Furosemide Augments the Effects of Captopril on Nuclear Studies in Renovascular Stenosis

RICHARD T. KOPECKY, F. DEAVER THOMAS, AND JOHN G. MCAFEE

SUMMARY Captopril facilitates detection of unilateral renovascular hypertension by selectively reducing glomerular filtration rate in affected kidneys. To determine if volume depletion augments this response, we compared the effects of captopril, furosemide, and combined furosemide plus captopril on individual kidney computer-derived clearances of $^{99m}$Tc-diethylenetriamine pentaacetic acid (DTPA) and $^{131}$I-iodohippurate in two-kidney, one clip Goldblatt hypertensive rats and normal controls. In clipped kidneys, captopril reduced DTPA clearance significantly from baseline (from 0.31 ± 0.02 to 0.19 ± 0.04 ml/min/100 g; p < 0.02) whereas furosemide alone had no effect (0.28 ± 0.03 ml/min/100 g). Combined furosemide plus captopril further reduced clipped kidney DTPA clearance to a level significantly less than captopril alone (0.10 ± 0.02 ml/min/100 g; p < 0.02). Clipped kidney o-iodohippurate clearance was not changed from baseline by any treatment. In contralateral unclipped and normal kidneys, DTPA clearance did not decline from baseline following either captopril or furosemide plus captopril treatment. Since the dose of captopril used (3 mg/kg by intraperitoneal injection) did not reduce systolic blood pressure of hypertensive rats significantly, these changes probably reflect intrarenal rather than systemic hemodynamic effects of converting enzyme inhibition and are consistent with the hypothesis that captopril interferes with glomerular filtration in stenotic kidneys by reducing efferent arteriolar vascular resistance. Prior volume depletion accentuates the effect of captopril on stenotic kidney glomerular filtration rate, providing improved functional discrimination of stenotic kidneys from contralateral unclipped and normal kidneys. These results indicate that furosemide-induced volume depletion may increase the diagnostic sensitivity of captopril-enhanced $^{99m}$Tc-DTPA renography in the detection of unilateral renovascular hypertension. (Hypertension 10: 181-188, 1987)

KEY WORDS • renovascular hypertension • captopril • furosemide • glomerular filtration • $^{99m}$Tc-diethylenetriamine pentaacetic acid

In unilateral renovascular hypertension, converting enzyme inhibition produces substantially different functional responses in the stenotic and the normal kidney.1 Maintenance of glomerular filtration in the stenotic kidney depends in part on angiotensin II–mediated efferent arteriolar vasoconstriction.2,3 By interfering with angiotensin II production and further lowering pressure distal to the fixed obstruction, converting enzyme inhibition can reduce the glomerular filtration rate in the stenotic kidney while renal plasma flow remains stable. The contralateral normal kidney, however, generally responds to converting enzyme inhibition with a modest increase or no change in glomerular filtration rate and renal plasma flow.4,5 $^{99m}$Tc-diethylenetriamine pentaacetic acid (DTPA) renal uptake studies provide noninvasive measurements of individual kidney glomerular filtration rate6 and can be used for the detection of renovascular hypertensive.7 Several reports suggest that concurrent administration of captopril may improve the diagnostic sensitivity of this technique by selectively reducing glomerular filtration rate in kidneys with unilateral vascular stenosis.8-10 Since volume status can influence the dependence of glomerular filtration on an intact renin-angiotensin system in the stenotic kidney,3 it could also influence the diagnostic sensitivity of captopril-enhanced radionuclide studies. Dietary sodium restriction and diuretic-induced volume depletion both appear to heighten the likelihood of acute renal failure during converting enzyme inhibitor therapy of renovascular hypertension.5-11-13 Conversely, volume ex-
pansion reduces the angiotensin II dependence of glomerular filtration in the stenotic kidney and could lessen the functional response to captopril. Substantial reductions in blood pressure can also reduce the glomerular filtration rate of stenotic kidneys by directly lowering renal perfusion pressure,\(^1\) even when the renin-angiotensin system remains intact. Thus, the systemic antihypertensive action of captopril could also influence stenotic kidney function.

