ -DTPA and ^{131}I -OIH clearance values were low, but ^{131}I -OIH clearance was affected less severely than that of $^{99\text{m}}\text{Tc}$ -DTPA. During the diuretic and recovery phases, there was a gradual improvement of both radionuclide clearance values, but normalization of mean values was not obtained until the end of the investigation.

The filtration fraction presented as $^{99\text{m}}\text{Tc}$ -DTPA and ^{131}I -OIH clearance value ratio was found significantly decreased in the oligoanuric phase of ARF. Six months after the onset of ARF, patients with initial ERPF values of 178–243 ml/min showed partial recovery of kidney function while those within 253–315 ml/min achieved

Fig. 1. ^{131}I -OIH clearance values in ARF patients with different initial kidney function. C = Control; 1 = irreversible ARF; 2 = partial recovery; 3 = complete recovery. ^a $p < 0.001$: vs. control; ^b $p < 0.001$: 6 months vs. 5–10 days; ^c $p < 0.001$: vs. group 1; ^d $p < 0.001$: vs. group 2.

Fig. 2. $^{99\text{m}}\text{Tc}$ -DTPA clearance values in ARF patients with different initial kidney function. C = Control; 1 = irreversible ARF; 2 = partial recovery; 3 = complete recovery. ^a $p < 0.001$: vs. control; ^b $p < 0.01$: vs. control; ^c $p < 0.001$: 6 months vs. 5–10 days; ^d $p < 0.001$: vs. group 1; ^e $p < 0.001$: vs. group 2.

Table 2. $^{99\text{m}}\text{Tc}$ -DTPA and ^{131}I -OIH clearance in different stages of ARF

Group	Patients	$^{99\text{m}}\text{Tc}$ -DTPA clearance ml/min	^{131}I -OIH clearance ml/min	Filtration fraction
1 Control	20	126.0 ± 13.0	589 ± 84	0.21 ± 0.15
2 Oligoanuric ARF	25	$19.2 \pm 7.8^{\text{a, c, d}}$	$190 \pm 70^{\text{a, c, d}}$	$0.10 \pm 0.11^{\text{b, e}}$
3 Diuretic ARF	25	$43.2 \pm 9.6^{\text{a, f}}$	$291 \pm 58^{\text{a, f}}$	0.14 ± 0.16
4 Recovery ARF	25	$92.4 \pm 13.2^{\text{a}}$	$469 \pm 87^{\text{b}}$	0.19 ± 0.15

^a $p < 0.001$, ^b $p < 0.01$: vs. control; ^c $p < 0.001$: 2nd group vs. 3rd group; ^d $p < 0.001$, ^e $p < 0.05$: 2nd group vs. 4th group; ^f $p < 0.001$: 3rd group vs. 4th group.

complete recovery (fig. 1). A significant difference was found in 5- to 10-day ERPF values between patients with irreversible and reversible ARF. There was no significant difference in $^{99\text{m}}\text{Tc}$ -DTPA clearance values among patient groups after ARF onset (fig. 2). At the end of the study, a similar pattern of GFR changes was obtained for ERPF.

The data of ^{131}I -OIH and $^{99\text{m}}\text{Tc}$ -DTPA clearances as well as filtration fraction recorded in patients with CRF are shown in table 3. Clearance values of $^{99\text{m}}\text{Tc}$ -DTPA and ^{131}I -OIH were considerably reduced in incipient CRF, being significantly lower in the advanced stage than the control. However, there was no significant decrease in the filtration fraction.

Discussion

ARF is a clinical syndrome that arises from a vast array of pathogenetic conditions and is defined as an abrupt decline in renal function [11]. The most frequent form of ARF is a reversible process, making early diagnosis of this disorder necessary for prognosis and adequate treatment [12].

