ABSTRACTS
77th Congress of the European Atherosclerosis Society
April 26–29, 2008
Istanbul, Turkey
Background and aims: Cilostazol, an antiplatelet drug, and probucol, a cholesterol-lowering drug, are reported to ameliorate atherosclerosis in animal models. However, their combined effect on atherosclerosis is unclear. We therefore evaluated their combined effect on atherosclerotic lesions in LDL receptor-deficient mice.

Methods: Male LDL receptor-deficient mice were fed a high fat diet with or without cilostazol alone, probucol alone, or with cilostazol and probucol in combination, for 8 weeks. Body weight and plasma lipid levels were measured before and during treatment. At the end of treatment, the size distribution of plasma lipoproteins was analyzed by HPLC and then plasma HDL cholesterol levels and en face aortic atherosclerotic lesion areas were measured.

Results: Probucol alone significantly decreased both total cholesterol and HDL cholesterol, while cilostazol alone did not decrease total cholesterol but significantly increased HDL cholesterol. Both cilostazol alone and probucol alone significantly decreased atherosclerotic lesion areas, and their combined administration showed more significant decreases than when each drug was administered singly.

Conclusion: The combination of cilostazol and probucol was more effective in preventing atherosclerotic lesion formation than the administration of each drug alone; this may provide us with a new strategy for treating atherosclerosis.

PO6-47

ATHEROGENESIS, Pancreatitis and Brain Dysfunction in LPL Deficient Mice with Severe Hypertriglyceridemia

X. Zhang, R. Qi, X. Xian, Y. Wang, W. Huang, G. Lu Institute of Cardiovascular Sciences, Peking University, Beijing, China

Background and Aim: Mice of homozygous lipoprotein lipase (LPL) gene deficiency could be rescued from neonatal lethality by somatic gene transfer of a beneficial mutant. These mice developed severe hypertriglyceridemia, which mimics that of human mutations in LPL gene.

Methods and results: At age over 15 months unexpected spontaneous atherosclerosis was detected in these mice and high levels of oxidative stresses and hypertriglyceridemia. In pancreatic acinar cells from wild type mice addition of CM to LPL deficient patients, these mice have increased susceptibility to acute pancreatitis. In pancreatic acinar cells from wild type mice addition of CM to LPL deficient patients, these mice have increased susceptibility to acute pancreatitis. After discovery of learning and memory deficit in these mice electrophysiology, one of the most important neuropathic marker, also reduced significantly.

Conclusions: The alterations in multi-organs suggested that severe HTG might exert pathological effects via certain common mechanisms to induce organ injury, which will provide new insights into lipid-related cellular stress.

PO6-48

THE BIOCHEMICAL AND CARDIOVASCULAR CONSEQUENCES OF LCAT DEFICIENCY

L. Calabresi, D. Daldassarre, E. Moleri, P. Conca, S. Castelnuovo, G. Franceschini. Center E. Grossi Paoletti, Department of Pharmacological Sciences, University of Milano, Italy

We have recently identified 14 Italian families with LCAT deficiency, carrying 19 different mutations in the LCAT gene. All carriers of two mutant LCAT alleles (n=17) had remarkably low plasma HDL-C, apoA-I, and apoA-II levels, associated with multiple alterations in HDL structure and particle distribution, with a selective depletion of LpA1/A-II particles, a predominance of small, pre-beta-migrating HDL and a complete lack of HDL2. Unesterified cholesterol, the unesterified/total cholesterol ratio, VLDL-cholesterol, and triglycerides were significantly elevated, whereas apoB was significantly lower compared to controls. Twenty-three out of 44 carriers of one mutant LCAT allele (53%) had a low plasma HDL-C; the average plasma HDL-C and apoA-I levels were significantly lower than in controls. Plasma LCAT activity was also significantly lower than in controls. Despite the atherogenic profile, only one of the 17 carriers of two mutant LCAT alleles, a 71 y.o. man with elevated LDL-C, hypertension, and diabetes, presented with premature coronary artery disease. The evaluation of carotid intima-media thickness (IMT) showed that carriers of two mutant LCAT alleles have IMT values comparable to age-sex matched controls, despite the severe hyperalphalipoproteinemia. Carriers of one mutant LCAT allele have widely distributed IMT values, showing on average IMT values comparable to controls. In a large series of subjects carrying mutations in the LCAT gene, the inheritance of a mutated LCAT genotype causes a gene-dose-dependent alteration in the plasma lipid/lipoprotein profile. No premature cardiovascular disease and no increase in carotid IMT was observed, despite the hyperalphalipoproteinemia, in the Italian LCAT deficient subjects.