

Cascade Screening in Familial Hypercholesterolemia: importance in early detection

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Introduction

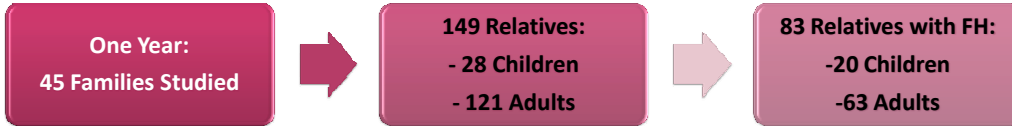
Familial hypercholesterolemia (FH) is a genetic condition mainly caused by mutations in *LDLR* but missense mutations in *APOB* and *PCSK9* can cause similar phenotypes. FH is characterized by increased levels of LDL cholesterol, leading to premature cardiovascular diseases (CVD). Cascade screening (CS) allows the rapid identification of new FH cases within a family.

The main goal of this work is to perform CS of FH families and to understand the importance of this approach to identify prematurely individuals that are at risk to develop CVD.

Methods

DNA was extracted from blood samples from family members of each index patient (with a previously identified mutation). The PCR amplification and sequencing of the fragments containing the mutations in *LDLR*, *APOB* or *PCSK9*, identified in each index was performed following the conditions already published. The sequencing results were analyzed using the software *staden package*[®]. The biochemical characterization, including total cholesterol (TC) and LDL cholesterol (LDL-c) of the FH patients was also performed through automated methods.

Results



48,2% of the relatives weren't under medication when diagnosed molecularly with FH.

Relatives and Medication

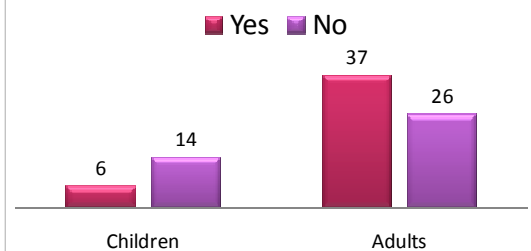


Fig.1 – number of relatives, children and adults, distributed by medication. 70% of children and 58,73% of the adults were not under medication.

The medium plasmatic concentration of TC and LDL-c in relatives with FH that are under medication are higher than the recommended values for individuals with this disease (TC <170 mg/dL and LDL-c <100 mg/dL).

Lipidic Plasmatic Concentrations with Medication

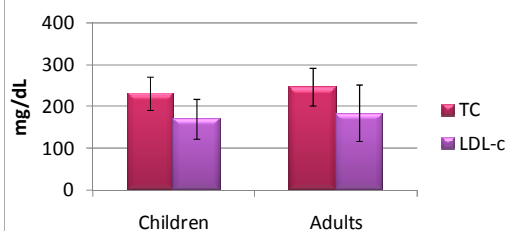


Fig.2 – Medium plasmatic concentration of TC, LDL-c and HDL-c in relatives that are under medication.

Discussion and Conclusion

CS is a cost effective method to identify FH patients for several reasons. First, the molecular study is done by searching the mutation that was found in the respective index case, saving time and money. Second, relative's phenotype, most of the times, is less severe and does not allow clinical identification. CS may allow the premature detection of FH and cardiovascular risk stratification, leading to the reduction of morbidity and mortality by implementation of adequate counseling and therapeutic measurements. It's important to refer that 48,2% of the studied relatives with FH were not under any medication. The relatives who were medicated have values of TC and LDL-c above the recommendation values, probably, because the therapeutics are not adequate for their condition. In this way, their risk to develop a premature CVD is still elevated.

FH is still under-diagnosed in Portugal, and so, efforts must be made to enlarge adherence of relatives to CS, maybe through increase disclosure of information to the community.