Based on these considerations, the diagnostic value of captopril-enhanced renal radionuclide studies in unilateral renovascular hypertension might be optimized by 1) volume depletion, to maximally stimulate the renin-angiotensin system and increase dependence of glomerular filtration on angiotensin II in the stenotic kidney, and 2) low dose captopril, to avoid substantial reductions in systemic blood pressure. To evaluate this hypothesis, we compared the effects of low dose captopril on radionuclide-determined individual kidney function in euvoelastic and diuretic-treated renovascular hypertensive rats and in normotensive sham-operated controls.

### Materials and Methods

#### Animal Preparation

Male Sprague-Dawley rats weighing 200 g (Taconic Farms, Germantown, NY, USA) were anesthetized with ether and underwent surgical placement of a solid silver clip (slit width, 0.20 mm) on the left renal artery (two-kidney, one clip [2K1C] rats). The right kidney was not disturbed. A separate group of rats underwent an identical operation, including dissection of the renal artery, but no clip was applied (sham-operated rats). The 2K1C and sham-operated rats were housed together with free access to standard chow (Purina Formulab 5008, 0.35% sodium; St. Louis, MO, USA) and water throughout the study.

Three weeks after operation, systolic blood pressure was determined by tail-cuff plethysmography with the rats under light ether anesthesia, using a photoelectric pulse sensor (Grass Instruments, Quincy, MA, USA) and a 20 × 12-mm tubular occluding cuff (Narco Biosystems, Houston, TX, USA) connected to a Statham pulse sensor (Grass Instruments, Quincy, MA, USA) and displayed on a Grass physiograph. The mean of six determinations over 2 to 3 minutes was taken as systolic blood pressure. Only 2K1C rats with systolic blood pressure over 150 mm Hg and acceptable expansion reduces the angiotensin II dependence of glomerular filtration in the stenotic kidney and could lessen the functional response to captopril. Substantial reductions in blood pressure can also reduce the glomerular filtration rate of stenotic kidneys by directly lowering renal perfusion pressure,\(^1\) even when the renin-angiotensin system remains intact. Thus, the systemic antihypertensive action of captopril could also influence stenotic kidney function.

Based on these considerations, the diagnostic value of captopril-enhanced renal radionuclide studies in unilateral renovascular hypertension might be optimized by 1) volume depletion, to maximally stimulate the renin-angiotensin system and increase dependence of glomerular filtration on angiotensin II in the stenotic kidney, and 2) low dose captopril, to avoid substantial reductions in systemic blood pressure. To evaluate this hypothesis, we compared the effects of low dose captopril on radionuclide-determined individual kidney function in euvoelastic and diuretic-treated renovascular hypertensive rats and in normotensive sham-operated controls.

### Experimental Protocol

From 3 to 6 weeks postoperation, systolic blood pressure and renal radionuclide studies were performed weekly on each rat after the following treatments: Week 3, diluent injection 1 hour prestudy (baseline); Week 4, captopril, 3 mg/kg, 1 hour prestudy by intraperitoneal (i.p.) injection dissolved in distilled water; Weeks 5 and 6, furosemide, 25 mg/kg i.p., 6 hours prestudy or furosemide plus captopril at the same doses. Rats randomly received furosemide alone or furosemide plus captopril on Week 5 and the alternate treatment on the following week. On study days, food was withheld and rats had access to distilled water. Renal radionuclide studies commenced immediately following systolic blood pressure determination. Diuretic response was assessed by change in body weight, measured just prior to and 6 hours after furosemide injection. On Week 7, blood was drawn, animals were killed, and the kidneys and heart removed and weighed. Two 2K1C rats died before completing the study and were excluded from data analysis.

