C23

Effect of lovastatin on glomerular TGF-b1 mRNA expression and progression of diabetic nephropahy in streptozotocin-induced diabetic rats.

HB Lee, SI Kim and DC Han
Hyonam Kidney Laboratory, Soon Chun Hyang University. Seoul, Korea.

We have previously shown that inhibition of HMG CoA reductase by lovastatin ameliorates albuminuria and glomerulosclerosis in 5/6 nephrectomized rats (Nephrol Dial Transpl 8: 1534, 1993) and in streptozotocin (STZ)-induced diabetic uninephrectomized rat (Kidney Int 44:1181, 1993) and that in STZ-diabetic rats lovastatin suppresses glomerular TGF-b1 mRNA expression as examined by in situ hybridization in 2 days after but not in 2 weeks after STZ (Kidney Int 48, Suppl 51 S61, 1995). We extended our observation to longitudinal study from 4 days to 12 months after induction of diabetes by STZ in rats. Urine albumin was measured by bromocresol green method. Glomerular surface area was measured with Image-pro (ver. 1.2, Media Cybernetics, USA) software program on PAS-stained tissue section and glomerular volume was calculated according to Weibel and Gomez method. Glomerular TGF-b1 mRNA was examined by Northern analysis. In untreated diabetic rats, a 4-fold increase in urinary albumin excretion, 50 % increase in glomerular volume, and 60 % increase in glomerular TGF- b1 mRNA expression were observed. In lovastatin treated diabetic rats all these changes were almost completely abrogated. There was a tendency for the blood glucose levels to decline in lovastatin-treated rats beginning 1 month after STZ but TGf-b1 mRNA remained suppressed on days 4, 14, and 28 when blood glucose levels were elevated. The results suggest that renal protective effect of lovastatin in diabetes may be due in part to suppression of TGF-b1.

C24

Enalapril suppresses glomerular TGF-b1 mRNA and progression of diabetic nephropathy in streptozotocin- induced diabetic rats.

HB Lee, DC Han, SI Kim.
Hyonam Kidney Labratory, Soon Chun Hyang University, Seoul, Korea.

Angiotensin converting enzyme (ACE) inhibition slows the progression of diabetic nephropathy presumably by controlling intraglomerular hypertension. Cellular and molecular mechanisms of this renal protective effect of ACE inhibition are not clearly understood although evidences from experimental studies would suggest that suppression of TGF-b/TGF-b receptor system may be involved. We, therefore, examined the effects of enalapril on the progression of diabetic nephropathy and on the glomerular expression of TGF-b1 mRNA in streptozotocin-induced diabetic rats. Urine albumin was measured by bromocresol green method. Glomerular surface area was measured with Image-pro (ver. 1.2, Media Cybernetics, USA) software program on PAS-stained tissue section and glomerular volume was calculated according to Weibel and Gomez method. Glomerular TGF-b1 mRNA was examined by Northern analysis. In untreated diabetic rats, up to 4-fold increase in urinary albumin excretion, 50 % increase in glomerular volume, and 60 % increase in glomerular TGF-b1 mRNA expression were observed. Enalapril attenuated all these changes without affecting blood glucose levels. The results suggest that the renal protective effect of ACE inhibition in diabetes may be due in part to suppression of TGF-b1.