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Simvastatin inhibits tissue factor and plasminogen activator inhibitor-1 expression of glomerular mesangial cells in hypercholesterolemic rabbits

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ABSTRACT

Tissue factor (TF) and plasminogen activator inhibitor-1 (PAI-1) activity and/or expression are upregulated in hypercholesterolemia. Despite extensive research on anti-thrombotic effect of statins, little is known about their effects on TF and PAI-1 expression in glomerular mesangial cells under hypercholesterolemic condition. Male rabbits were fed on either normal or high-cholesterol diet for 8 weeks. Then cholesterol-fed rabbits were randomly assigned to simvastatin or starch. At the end of 12 weeks, glomerular mesangial cells were collected. The concentrations of TF and PAI-1 mRNA were detected by RT-PCR. The plasma activities of TF and PAI-1 were determined with enzyme linked immunosorbent assay (ELISA) and chromogenic substrate method, respectively. The atherogenic diet caused a consistent increase in serum concentrations of total cholesterol (TC) and serum triglyceride (TG) (p < 0.05), increased TF and PAI-1 mRNA expression in glomerular mesangial cells and plasma activities as compared to the normal diet (p < 0.01). Four-week simvastatin treatment resulted in significant decrease of mesangial TF and PAI-1 mRNA (p < 0.01), and also of the plasma activities of TF (p < 0.05) and PAI-1 (p < 0.01). These results suggest that simvastatin might protect kidney from the formation of microthrombus under hypercholesterolemic condition and might be a possible pathogenesis of obesityrelated glomerulopathy.

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