Determination of sdLDL particles in patients with Familial Hypercholesterolaemia and Familial Combined Hyperlipidaemia

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Background

Cardiovascular disease (CVD) is a multifactorial disorder depending on both genetic and environmental factors. Low density lipoprotein (LDL) comprises a heterogeneous population of particles in terms of size, biochemical properties and atherogenic potencial. Several studies have demonstrated that small dense LDL (sdLDL) particles are an emerging cardiovascular (CV) risk factor due to its atherogeneicity. The objective of this study was the measurement of sdLDL in patients with genetic diagnosis of Familial Hypercholesterolaemia (FH) and clinical diagnosis of Familial Combined Hyperlipidaemia (FCHL) to establish a relation between sdLDL, CV risk and the efficacy of therapeutics.

Methods

Lipid profile was determined by the measurement of LDL particle size and its cholesterol concentration using a polyacrylamide gel electrophoresis method (Lipoprint system, Quantimetrix) that separates the LDL subfractions present in fasting serum samples. The lipidogram obtained classifies the patients as being profile A (low CV risk) or B (high CV risk) depending mainly on the sdLDL concentration. Total, LDL and high density lipoprotein (HDL) cholesterol, apolipoprotein AI (ApoAI), ApoB, lipoprotein(a) and triglycerides were also measured in an automated analizer (Cobas 400, Roche).

Results

- The lipid profile was obtained from **43 FH adults** and **46 FCHL adults**, index and relatives.
- Significant results were found for patients <u>without medication</u> and with high sdLDL (>6mg/dl) where **FH patients** presented higher levels of total cholesterol, LDL and ApoB and **FCHL patients** presented higher levels of total cholesterol, LDL , ApoB and triglycerides (TG), compared to patients with sdLDL under recommended values (Fig. 1).
- <u>Under medication</u> **FH patients** have significant higher ApoB levels and lower HDL, and **FCHL patients** have significant higher total cholesterol, LDL and ApoB levels (Fig. 1).
- In Figure 2 there are presented some examples of lipidograms of the patients of this study obtained from the Lipoprint System.
- In the FCHL patients group that were on medication 71,4% still presented a high CV risk profile (profile B) (Fig. 3).

