Evaluation of Renal Ischemia with $^{99m}$Tc-Pyrophosphate

Henrik S. Thomsen and Andrew Taylor Jr.

Department of Radiology S-004, University of California San Diego, La Jolla, CA 92093 and
Department of Nuclear Medicine, Veterans Administration, Medical Center San Diego, La Jolla, CA 92161, USA

Abstract. Renal ischemia injury was induced by transient 30-min occlusion of the main renal artery in five rabbits and by transient 60-min occlusion in four rabbits. The vessels to the contralateral kidneys were ligated in all nine animals and in six additional control rabbits. Renal blood flow was restored immediately following the transient ischemia. Twenty-four hours later, $^{99m}$Tc-pyrophosphate was injected and renal uptake was monitored for 100 s at 10-min intervals for 90 min following injection. At 90 min postinjection, the animals were killed and the percent injected dose remaining in the kidneys was calculated for three animals in each group. At 60 min postinjection, in vivo activity in the 30-min ischemic kidneys was 2.3 times greater than that of controls, and activity in the 60-min ischemic kidneys 4.6 times greater than that of controls. These results suggest that $^{99m}$Tc-pyrophosphate scanning may be useful in assessing slight ischemic damage to the kidney.

Introduction

Previous studies have shown that the renal uptake of $^{99m}$Tc-Sn-Hydroxyethylidenediphosphonate (HEDP) is significantly increased in acute tubular necrosis (ATN) (Lavelle et al. 1979; Lavelle et al. 1980). Evaluation of ischemic damage to a kidney graft may be quite important during the first days following transplantation since the degree of ischemic damage may be reflected in the severity of ATN, and ATN must be distinguished from rejection if proper treatment has to be instituted. Since $^{99m}$Tc-pyrophosphate (PYP) has been extensively used and widely accepted in the evaluation of acute myocardial necrosis (Willems et al. 1980), we undertook a study to determine if the concentration of PYP is increased in ATN. Furthermore, if postischemic renal tissue did preferentially accumulate PYP we wanted to determine if the renal accumulation of $^{99m}$Tc-PYP correlated with the duration of warm ischemia.

Materials and Methods

Eighteen New Zealand White (NZW) rabbits each weighing between 2.0 and 3.0 kg were used. The rabbits were given water and food ad libitum prior to the operation. They were preanesthetized with IM 0.4 mg/ml fentanyl and 20 mg/ml droperidol (Innovar Vet) in doses of 0.1 ml/kg body weight and anesthetized with IV pentobarbital 20–40 mg/kg body weight. Additional pentobarbital in doses of 10 mg was given as needed to maintain anesthesia. In all animals the right renal artery and vein were ligated under sterile conditions through a right Bergmann’s incision with a 1-0 silk suture (Ethicon). In six cases the left renal artery was left untouched. In the remaining twelve animals the left renal artery was isolated by careful non-touch technique through a left Bergmann’s incision and clamped by an Inox artery clamp (Diefenbach 13-114-04, Simonsen and Weel) for 30 min (six animals) and 60 min (six animals), respectively. Complete arterial occlusion was verified by observing the kidney surface, which immediately shrank and turned pale. Immediately after removal of the clamp all kidneys became red and firm. The rabbits were allowed to recover for 24 h. During the recovery period one 30-min ischemic animal and two 60-min ischemic animals died. The remaining animals were then reanesthetized with IM ketamine hydrochloride (Ketaset) in doses of 0.2–0.3 ml/kg body weight. $^{99m}$Tc-PYP (0.6–1.0 mCi/kg body weight) was injected through an ear vein and the animals were restrained in a ventral position underneath a scintillation camera (Searle pho-gamma 3) equipped with a pinhole-collimator. The position was adjusted by viewing the image in the camera’s persistence scope. Counts were obtained for 100 s at 10-min intervals for 90 min following injection. The animals were then killed and the left kidney was removed. The kidneys were counted separately in a gamma well counter (Searle auto-gamma well counter, 1185 R) to determine the percent of the injected activity accumulated in each kidney. Counts from six kidneys had to be deleted due to technical reasons. The remaining nine kidneys consisted of three kidneys from each group. All counts were corrected for decay.

