Effect of Captopril on Renal Hemodynamics in the Treatment of Resistant Renal Hypertension

STAFFAN BJÖRCK, M.D., HANS HERLITZ, M.D., GUDRUN NYBERG, M.D., GÖRAN GRANERUS, M.D., AND MATTIAS AURELL, PROF.

SUMMARY The effects of 6 weeks of treatment with captopril on the renal hemodynamics of 16 patients with treatment-resistant renal hypertension (six had diabetic nephropathy, seven had other renal parenchymatous disease, and three had renovascular disease) were studied. Significant changes in glomerular filtration rate, filtration fraction, plasma renin activity, urinary aldosterone, and mean blood pressure were noted in the patients with renal parenchymatous disease, but not in those with diabetic nephropathy. Renal blood flow remained unchanged in all patients. Captopril was well tolerated. (Hypertension 5 (supp III): HI-152-HI-153, 1983)

Key Words • glomerular filtration rate • renal plasma flow • diabetic nephropathy • renal insufficiency • renin-angiotensin system

The renin-angiotensin system is involved in the regulation of the glomerular filtration rate (GFR) and renal blood flow (RBF). Its importance is enhanced when the renin-angiotensin system is activated, for instance in the salt-depleted state, when angiotensin converting-enzyme (ACE) blockade can induce a pronounced increase in renal blood flow, even in the face of reduced blood pressure. The renal hemodynamic response to ACE-blockade in the presence of renal disease is not as well investigated. Captopril has been found to decrease GFR when used in patients with reduced renal function and, especially so, in bilateral renovascular disease. The efficacy and tolerability of captopril in diabetes and diabetic nephropathy have not been reported. In the present study, the renal hemodynamic functions before and during captopril treatment were investigated in patients with renal disease and treatment-resistant hypertension.

Patients and Methods

Patients

Sixteen patients with therapy-resistant renal hypertension, defined as a diastolic blood pressure repeatedly greater than 95 mm Hg despite treatment with at least three drugs (a beta-blocker, a diuretic, and a vasodilating drug) were included in the study. Six of the patients had diabetic nephropathy (DN), seven had other renal parenchymatous disease (RPD), and three had renovascular disease (RVD). The RVD group was comprised of one patient with bilateral and two with unilateral renal artery stenoses. The previous antihypertensive treatment was changed to captopril in addition to a diuretic. The daily captopril dose was 37.5 to 300 mg, depending on the renal function. In four patients, the beta-blocker therapy had to be continued because of other diseases.

Methods

Glomerular filtration rate (GFR), renal plasma flow (RPF), plasma renin activity (PRA), angiotensin II (All) levels, and urinary aldosterone excretion were investigated before, 1 week after, and 6 weeks after initiation of captopril therapy. GFR was measured according to Bröchner-Mortensen’s method using $^{51}$Cr-EDTA as filtration marker and RPF measured as PAH-clearance. PRA was analyzed using radioimmunoassay for angiotensin I according to the method of Giese et al., and All according to Dusterdieck and McElwee with the modification described by Kappelgaard et al.

Results

The effect of captopril on renal hemodynamics, PRA, All, and urinary aldosterone in patients with DN and other RPD are shown in table 1. Significant changes of GFR, filtration fraction, PRA, and urinary aldosterone were noted in the group with renal parenchymatous disease, but not in patients with diabetic nephropathy. The three patients with renovascular disease were not included in table 1 and had decreases in blood pressure ($-18\%$), All ($-92\%$), GFR ($-21\%$), and urinary aldosterone ($-77\%$). The RPF, however, remained unchanged at the three investigations (176.3; 193.0; 158.3 ml/min/1.73 m$^2$).
CAPTOPRIL AND RENAL HEMODYNAMICS/Björck et al.

In conclusion, we have found no significant alteration in renal plasma flow after 6 weeks of captopril therapy in 16 patients with renal hypertension. The GFR decreased by 13% in patients with renal parenchymatous diseases while it was unchanged in patients with diabetic nephropathy.

References


Captopril was well tolerated by all patients. The MAP decrease was 9.9% (p < 0.01) in the RVD and RPD groups after 6 weeks. The DN group had no blood pressure reduction. However, combination of furosemide and captopril in these patients resulted in a blood pressure control equal to the earlier three-drug therapy.

After 6 weeks GFR had decreased in two of the three patients with RVD and in all patients with RPD. It remained unchanged in the diabetic group. The greatest fall in GFR occurred in two patients with renal artery stenoses, who also had the greatest blood pressure decrease. Blood pressure reduction and decrease in GFR were not related to each other in the other patient groups.

Mean RPF tended to increase, but the interindividual variation was considerable. The greatest increase was 80% after 1 week in one patient with diabetic nephropathy. The individual response after 1 week persisted, but to a lesser degree after 6 weeks. The RPF response could not be predicted from the level of All, PRA, or from the degree of blood pressure reduction. We don’t think that the withdrawal of beta-blockade contributes to the increase in RPF since concomitant therapy with vasodilating drugs has been shown to counteract the RPF-lowering effect of beta-blockade, and the vasodilator was withdrawn at the same time as the beta-blocking drug.

The filtration fraction decreased significantly in the RPD and RVD group. The most plausible mechanism for this is a dilatation predominantly of the postglomerular arteriole by the ACE blockade, as has been suggested by Hall et al. The filtration fraction in the diabetic group was already low before treatment, which could be due to changed membrane properties caused by their renal disease.

As expected, after ACE blockade, PRA increased and All decreased, but the changes from the initial values were slightly smaller in the DN group than in the other groups. In the DN group, urinary aldosterone levels remained completely unchanged after captopril, in contrast to a marked reduction in the other patients. The reason for this is not known, but it might be due to a disturbed prostaglandin system in diabetics, since inhibition or prostaglandin synthesis can induce a similar pattern of reaction.
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S Björck, H Herlitz, G Nyberg, G Granerus and M Aurell

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