



Reconstituted HDL improves endothelial function in type 2 diabetes

Patients with type 2 diabetes are typically characterised by dyslipidaemia (low levels of high-density lipoprotein [HDL] cholesterol, elevated triglycerides and an increase in small, dense, low-density lipoprotein [LDL] particles) and endothelial dysfunction, which contribute to a high risk for cardiovascular disease. However, lowering LDL cholesterol with statin treatment has been shown to be inadequate in restoring vascular dysfunction in these patients. Researchers at the Amsterdam Medical Center, University of Amsterdam, The Netherlands, therefore investigated the value of infusion of reconstituted HDL (apolipoprotein A-I [apoA-I]/ phosphatidylcholine discs) in type 2 diabetes.

Endothelial dysfunction was evaluated using venous occlusion plethysmography in 7 patients with uncomplicated type 2 diabetes and 7 normolipidaemic controls. Forearm blood flow responses were measured to intra-arterial infusion of cumulative doses of the vasodilators serotonin and sodium nitroprusside, as well as NG-monomethyl-L-arginine (L-NMMA), an inhibitor of nitric oxide synthase, responsible for production of nitric oxide (NO), which has vasodilatory activity. Reconstituted HDL 80 mg/kg was infused over a 4-hour period, and measurements of basal and stimulated NO activity as well as endothelium-independent vasodilation were repeated. Plasma levels of apoA-1 and oxidised LDL were measured before and 4 hours after HDL infusion.

In patients with type 2 diabetes, infusion of reconstituted HDL restored forearm blood flow responses to serotonin and L-NMMA. No effect was observed in control subjects. Infusion of reconstituted HDL also increased plasma levels of apoA-I ($p < 0.01$) and decreased levels of oxidised LDL ($p < 0.05$) in patients with type 2 diabetes and controls.

The data suggest that infusion of reconstituted HDL can exert direct beneficial effects on the arterial wall in patients with type 2 diabetes via restoration of basal and stimulated NO bioavailability. These findings provide support for therapeutic strategies that increase the vasodilatory properties of HDL.

Reference

1. Nieuwdorp M, Stroes ES. Restoration of endothelial function after infusion of reconstituted high-density lipoprotein in subjects with type 2 diabetes mellitus. Presented at the American Heart Association Scientific Sessions 2006, Abstract 1344.