90 UPDATE OF THE BIOCHEMICAL AND MOLECULAR RESULTS OF PORTUGUESE PATIENTS WITH FAMILIAL COMBINED HYPERLIPIDAEMIA

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FCHL is a complex disorder with a highly atherogenic profile. The aim of this study is the biochemical/molecular characterization of FCHL patients.
Molecular study of *LPL*, *APOAIV*, *APOAV*, *APOCIII* and *USF1* (s1,s2) was performed in 35 index patients by PCR amplification and sequencing. Total cholesterol (TC), HDL-c, sdLDL, triglycerides (TG), apoB and apoCIII were measured in automated analysers. sdLDL was also analysed by electrophoresis with Lipoprint®. ApoAIV and ApoAV were measured by ELISA. For all patients, biochemical characterization of apolipoproteins and sdLDL before treatment was not possible to determine.
Prior to medication the levels of TC (305±62 mg/dL) and TG (380±269 mg/dL) were high but HDL-c was normal (44±11 mg/dL). Even under medication these patients presented high levels of CT (205±58 mg/dL), TG (233±109 mg/dL) and ApoCIII (15±4 mg/dL) and normal levels of HDL-c (44±9 mg/dL). ApoAIV (17±10 mg/dL), ApoAV (156±140ng/mL) and ApoB (89±41 mg/dL) levels were within normal range in majority of cases. Lipoprint® analysis of 8 patients under medication revealed an atherogenic pattern.
Two new alterations were found. One patient with TC=271 mg/dl and TG=275 mg/dL carried APOAIV Q359_E362 (values without medication). Another patient with TC=419 mg/dL and TG=1095 mg/dL presented APOAV D332fsX336 and, even under medication, had high sdLDL (39 mg/dL, cut-off value 35 mg/dl) and an atherogenic pattern with Lipoprint® analysis (pattern B). Some patients had a novel alteration APOCIII 3269C>A that was proven later that was a polymorphism.
Patients with FCHL have increased cardiovascular risk that can be prevented with an early genetic identification and an extensive biochemical characterization that can be important to evaluate the efficacy of treatment.

91 THE EFFECTS OF COMBINING ROSUVASTATIN WITH SARTANS OF DIFFERENT PPARγ ACTIVATING CAPACITY ON LOW-DENSITY LIPOPROTEIN SUBFRACTIONS AND LIPOPROTEIN-ASSOCIATED PHOSPHOLIPASE A_2

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Aims: Sartans differ in their capacity to partially active the peroxisome proliferator-activated receptor γ (PPARγ). The aim of this study was to evaluate whether this characteristic is associated with changes in low-density lipoprotein (LDL) subfraction phenotype or plasma lipoprotein-associated phospholipase A_2 ($LpPLA_2$) when co-administrating a sartan with a statin.
Methods: Patients (n = 151) with mild hypertension, impaired fasting plasma glucose (FPG), elevated triglycerides (⩾150 mg/dL) and LDL cholesterol (⩾160 mg/dL) were given dietary intervention and rosuvastatin (10 mg/day). Patients were randomized to: (1) a sartan which partially activates PPARγ (telmisartan 80 mg/day; RT group), (2) a sartan with low efficacy in activating PPARγ (irbesartan 300 mg/day; RI group) and (3) a sartan with no efficacy in activating PPARγ (olmesartan 20 mg/day; RO group). Patients were re-evaluated 6 months after treatment onset.
Results: The lipidemic profile was similarly altered in all groups. Small dense LDL cholesterol decreased vs baseline in the RT (−67%), RI (−58%) and RO (−61%) groups ($p < 0.001$). All regimens increased LDL particle size vs baseline (RT +1.4%; $p = 0.002$, RI +1.0%; $p < 0.04$ and RO +1.4%; $p = 0.001$). Plasma Lp-PLA_2 activity equally decreased vs baseline in all groups (RT −38%, RI −38%, RO −43%) ($p < 0.001$). Plasma Lp-PLA_2 mass similarly decreased in all groups vs baseline (RT −28%; $p = 0.001$, RI −32%; $p = 0.01$ and RO −27%; $p = 0.001$). No difference for any parameter change was noticed among groups.
Conclusions: Co-administrating rosuvastatin with sartans of different degree of PPARγ activating capacity was not associated with differential changes in LDL subfractions or plasma $LpPLA_2$ activity and mass.