### Renal Radionuclide Studies

With the rats under ether anesthesia, tail-vein injections of 1 mCi of \(^{99m}\text{Tc-DTPA}\) or 200 \(\mu\)Ci of \(^{131}\text{I-Iodohippurate}\) sodium (Hippuran) preceded scintillation camera imaging; 15-second interval images were computer-digitized for 3 minutes, followed by 60-second images for an additional 12 minutes. The 0.5- to 1.5-minute interval image was quantitated as the percentage of the injected dose in each kidney, as reported previously.\(^1\) Estimation of DTPA plasma clearance (\(C_{\text{DTPA}}\)) or Hippuran plasma clearance (\(C_{\text{HIPP}}\)) was obtained from regression equations relating plasma clearance to renal uptake. Regression equations were developed from previous rat plasma clearance studies for DTPA (\(n = 60\)) and Hippuran (\(n = 48\)), done concurrently with renal uptake studies (see Appendix). Plasma clearances were quantitated using the two-exponential model of Sapirstein et al.\(^1\)

Plasma creatinine was determined by a modified Jaffé reaction.\(^1\) Data are expressed as means ± SEM. Filtration fraction was calculated as the ratio of \(C_{\text{DTPA}}\) (glomerular filtration rate) to \(C_{\text{HIPP}}\) (renal plasma flow). Comparisons between treatments in each group and between groups were made using a two-tailed Student’s \(t\) test for paired and unpaired data, respectively. Statistical significance was defined as a \(p\) value less than 0.05.

### Results

Characteristics of 2K1C and sham-operated rats appear in Table 1. 2K1C rats remained healthy despite being hypertensive as evidenced by growth comparison to sham-operated rats during the study. At death, the 2K1C group had a higher mean plasma creatinine value than that of the sham-operated group, but this difference was not statistically significant. The degree of volume depletion, as assessed by weight loss, was similar in 2K1C and sham-operated rats following furosemide alone and furosemide plus captopril. Within each group, the order of drug administration during Weeks 5 and 6 had no effect on the diuretic response to either treatment.

In response to systemic hypertension, cardiac hypertrophy developed in 2K1C rats, with heart weights significantly greater than those of sham-operated rats. Clipped left kidneys of 2K1C rats (1.07 ± 0.03 g) were comparable in size to sham-operated left kidneys
Table 1. Characteristics of 2K1C and Sham-operated Rats

<table>
<thead>
<tr>
<th>Parameter</th>
<th>2K1C (n = 12)</th>
<th>Sham (n = 6)</th>
</tr>
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<tbody>
<tr>
<td>Weight gain, Weeks 3-7 (g)</td>
<td>47 ± 9</td>
<td>55 ± 6</td>
</tr>
<tr>
<td>Plasma creatinine (mg/dl)</td>
<td>0.53 ± 0.05</td>
<td>0.43 ± 0.03</td>
</tr>
<tr>
<td>Diuretic response (g)</td>
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<td></td>
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<tr>
<td>Furosemide</td>
<td>-18 ± 1</td>
<td>-22 ± 3</td>
</tr>
<tr>
<td>Furosemide and captopril</td>
<td>-18 ± 2</td>
<td>-22 ± 4</td>
</tr>
<tr>
<td>Organ weight (g)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>1.31 ± 0.03</td>
<td>1.03 ± 0.06*</td>
</tr>
<tr>
<td>Left kidney</td>
<td>1.07 ± 0.03</td>
<td>1.17 ± 0.06</td>
</tr>
<tr>
<td>Right kidney</td>
<td>1.44 ± 0.05†</td>
<td>1.16 ± 0.05†</td>
</tr>
</tbody>
</table>

Values are means ± SEM. Plasma creatinine values were determined at death in Week 7, 1 week after administration of captopril or furosemide plus captopril for the final radionuclide study. For studies involving furosemide, the weight loss between measurements made just before and 6 hours after injection of the diuretic was taken as the diuretic response.

*p < 0.001, †p < 0.01, compared with 2K1C rats, by unpaired t test.

*p < 0.05, compared with value in clipped left kidney, by paired t test.