In this study, the oligoanuric phase of ARF measured with $^{99\text{m}}\text{Tc}$ -DTPA showed more of a decrease than ERPF assessed with ^{131}I -OIH. Markedly decreased $^{99\text{m}}\text{Tc}$ -DTPA clearance could have resulted from prolonged vasoconstriction, a decrease in hydrostatic glomerular pressure, tubular obstruction and back leakage of tubular urine

Table 3. ^{99m}Tc -DTPA and ^{131}I -OIH clearance in patients with CRF

Group	Patients	^{99m}Tc -DTPA clearance ml/min	^{131}I -OIH clearance ml/min	Filtration fraction
1 Control	20	126.0 ± 13.0	589.0 ± 84	0.21 ± 0.15
2 Incipient CRF	26	48.6 ± 10.8^a	240.0 ± 67^a	0.20 ± 0.16
3 Advanced CRF	20	$14.4 \pm 4.8^{a,b}$	$91.8 \pm 35.4^{a,b}$	0.15 ± 0.13

^a $p < 0.001$: vs. control; ^b $p < 0.001$: 2nd group vs. 3rd group.

[13]. Reduced values of ^{131}I -OIH clearance demonstrated a reduction of ERPF and tubular secretion. Tubular uptake and secretion of ^{131}I -OIH appears to be a two-step process involving an active transport of the tracer from the peritubular fluid into the tubular cells and transport from the tubular cells into the tubular urine [14]. The parenchymal retention of ^{131}I -OIH may occur when the first step is maintained while the second step is interrupted [15]. The greater reduction in GFR compared to ERPF found in the early phase of ARF is in agreement with previous reports obtained in clinical and animal models of renal ischemia, acute glomerulonephritis and obstructive nephropathy [16, 17]. There was less difference in the decrease in ^{99m}Tc -DTPA and ^{131}I -OIH clearance in the diuretic phase, and this difference disappeared in the recovery phase. Although absolute values of GFR and ERPF in the recovery phase of ARF were still significantly lower than control values, normalization of the filtration fraction indicated that there was more prominent improvement of glomerular than tubular function.

In the previous study, high renal uptake was demonstrated in ARF patients with recovered kidney function [18]. The present study suggests that a high renal clearance value of ^{131}I -OIH in ARF patients is associated with a favorable outcome. The group with the lowest initial ^{131}I -OIH clearance values had no improvement of kidney function during the period of investigation. Partial or complete recovery was demonstrated in patients with less of a reduction of ERPF 5–10 days after disease onset. Therefore, the degree of an initial fall of ERPF does have prognostic significance and should be obtained when patients present with ARF. On the other hand, GFR falls out of proportion to ERPF and does not serve as a prognostic indicator.

CRF demonstrates a progressive, irreversible impairment of global kidney function. It is shown by equally deteriorated glomerular and tubular function estimated by ^{99m}Tc -DTPA and ^{131}I -OIH clearance, respectively, in

incipient insufficiency and slightly more damaged GFR in advanced stages. The absence of significant alteration in the filtration fraction of these groups suggests that ^{99m}Tc -DTPA and ^{131}I -OIH clearance decreased concurrently in this patient population. Measurement of either parameter should give a comparable estimate of renal function. These findings are compatible with the intact nephron hypothesis which states that residual nephrons of the diseased kidney do retain their functional integrity [19]. Due to its higher renal extraction, delayed ^{131}I -OIH scintigraphy could be used for estimation of residual renal function and prediction of the time when kidney replacement therapy should be necessary [18, 20]. Extremely low ^{131}I -OIH clearance as well as the lack of kidney visualization on delayed scintigraphy with ^{131}I -OIH indicate a necessity for kidney replacement therapy in the very near future [21, 22].

Conclusions

There is a greater reduction of GFR measured by ^{99m}Tc -DTPA clearance than ERPF determined by ^{131}I -OIH clearance in the oligoanuric phase of ARF. The filtration fraction in recovered patients had a tendency toward normalization due to faster improvement of GFR. The recovery of ARF patients was in accordance with the values of ^{131}I -OIH clearance recorded in the oligoanuric phase. In incipient CRF, reductions of GFR and ERPF were equivalent while in the advanced stage there was a more marked decrease in GRF than ERPF. This study suggests that ^{131}I -OIH has a favorable prognostic value based on prediction reversibility in acute failure and assessment of residual function in chronic evolution.

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