DIABETES

Early blockade of the renin–angiotensin system in type 1 diabetes mellitus

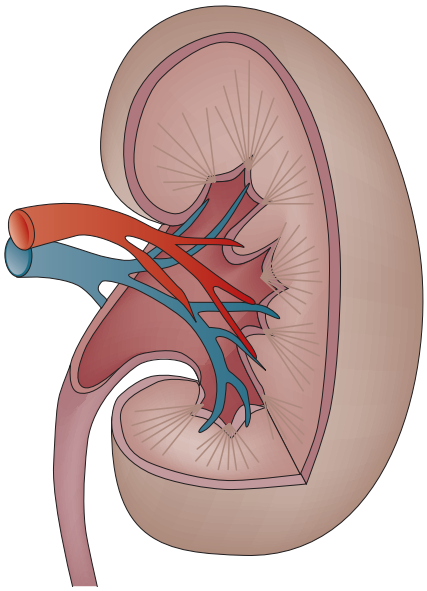
Progression of nephropathy cannot be delayed by blocking the renin–angiotensin system before the onset of albuminuria in patients with type 1 diabetes mellitus, report the researchers of a multicenter study published in the *New England Journal of Medicine*. Such treatment, however, slows the progression of diabetic retinopathy.

Previously, blockade of the renin–angiotensin system has been suggested to decrease progession of nephropathy and proteinuria in patients with diabetes mellitus who have diabetic nephropathy at a relatively advanced stage (characterized by proteinuria and a decreased glomerular filtration rate). In addition, treatment with renin–angiotensin system blockers decreases the risk of the development of retinopathy in patients with diabetes mellitus. In this study, treatment with such agents had beneficial effects on structural changes related to type 1 diabetes mellitus in the retina, but not in the kidneys.

Mauer and colleagues performed a randomized, controlled, multicenter trial to assess the renal and retinal effects of treatment with the angiotensin-receptor blocker losartan (50 mg per day, followed by 100 mg per day), the angiotensin-converting enzyme enalapril (10 mg per day, followed by 20 mg per day) and placebo. The study group included 285 patients with type 1 diabetes mellitus for 2–20 years who did not have hypertension, albuminuria or proliferative diabetic retinopathy. Participants were followed up for 5 years.

The primary renal end point, fraction of glomerular volume occupied by mesangium, was determined at baseline and at 5 years. Morphometric measurements, which were performed on electron micrographs of renal biopsy specimens, revealed that changes in mesangial fractional volume during the study period did not differ substantially between either treatment group and the placebo group. Decreases in glomerular filtration rate were also similar in all three groups. The discrepancy between these results and those reported in earlier studies might be explained by the fact that participants of this study were at a lower risk of diabetic nephropathy at baseline than those of previous studies.

Surprisingly, the incidence of microalbuminuria was markedly higher in patients who received losartan than in those who received placebo. Therefore, the authors recommend careful monitoring of albumin excretion rate in patients who receive treatment with angiotensin-receptor blockers.



The risk of progression of retinopathy by at least two steps on a 15-step diabetic retinopathy severity scale was reduced by 65% in the enalapril group and by 70% in the losartan group compared with the placebo group. These changes were not related to the patients' HbA_{1C} levels. The authors hypothesize that the observed improvements are related to either the blood pressure-lowering effects of enalapril and losartan or their direct effect on the renin–angiotensin system in the retina.

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Original article Mauer, M. *et al.* Renal and retinal effects of enalapril and losartan in type 1 diabetes. *N. Engl. J. Med.* **361**, 40–51 (2009).