Results

Since the injected dose and counting geometry varied from rabbit to rabbit, the results are expressed as a percentage of the activity present 10 min after the injection (Fig. 1) or as counts per 100 s per mCi injected per kg body weight (Fig. 2). At 10 min postinjection there was no significant difference between the mean activity in six normal kidneys, five 30-min ischemic kidneys, and four 60-min ischemic kidneys. During the next 40 min after injection, the mean renal activity in both the normal kidney and the 30-min ischemic kidney steadily decreased although the rate of decrease was greater in the normal kidney. In contrast, the renal activity in the 60-min ischemic kidney steadily increased and then remained relatively constant. From 40 min postinjec-
Fig. 1. The activity in the kidneys expressed as a percentage of the activity present 10 min after the injection of 99mTc-PYP 24 h after no occlusion (△), 30 min of ischemia (●) and 60 min of ischemia (○), respectively. (Mean ± SD)

Fig. 2. The activity in the kidneys expressed as counts/100 sec x mCi x kg injected/kg body weight at 10-min intervals from 10 min to 90 min after the injection of 99mTc-PYP. The injection was performed after 24 h of recovery after no occlusion (△), clamping of the renal artery for 30 min (●), and clamping of the renal artery for 60 min (○), respectively. (Mean ± SD)

Table 1. Activity 90 min after the injection of 99mTc-PYP in the kidney in percent of the total injection in the three groups

<table>
<thead>
<tr>
<th>Duration of ischemia (min)</th>
<th>Number of kidneys</th>
<th>% Injected dose</th>
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<tbody>
<tr>
<td></td>
<td>3</td>
<td>0.5 ± 0.1</td>
</tr>
<tr>
<td>30</td>
<td>3</td>
<td>5.3 ± 0.7</td>
</tr>
<tr>
<td>60</td>
<td>3</td>
<td>17.8 ± 6.9</td>
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</tbody>
</table>

Discussion

Rabbits are excellent for functional studies of ischemic damage independent of macroscopic structure: (1) Since clamping of the renal artery results in ischemic damage comparable to anoxic trauma observed in the human cadaver kidney (Løkkegaard and Bilde 1972). (2) Since the collateral circulation in the rabbit is approximately 0.2% of the total renal blood flow (Dahlager and Bilde 1976).

Ischemia for 30 and 60 min resulted in minimal morphological damage to the rabbit kidney when the kidney was sectioned following a 24-h recovery period. Lavelle et al. (1980) found no changes 24 h after 30 min of ischemia, but tubular necrotic cells could be seen after the 60-min ischemia. Thomsen et al. (1981) found cytoplasmic vacuoles and a moderate degree of nuclear pyknosis of tubular cells in kidneys removed right after 30 and 60 min of occlusion. No regular necroses were detectable so early after the ischemia. Two hours or more of ischemia were required before damage to the blood vessels was found (Bilde et al. 1977).

In our studies, we found good agreement between the ischemic damage and the renal accumulation of PYP. Based on counts from the kidneys of intact animals, the activity in the 30- and 60-min ischemic kidneys exceeded the activity in the control kidneys at 60–90 min by ratios of 2.3 and 4.6, respectively. These results are similar to those reported by Lavelle et al. (1980) who, based on extrapolated data, found that the HEDP accumulations in the 30- and 60-min occluded kidneys exceeded the control kidneys by ratios 1.3 and 2.9, respectively. In both studies renal accumulation of technetium phosphorus compounds increased with increasing ischemia.

In our study the in vivo ratios of activity in the 30-min and 60-min ischemic kidneys to the control kidneys were 2.3 and 4.6, respectively. When the isolated kidneys were counted in vitro, the 30- and 60-min ischemic kidneys had 10 and 34 times as much activity as the control kidneys. The differences...