Role of angiotensin in the vascular response to chronic renal tubular obstruction

by

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ABSTRACT

Chronic (24 hour) obstruction of single tubules of the rat kidney causes a decrease in glomerular blood flow as a result of afferent arteriolar constriction. Since all of the components of the renin-angiotensin system are present in the juxtaglomerular apparatus of each nephron, we investigated the possibility that obstruction-induced vasoconstriction is mediated by intrarenal angiotensin generation. In pentobarbital anesthetized rats, micropuncture techniques were utilized to inject long viscous castor oil blocks into the lumens of 15-20 proximal tubules. The next day, the animals were anesthetized with Inactin and 9 μm microspheres were injected into the circulation at the left ventricle. For each rat, glomerular blood flow was calculated from the number of trapped microspheres visualized in microdissected normal and obstructed nephrons. Three sets of rats and their vehicle controls were examined by this procedure. The treatments given were (I) captopril, 10 mg/kg, p.o., (II) saralasin, 10 μg/kg/min, i.v., or (III) high salt intake administered in drinking water plus desoxycorticosterone (DOC) injections at an average dosage of 2.7 mg/kg/day for 2-3 weeks.

Glomerular blood flow of normal nephrons in control animals averaged 226 ± 12 nl/min (S.E.M., n=17 rats), while blood flow to blocked nephrons was 130 ± 9 nl/min, a 41% decrease in glomerular perfusion ($p<0.001$). In 5 rats

treated with captopril, a converting enzyme inhibitor, blood flow to normal nephrons and obstructed nephrons averaged 296 ± 40 and 252 ± 31 nl/min, respectively, representing a significant improvement in flow to blocked tubules ($p<0.005$). In six rats treated with saralasin, an angiotensin antagonist, blood flow to unobstructed nephrons was 210 ± 11 nl/min, while flow to blocked nephrons averaged 152 ± 4 nl/min, a significant reduction of the vasoconstriction response to obstruction when compared to control rats ($p<0.05$). In 6 renin depleted rats (high salt intake and DOC), blood flow to normal and tubule-obstructed nephrons was 229 ± 20 and 181 ± 21 nl/min, respectively, a significant decrease in the difference in flow between normal and blocked nephrons ($p<0.0005$).

Therefore, both renin suppression and pharmacologic intervention of angiotensin action with captopril or saralasin improved glomerular perfusion of obstructed nephrons. This strongly supports the dependence of obstuction-induced changes in arteriolar resistance upon angiotensin activity. These observations support the theory that angiotensin functions as a locally acting hormonal factor controlling glomerular hemodynamics.

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