Effect of Tetranectin-apoA-I infusions on atherosclerosis progression/regression in hypercholesterolemic rabbits

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Experimental and clinical studies have shown that intravenous administration of synthetic HDL (sHDL) containing human apolipoprotein A-I (apoA-I) cause a significant atherosclerosis regression. A possible limitation of this therapeutic approach may be a rapid apoA-I turnover that can be partially circumvented by the use of apoA-I variants characterized by a slower catabolism, such as apoA-I_{Milano}. Tetranectin-apoA-I, a trimeric human apoA-I, was designed to reduce renal clearance and thus prolongue half-life and, possibly, efficacy. Aim of the study was to evaluate the effect of Tetranectin-apoA-I infusion on atherosclerosis regression in a rabbit model widely used to test the efficacy of synthetic HDL. 36 rabbits underwent a perivascular injury at both carotids, followed by a 1.5% cholesterol diet. At 90 days after surgery, rabbits were randomly divided into 4 groups and i.v. treated, five times, once every three days, with different doses of Tetranectin-apoA-I (8, 40, 100 mg/kg) or with placebo. Plaque changes were evaluated *in vivo* by intravascular ultrasound (IVUS), performed before and at the end of the treatment period. Total atheroma volume in the placebo group increased in the time between the first and the second IVUS evaluation (+11.7±4.5% from baseline). A reduced progression or a regression was observed vs baseline in Tetranectin-apoA-I treated groups (+1.3±1.9% in 8 mg/kg; -0.03±4.80% in 40 mg/kg; -1.6±4.3% in 100 mg/kg treated rabbits). Absolute and percent changes of total atheroma volume in each Tetranectin-apoA-I group were significantly different from those found in the placebo group ($p<0.005$). On summary, five Tetranectin-apo-A-I administrations proved effective in reducing carotid plaque progression (8 and 40 mg/kg dose) or in inducing regression (100 mg/kg dose) in hypercholesterolemic rabbits.