High lipoprotein(a) cholesterol in patients with Familial Hypercholesterolemia

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Estudo Português de Hipercolesterolemia Familiar

Aim:

Familial Hypercholesterolemia (FH) patients have an increased cardiovascular risk due to high TC or LDL-C levels. Lp(a) chemical structure is similar to LDL and elevated Lp(a) is considered an independent risk factor for cardiovascular disease (CVD). Recently, it has been described that in patients with high Lp(a), the Lp(a)-C can contribute up to 25% to 50% of all LDL-C. In the present work we aim to determine if elevated Lp(a) concentrations can contribute to clinical phenotype of FH.

Methods:

A cohort of 1374 individuals (875 adults and 499 children) with clinical diagnosis of FH was analysed. Lipid profile was determined, using an automatic biochemical equipment, by enzymatic colorimetric and immunoturbidimetric methods. Molecular study of *LDLR*, *APOB* and *PCSK9* genes was performed by PCR and Sanger sequencing. Data was analysed by SPSS using Mann-Whitney and Qui-square tests.

Results:

The cohort was divided according to the genetic diagnosis in FH mutation positive (FHM+), individuals identified with pathogenic or likely pathogenic mutation, and FH mutation negative (FHM-), individuals without a mutation in *LDLR*, *APOB* and *PCSK9* genes.

Children

- Lp(a) mean levels were statistically significant higher in FHM- when compared with FHM+ (Table 1).
- 33.1% of children present Lp(a)>50mg/dL (Figure 1).
- In the group of children with Lp(a)>50mg/dL, 56.3% are FHM- vs 43.7% FHM+ (p<0.001) (Figure 1).

Table 1. Lipid profile of children with clinical diagnosis of FH			
	FHM-	FHM+	P value
TC	224.7±36.2	253.0±51.2	<0.001
LDL-C	147.4±33.3	185.3±49.0	<0.001
HDL-C	60.3±16.1	50.8±12.3	<0.001
TG	92.0±46.0	80.7±41.6	<0.001
Lp(a)	59.9±65.7	41.2±43.4	0.008
APOA1	157.9±30.8	131.8±22.2	<0.001
APOB	97.5±26.2	122.9±32.3	<0.001

Adults

- Lp(a) mean levels were higher in FHM- but not statistically significant (55.9mg/dL vs 52.7mg/dL) (Table 1).
- 37.3% of adults present Lp(a)>50mg/dL; no statistically significant differences were found between FHM- and FHM+.
- 15.8% of adults present a premature CVD (mean age 46.3 years).
- In the group of adults with Lp(a)<50mg/dL 12% present pCVD, while 22% present pCVD in the group of adults with Lp(a)>50mg/dL (p<0.001) (Figure 2).

Table 2. Lipid profile of adults with clinical diagnosis of FH			
	FHM-	FHM+	P value
TC	233.7±66.2	280.2±75.5	<0.001
LDL-C	147.4±50.9	200.7±69.8	<0.001
HDL-C	56.4±16.7	53.7±15.3	0.014
TG	172.9±315.2	126.9±87.1	<0.001
Lp(a)	55.9±61.3	52.7±58.4	0.959
APOA1	161.3±35.6	147.4±31.9	<0.001
APOB	109.9±36.6	144.6±48.2	<0.001

Conclusions:

Almost 50% of these FH mutation negative children have Lp(a)>50 mg/dL that can be contributing to elevated LDL-C levels resulting in a FH-like phenotype. Most probably in these cases the genetic cause of their hypercholesterolaemia is not FH but hyper Lp(a).

We've also observed that in the group of adults 37% present an elevated Lp(a), that is an additional risk factor to their hypercholesterolemia. Since LDL-C levels of patients with elevated Lp(a) cannot be reduced if the Lp(a) remains elevated, specific therapies to lower Lp(a) are necessary in these patients.