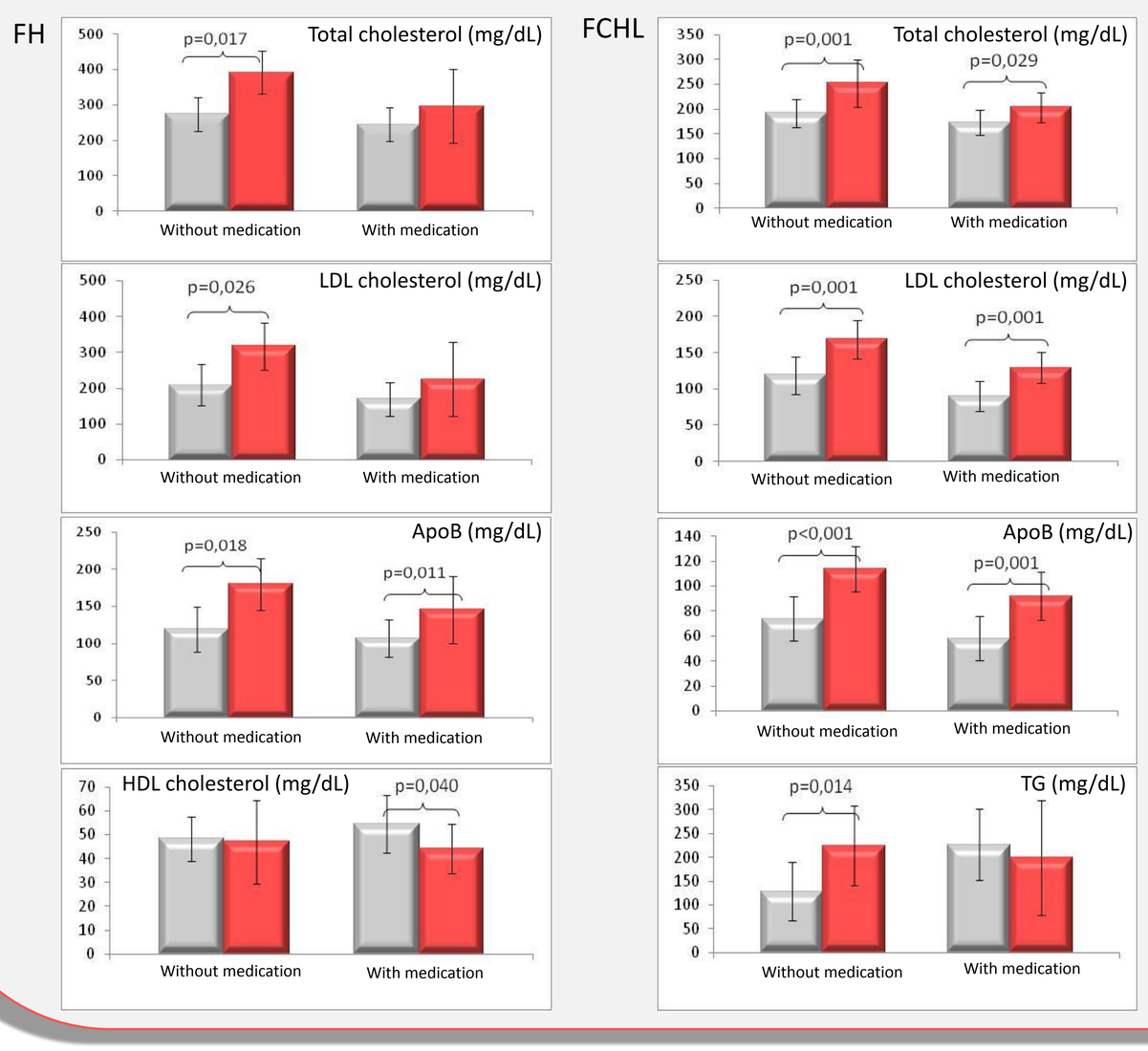

Figure 1 – Comparison between biochemical parameters in FH and FCHL patients according to sdLDL CV risk cutoff and medication.

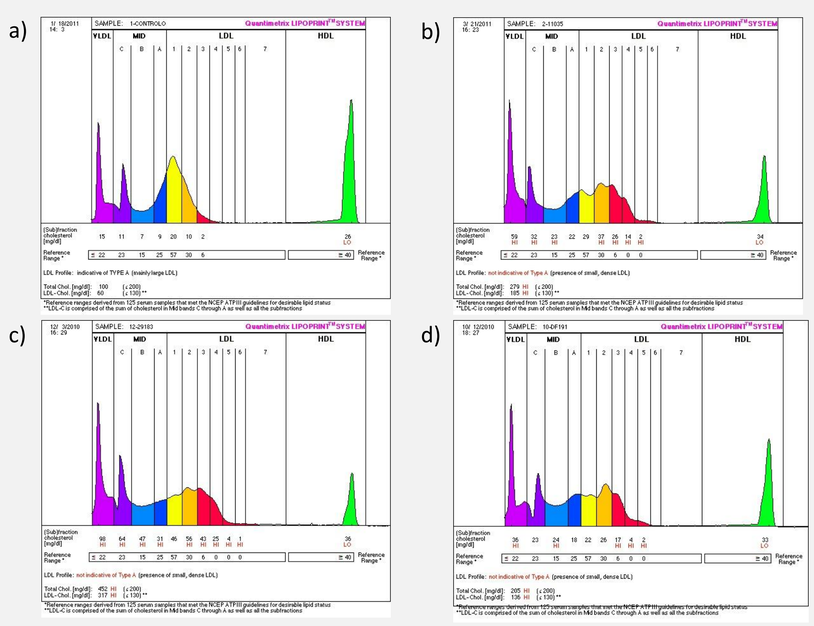

Figure 2 – Lipidograms examples obtained by the Lipoprint System of a control (a), FH (b, c) and FCHL (d) patients.

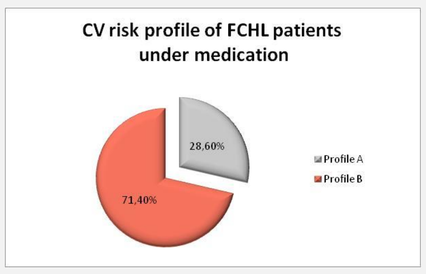

Figure 3 – CV risk profile of FCHL patients under medication (profile A – 29,6%; profile B – 71,4%).

Discussion and Conclusions

Total, LDL and HDL cholesterol and also ApoB and TG levels seem to be differentially distributed between FH ad FCHL patients when taking into account the presence of sdLDL and the use of medication.

71,4% of the FCHL patients under medication still presented a high CV risk profile, showing that statins seem not to decrease sdLDL levels and neither CV risk. Also FCHL patients are not well medicated or do not respond to usual medication to decrease cholesterol.

These preliminary results indicate that the measurement of sdLDL could be a good biomarker for treatment control but further studies are needed to evaluate the effect of medication in sdLDL levels in FH and FCHL patients.

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