(1.17 ± 0.06 g); however, unclipped right kidneys (1.44 ± 0.05 g) were significantly larger than clipped kidneys and normal right kidneys (1.16 ± 0.05 g).

As shown in Figure 1, systolic blood pressure of 2K1C rats exceeded that of sham-operated rats at baseline (177 ± 5 vs 130 ± 3 mm Hg; p < 0.001) and throughout the study (p < 0.001, all treatments). Treatment with captopril alone or furosemide plus captopril did not change systolic blood pressure significantly from baseline in either group. Furosemide treatment alone increased systolic blood pressure from baseline in 2K1C rats (189 ± 6 mm Hg; p < 0.05) but had no effect on systolic blood pressure of sham-operated rats.

The effects of captopril, furosemide, and combined furosemide plus captopril on the function of clipped kidneys of 2K1C rats are shown in Figure 2. Captopril alone reduced C DTPA significantly from baseline (0.31 ± 0.02 to 0.19 ± 0.04 ml/min/100 g; p < 0.02) whereas furosemide alone had no effect (0.28 ± 0.03 ml/min/100 g). Combined furosemide plus captopril treatment caused a further marked reduction in clipped kidneys.
kidney $C_{DTPA}$ to $0.10 \pm 0.02$ ml/min/100 g, a level significantly less than that observed with captopril alone ($p < 0.02$). This effect was reversible, since the six 2K1C rats that received furosemide plus captopril in Week 5 had $C_{DTPA}$ values following furosemide alone in Week 6 that were not significantly different from baseline. $C_{Hipp}$ in clipped kidneys of 2K1C rats was unchanged from baseline ($1.17 \pm 0.04$ ml/min/100 g) by any treatment. Reductions in $C_{DTPA}$ combined with stable $C_{Hipp}$ values resulted in a significant fall in the filtration fraction of clipped kidneys, from $0.26 \pm 0.02$ at baseline to $0.14 \pm 0.03$ following captopril alone and to $0.08 \pm 0.02$ following furosemide plus captopril.

In unclipped kidneys of 2K1C rats, the response to captopril and furosemide plus captopril was quite different (Figure 3). $C_{DTPA}$ was unchanged from the baseline value of $0.42 \pm 0.02$ ml/min/100 g by any treatment. $C_{Hipp}$ in unclipped kidneys increased from baseline ($1.37 \pm 0.05$ ml/min/100 g) following captopril alone ($1.63 \pm 0.04$ ml/min/100 g; $p < 0.005$) and captopril plus furosemide ($1.66 \pm 0.11$ ml/min/100 g; $p < 0.05$). Unclipped kidney filtration fraction fell significantly from a baseline value of $0.30 \pm 0.01$ to $0.22 \pm 0.03$ after treatment with furosemide plus captopril. Unlike clipped kidneys, the decrease in unclipped kidney filtration fraction was due primarily to an increase in $C_{Hipp}$ rather than a decrease in $C_{DTPA}$.

Baseline $C_{DTPA}$ of unclipped kidneys of 2K1C rats exceeded that of clipped kidneys ($p < 0.01$). To determine if this difference reflected anatomical enlargement of the unclipped kidney versus the clipped kidney or functional hypertrophy on a per unit tissue basis, $C_{DTPA}$ data was normalized for kidney size. As shown in Figure 4, unclipped and clipped kidneys exhibited similar baseline $C_{DTPA}$ values per gram of kidney tissue. The functional response to treatment was qualitatively similar to that seen using clearance values normalized to body weight. Although captopril alone reduced clipped kidney $C_{DTPA}$ from baseline, this difference did not achieve statistical significance when compared with that of the unclipped kidney. However, treatment with furosemide plus captopril reduced clipped kidney $C_{DTPA}$ to a level significantly less than that of the contralateral unclipped kidney.