92 THE PRESENCE OF REMNANT LIPOPROTEINS IN THE FASTING PLASMA WITH TG LEVELS LESS THAN 150 MG/DL

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Introduction: Remnant-like lipoprotein particles (RLP) have been measured by cholesterol as RLP-C for CHD risk assessment. However, RLP-TG is a better marker to detect the presence of remnant lipoproteins in plasma with TG levels less than 150 mg/dL.
Method: Serum RLP-TG levels in health-check populations, cardiovascular disease, diabetes and oral fat load cases were determined. Serum TC, TG, HDL-C, LDL-C and RLP-C concentrations were also determined in the same cases.
Results: Cut-off value (75 percentile) of RLP-TG determined in the fasting normal control cases in Japanese population was 13 mg/dl in men and 10 mg/dL in women. Ninety fifth percentile of RLP-TG less than TG levels 150 mg/dL was 20 mg/dL. In patients with diabetes, metabolic syndrome, cardiovascular disease, RLP-TG levels were significantly higher than those in normal control subjects. RLP-TG levels increased significantly in postprandial plasma with TG levels less than 150 mg/dL. When fasting TG levels were less than 150 mg/dl, the frequency of the cases in normal control group RLP-TG >20 mg/dL was 4.8% and the frequency in disease cases were significantly higher.
Conclusion: RLP-TG levels were shown to be significantly higher in cases with diabetes, metabolic syndrome, cardiovascular disease. Moreover, the frequency of higher RLP-TG levels above 20 mg/dL in the fasting state when TG < 150 mg/dL was significantly higher in disease cases than in normal controls. These results revealed that TG therapy should be targeted to reduce less than 150 mg/dL of TG using RLP-TG as a parameter.

93 HYPERLIPIDEMIA AND OXIDATIVE STRESS ARE THE MAIN DETERMINANTS OF INTIMA-MEDIA THICKNESS IN CHILDREN WITH CHRONIC KIDNEY DISEASE

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Objective: Roles of dyslipidemia and oxidative stress in early phases of atherosclerosis were tested in renal disease (RD) children. We have used intima-media thickness of common carotid arteries (IMT CCA) as a measure of early atherosclerosis.
Methods: Fifty-two pediatric patients were enrolled in the study (10 chronic renal insufficiency − CRI, 22 renal transplant − RT and 20 haemodialysis − HD patients) and 36 healthy children (CG). Lipid status was assessed by measuring total, LDL, HDL, free-cholesterol and tryglicerides (TC, LDL-C, HDL-C, FC, TG). Oxidative status was determined through malondialdehyde (MDA) concentration and superoxide-dismutase (SOD) activity. IMT measurement was performed by using Siemens SONOLINE B-mode ultrasound apparatus. Multiple linear regression analysis with backward selection has been used to estimate influence of dyslipidemia, oxidative status and renal function markers on patients' IMT value.
Results: Renal disease children had disturbed lipid content, which was the most pronounced in HD children. They have significantly higher FC, and TG compared to healthy children (FC: 1.50±0.391 vs. 1.06±0.227, $p < 0.001$; TG: 1.934±0.917 vs. 0.703±0.359, $p < 0.001$). Oxidative stress was markedly increased (MDA: CRI 1.498±0.26226, RT 1.548±0.3969, HD 1.773±0.3426, CG 0.975±0.3329, $p < 0.001$) and antioxidative defense was compromised (SOD:CG 120±21, CRI 84±25, RT 93±12, HD 119±37 $p < 0.001$) in RD children. Multiple linear regression analysis revealed that model which has included lipid and oxidative status parameters had more than 90% of influence in variability of IMT values.
Conclusion: Early atherosclerosis in renal disease children is caused, at least in part, by dyslipidemia and oxidative stress.

94 IN SILICO MODELLING OF HUMAN LIPOPROTEIN METABOLISM

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Introduction: Lipoproteins play an important role in the genesis of atherosclerosis and cardiovascular diseases. High density lipoproteins (HDL) and low density lipoproteins (LDL) are of great interest in lipid research. However, lipoprotein analysis is elaborate and expensive. A model predicting the risk of cardiovascular disease depending on the lipid metabolism may be of great benefit.
Methods: Here, we present a refined version of a previously described model of the human lipoprotein metabolism. The model describes the behaviour of particular lipoproteins dependent on a set of reaction rates. Due to the large number of possible lipoprotein compositions, the computation is mostly done by the stochastic Gillespie algorithm and only in special cases deterministically. The now presented model is based on a dataset of lipoprotein measurements (circa 2000 patients) and contains several changes and refinements to the prior approach. One important enhancement is the remodelling of the cholesteryl ester transfer protein (CETP) dynamics.