Captopril Renography in Goldblatt Hypertension

TO THE EDITOR: In a recently published paper (1) Nally and co-workers investigated the effect of angiotensin converting enzyme (ACE) inhibition in dogs with either two kidneys, one clip (2K1C) or one kidney, one clip (1K1C) hypertension. The aim of their study was to improve the sensitivity of renography for the noninvasive detection of renal artery stenosis (RAS). For technetium-99m diethylenetriaminepentaacetic acid ([99mTc]DTPA) as well as for iodine-131 iodohippurate ([131I]IOH), captopril studies were found to be more sensitive in comparison to renography without ACE inhibition; however, RAS was most evident in the 15-min [99mTc]DTPA studies. For the assertion of RAS, time-activity curves from the kidneys were analyzed by integrating the area under the curve (integration period: first 5 min for 15-min [99mTc]DTPA and 30-min [131I]IOH; initial 30 sec for 90-sec [99mTc]DTPA). The ratio of the areas under the curves (stenotic/contralateral kidney) was used to demonstrate the diagnostic effect of ACE inhibition.

From renography and from the effects of ACE inhibition in 2K1C hypertension, as well as from our own observation in patients with unilateral RAS we think this ratio inappropriate for RAS detection in captopril renography. It is generally accepted that the renogram A(t) can be described by the convolution integral of the arterial tracer concentration cA(t) and the impulse retention function R(t), multiplied by the renal extraction for the tracer. Therefore the renogram is given by the equation 

\[ A(t) = GFR \int cA(t) \cdot R(t) \cdot dt \]

for DTPA and 

\[ A(t) = ERPF \int cA(t) \cdot R(t) \cdot dt \]

for IOH. ACE inhibition causes a rapid decrease in glomerular filtration rate (GFR) in RAS, but has little effect on the contralateral side. As a consequence in RAS with ACE inhibition [99mTc]DTPA uptake is diminished on the stenotic side, accompanied by a prolonged retention for the radiopharmaceutical in the kidney. Since the integration time of 5 min is long compared to minimal transit times for [99mTc]DTPA—especially in well-hydrated individuals—the area under the stenotic kidney curve should increase. On the other hand the diminished uptake reduces the integral value. Thus in calculating the area for the stenotic side in 15-min [99mTc]DTPA in this manner the effects interfere and the sensitivity for RAS detection is reduced. Another puzzling point is the finding of an ~50% reduction for the [131I]IOH ratio after captopril. In RAS, ACE inhibition decreases selectively the efferent arteriolar resistance, causing a dissociation of the autoregulation of the kidney.

Frederick L. Datz
Paul E. Christian
John G. Moore
University of Utah Medical Center
Salt Lake City, Utah


FIGURE 1

[131I]IOH and [99mTc]DTPA renograms without captopril (upper row) and with captopril (lower row). A 70% stenosis of the right kidney (dotted line) was confirmed angiographically.
by maintaining renal blood flow despite an abrupt decrease in GFR (3,4). This is even supported by the PAH clearance measurements of the authors (1,2). No significant effect of ACE inhibition on ERPF was found for the stenotic as well as the nonstenotic kidney. This fact is also in conflict with the curves given in Fig. 1(1) for the 90-sec $^{99m}$Tc-DTPA studies with and without captopril.

With unilateral RAS we found in our patients regularly an unchanged first phase for $^{99m}$Tc-DTPA and an unchanged $^{[123]}$I-OIH uptake after captopril, together with a reduced uptake for $^{99m}$Tc-DTPA and a prolonged retention for DTPA and OIH. The figure shows renogram curves for a patient with an angiographically confirmed 70% stenosis of the right kidney. Ratios in the patient calculated according to Nally’s and co-workers method amount to 0.98, 0.97, and 0.90 for 15-min $^{[123]}$I-OIH 15-min $^{99m}$Tc-DTPA and 90-sec $^{99m}$Tc-DTPA in studies without captopril and to 1.20, 0.92, and 0.86 in studies with captopril. The uptake of $^{99m}$Tc-DTPA 90 sec postinjection was 72% for the stenosed kidney in comparison to the nonstenotic kidney for the captopril renogram, and 98% for the study without captopril. The mean transit time for the stenotic kidney increased from 2.5 min for the baseline study to 9.5 min (OIH) resp. 7.8 min (DTPA) after captopril. In contrast to the calculated ratios, both parameters were judged as diagnostic for RAS detection in this patient.

References


K. Kletter
H. Frischauf
University of Vienna
Vienna, Austria

REPLY: We would like to thank Dr. Kletter for his comments and agree with his basic assertions. However, several points deserve clarification and emphasis.

In a two-kidney, one-clip model of hypertension, angiotensin converting enzyme (ACE) inhibition results in decrease in GFR of the stenotic kidney. This physiologic response may be manifest by either patterns of retention or a marked decrease in uptake of $^{99m}$Tc-DTPA. In the acute dog model, the latter pattern was seen uniformly in all of our studies. Consequently, the area under the curve for the stenotic kidney decreased as did the ratio of stenotic kidney/contralateral kidney. In patients with unilateral renal artery stenosis, either pattern of retention or depression of $^{99m}$Tc-DTPA uptake may be seen after captopril. We have seen many patients similar to the one described by Dr. Kletter. Obviously, such a pattern of retention would skew the ratio of area under the curve in the positive direction.

Second, the Results section of our paper clearly states that the decrease in ratio (stenotic/contralateral) for the Hippuran renogram actually results from little change in the stenotic kidney and an increase in area under the curve for the contralateral kidney. These changes are consistent with our observations of a negligible change in ERPF of the stenotic kidney and a 22% increase in ERPF of the contralateral kidney.

In general, Dr. Kletter’s comments correctly emphasize the dangers of blindly applying observations in an experimental animal model to human studies. ACE inhibition clearly does have a marked effect upon both the $^{99m}$Tc-DTPA and $^{[123]}$I-Hippuran renograms in man and dog with unilateral renal artery stenosis. However, we would agree with the assertion that utilization of area under the curve parameters with captopril renography in patients may yield conflicting results.

Joseph V. Nally, Jr.
Cleveland Clinic Foundation
Cleveland, Ohio
William J. Potvin
Medical College of Ohio
Toledo, Ohio
Joe P. Windham
Henry Ford Hospital
Detroit, Michigan

The Superconducting Super-Collider: Impact on Nuclear Medicine

TO THE EDITOR: In her review of the status of Department of Energy (DOE) facilities (1), Linda Ketchum overlooked a DOE facility that has been producing radionuclides for nuclear medicine. Argonne National Laboratory also has a 60-inch, multi-particle cyclotron that has been solely devoted to isotope production for the last 10 years. Since the beginning of this year, the operation of the cyclotron has been the responsibility of the nuclear medicine research program.

While the superconducting super-collider (SSC) was discussed as a potential drain on the resources of existing programs, it should be noted that this new machine could also be a source of isotopes. The circular accelerators used for high-energy physics accelerate the particles in stages. It would be appropriate at this point in the planning of this accelerator for the members of the nuclear medicine community to propose that an isotope production facility be built after the first stage of acceleration. This would be similar to the Brookhaven Linac Isotope Production (BLIP) facility and would use beam otherwise “wasted” while the large ring accelerates the protons for high energy physics experiments. If such a facility were made a part of the design from the beginning, the problems that nearly forced the closing of the Los Alamos Meson Physics Facility (LAMPF) could potentially be avoided. Advance planning would also keep the cost of such a facility lower than if it were added on at a later date.

References

1. Ketchum LE. Physics experiment may cloud future of Los Alamos nuclear medicine program; erratic supply of