The effects of captopril, furosemide, and combined furosemide plus captopril on kidney function in sham-operated rats are shown in Figure 5. Baseline values of $C_{DTPA}$ and $C_{Hipp}$ were unchanged by any treatment in the untouched right kidney (see Figure 5, upper panel) of sham-operated animals. In sham-clipped left kidneys (see Figure 5, lower panel), $C_{DTPA}$ was reduced slightly but significantly from baseline ($0.41 \pm 0.03$ ml/min/100 g) by furosemide treatment alone ($0.29 \pm 0.01$ ml/min/100 g; $p < 0.05$) but was unaffected by captopril ($0.41 \pm 0.05$ ml/min/100 g) and furosemide plus captopril ($0.36 \pm 0.07$ ml/min/100 g). Sham-clipped kidney $C_{Hipp}$ was increased by captopril alone and remained unchanged from baseline following furosemide and furosemide plus captopril treatments.

**Discussion**

Activation of the renin-angiotensin system is the physiological hallmark of unilateral renovascular hypertension. Numerous studies have examined the effects of perturbations in the renin-angiotensin system on kidney function in an effort to understand the pathogenesis of this disorder. However, clinical strategies for the detection of renovascular disease have generally aimed at demonstrating the presence of angiotensin
FUROSEMIDE AND CAPTOPRIL IN RENOVASCULAR HYPERTENSION/Aroky et al.

FIGURE 4. Clearance of DTPA (C_{DTPA}) of unclipped right (UnC) and clipped left (Cl) kidneys of 2K1C rats, normalized for kidney size, at baseline and following treatment. Asterisk indicates significant difference compared with UnC (p<0.005).

II-dependent hypertension and stimulated renin production by the involved kidney, while alterations in kidney function per se have received relatively little attention in recent years.

Stenosed and normal kidneys have substantially different hemodynamic responses to blockade of the renin-angiotensin system. In the 2K1C Goldblatt rat (in which hypertension is angiotensin II-dependent during the acute phase), Huang et al. showed that converting enzyme inhibition reduces glomerular filtration rate and excretory function of the clipped kidney while having the opposite effects on the contralateral unclipped kidney. These workers attributed the effects of converting enzyme inhibition on the clipped kidney to reductions in arterial pressure. However, consideration of the intrarenal actions of angiotensin II provides another explanation. Hall et al. demonstrated that autoregulation of glomerular filtration rate at low renal perfusion pressures is dependent on an intact renin-angiotensin system, whereas renal blood flow autoregulation is not. These observations suggest that angiotensin II–mediated effenter arteriolar vasoconstriction is important for maintenance of clipped kidney glomerular filtration. This contention is supported by several studies indicating that angiotensin II acts primarily as an effenter vasconstrictor in the kidney, although this view has recently been challenged.

The recognition that captopril could cause acute, reversible renal failure in patients with bilateral renal artery stenosis or stenosis of a solitary kidney lent increased clinical significance to the physiology of glomerular filtration rate autoregulation. Since the entire renal mass is affected in such cases, variations in renal function are readily detectable. However, converting enzyme inhibitor–induced changes in stenotic kidney glomerular filtration rate can easily be missed in the presence of a normal contralateral kidney. This limitation can be overcome with radionuclide techniques, which allow repeated, noninvasive measurement of individual kidney glomerular filtration rate and renal plasma flow. Wenting et al. demonstrated that a single dose of captopril reduces the uptake of 99mTc-DTPA by the stenotic kidney of some patients with unilateral renovascular hypertension. Although stenotic kidney glomerular filtration rate is reduced in this setting, simultaneous measurements of perfusion by [131I]Hippuran renography or 99mTc-albumin microspheres indicate that renal blood flow is preserved; these findings are in striking concordance with the earlier reports of Hall et al. in the dog.

More recently, attempts have been made to refine this approach into a useful diagnostic test for renovascular hypertension. Since alterations in volume status and systemic blood pressure may influence clipped kidney function, we examined the effects of converting enzyme inhibition during control of these variables. With the use of a noninvasive radionuclide technique, the present study demonstrates that furosemide accentuates the differential effect of captopril on clipped and unclipped kidney function in the 2K1C Goldblatt hypertensive rat. Captopril alone reduced clipped kidney glomerular filtration rate (measured as C_{DTPA}) by 39%, whereas captopril treatment following furosemide-induced volume depletion caused a 68% reduction from baseline. Neither treatment had a significant effect on unclipped kidney C_{DTPA}.

The exact mechanism through which furosemide accentuates the effects of captopril on clipped kidney
glomerular filtration rate is uncertain. Animal and clinical data both suggest that volume depletion increases the dependence of glomerular filtration rate on angiotensin II at reduced perfusion pressures. Volume contraction itself might further limit blood flow across a fixed renal artery obstruction, rendering the glomerular circulation more vulnerable to hypotension when efferent tone is decreased by captopril. In the present study, clipped kidney plasma flow (measured as $C_{\text{HMP}}$) was not decreased by treatment with furosemide or furosemide plus captopril, arguing against this explanation. In addition, since furosemide treatment alone did not reduce mean systolic blood pressure in 2K1C rats, it would not be expected to hamper clipped kidney perfusion. An unequal degree of volume depletion following treatment with furosemide alone and furosemide plus captopril was unlikely, since the order of treatment was randomly varied. Moreover, the degree of volume depletion as assessed by weight loss was similar with both treatments. However, the failure of clipped kidney blood flow to increase following furosemide plus captopril treatment could still be interpreted as an insufficient (volume-limited) response if efferent vascular resistance was reduced to a greater extent by furosemide plus captopril than by captopril treatment alone. Since volume depletion causes additional stimulation of the renin-angiotensin system in the clipped kidney and angiotensin II is capable of down-regulating the density and affinity of its own vascular receptors, prior volume depletion could result in a more profound loss of efferent tone (and glomerular filtration rate) when angiotensin II levels are reduced by captopril than would otherwise occur with normal receptor function.

Furosemide stimulates synthesis and inhibits catabolism of renal prostaglandins, producing an increase in vasodilator prostaglandin excretion from stenotic kidneys. Since some of the vasodilator effects of converting enzyme inhibition are prostaglandin-mediated, furosemide could also potentiate the action of captopril through a prostaglandin-dependent mechanism. Additional studies using prostaglandin synthesis inhibitors would be necessary to evaluate this possibility; however, the fact that volume depletion induced by dietary sodium restriction without furosemide also accentuates the effects of captopril on clipped kidney glomerular filtration rate argues against a major role for prostaglandins.

Captopril treatment caused a small (12 mm Hg) but significant decrease in systolic blood pressure of 2K1C rats. This response may reflect an exacerbation of the negative sodium balance and peripheral vasoconstriction already present in this model. In support of this concept, Swales and Tange demonstrated that acute sodium and volume removal by peritoneal dialysis of 2K1C hypertensive rats causes either an acute increase in blood pressure or no response but does not lower blood pressure. Results of the present study were similar. Seven of 12 2K1C rats manifested a substantial hypertensive response to acute volume depletion (average increase of 25 mm Hg from baseline), whereas the five remaining animals had essentially no response (average decrease of only 6 mm Hg). In addition, it is also possible that non-volume-mediated renin release contributed to the increased systolic blood pressure in some animals, since furosemide is capable of directly stimulating renin secretion, even in volume-expanded rats.

Reduction of renal perfusion pressure with antihypertensive treatment can interfere with stenotic kidney function, although non-converting enzyme inhibitor drugs produce much less renal dysfunction than do equipotent doses of converting enzyme inhibitors. To minimize changes in renal perfusion pressure, we used a relatively small dose of captopril (3 mg/kg). This dose has a minimal effect on renal perfusion pressure in anesthetized two-kidney renovascular hypertensive rats, although diastolic blood pressure is reduced. In the present study, systolic blood pressure measured by tail-cuff plethysmography was unchanged by captopril treatment. Although we cannot exclude the possibility that mean blood pressure was somewhat reduced by captopril (with systolic pressure remaining stable), it seems unlikely that a large enough decrease in renal perfusion pressure could have occurred to produce such profound changes in clipped kidney glomerular filtration rate. Rather, it points out the exquisite sensitivity of clipped kidney function to even low doses of a converting enzyme inhibitor.

In clipped kidneys, glomerular filtration rate was reduced by captopril while renal plasma flow remained stable. Consequently, the filtration fraction was decreased. Unclipped kidneys responded to captopril with an increase in renal plasma flow, probably representing release of tonic vasoconstriction from circulating angiotensin II. Since glomerular filtration rate was unchanged, unclipped kidney filtration fraction was also decreased by converting enzyme inhibition. These findings are consistent with previous data suggesting that angiotensin II acts primarily at the efferent arteriolar level.

The glomerular filtration rate of clipped kidneys at baseline was less than that of contralateral unclipped kidneys. Since unclipped kidneys were enlarged while clipped kidneys remained of normal size, we compared their function factored by kidney weight. On a per-gram-tissue basis, clipped and unclipped kidney glomerular filtration rate was not significantly different. In preliminary experiments using larger renal artery clips (0.23 mm), we noted less difference in clipped and unclipped whole kidney glomerular filtration rate at baseline. The reduction of clipped kidney glomerular filtration rate following captopril treatment was less marked in these animals; however, superimposed volume depletion was not attempted. Additional studies are required to determine the minimum degree of renal artery stenosis required to sensitize clipped kidney glomerular filtration rate to furosemide and captopril treatment.

In summary, the results of this study indicate that furosemide accentuates the differential effect of captopril on kidney function in the 2K1C rat by causing a
Further selective decline in glomerular filtration rate of the clipped kidney. This decline can occur without a substantial change in systemic blood pressure and can be demonstrated with a noninvasive radionuclide technique. Although the mechanism through which furosemide influences the response to converting enzyme inhibition is not certain, it appears to be directly or indirectly related to the effects of volume depletion on the clipped kidney. Based on these results, furosemide-induced volume depletion should be evaluated as a potentially useful adjunct to captopril-enhanced $^{99m}$Tc-DTPA renography in the detection of unilateral renovascular hypertension.

Acknowledgments

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References


Appendix

The regression equations (Table A) for estimating plasma clearance from in vivo renal uptake measurements were derived from data generated for a previous publication.15 Plasma clearances obtained from multiple plasma samples were correlated with the summed uptake of right and left kidneys quantitated by gamma camera computer techniques in two series of rats. Both of these included controls and rats with glomerular damage induced by graded doses of puramycin aminonucleoside. The 99mTc-DTPA series of 60 rats and the [131I]Hippuran series of 48 rats each contained 24 controls. For the purposes of the present study, the plasma clearances of the right and left kidneys of those animals were assumed to be equal. Hence, the renal uptake of the individual kidneys were regressed against half the plasma clearance values.

**Table A. Linear Regression Equations for Calculating Clearances of Individual Rat Kidneys from in Vivo Early Renal Uptake**

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<th>Kidney</th>
<th>Clearance</th>
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<th>Right</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTPA</td>
<td>ml/min/100 g body wt</td>
<td>y = 0.0677x - 0.116</td>
<td>y = 0.0623x - 0.0698</td>
</tr>
<tr>
<td>ml/min/g kidney</td>
<td>y = 0.108x - 0.281</td>
<td>y = 0.103x - 0.233</td>
<td></td>
</tr>
<tr>
<td>Hippuran</td>
<td>ml/min/100 g body wt</td>
<td>y = 0.0732x - 0.499</td>
<td>y = 0.0796x - 0.284</td>
</tr>
<tr>
<td>ml/min/g kidney</td>
<td>y = 0.0427x - 1.08</td>
<td>y = 0.0627x - 0.733</td>
<td></td>
</tr>
</tbody>
</table>

x = in vivo early renal uptake.
Values of x are expressed as percentage of administered activity per kidney.

* = in vivo early renal uptake.

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