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BRIEF REPORT

Familial hypercholesterolemia: Experience in the Lipid Clinic of Alava☆

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KEYWORDS
Familial hypercholesterolaemia;
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Abstract
Introduction: Familial hypercholesterolaemia (FH) is the autosomal dominant genetic disorder most frequently associated with premature cardiovascular disease (CVD).
Materials and methods: A retrospective, observational study was conducted to determine the clinical characteristics, analytical parameters and cardiovascular risk factors of 133 patients with a genetically confirmed diagnosis of FH on follow-up in the Lipid Clinic of Alava.
Results: CVD was observed in 8.30% of the patients (ischaemic heart disease in 100% of the cases). The LDL concentration goal was achieved in 40.6% (45.50% in primary prevention and 27.30% in secondary prevention). The large majority (81.80%) of patients with coronary heart disease (CHD) were male. The odds ratio (OR) of males having CHD compared to females is 4.97 (1.03–23.93, $p = 0.03$). The OR of developing CHD in patients with a family history of premature CVD is 6.86 (1.32–35.67, $p = p.02$). A statistically significant association was found between smoking and the risk of CVD ($p = 0.005$), and also between having diabetes and the risk of CVD ($p = 0.0001$). If the treatment with statins begins at older than 40 years, the OR of suffering CHD is 6.40 (1.53–26.5) ($p = 0.009$). The mean time from diagnosis to the cardiovascular event in the group of ex-smokers is 10.80 ± 5.80 years, and in the non-smoking group it is 17.50 ± 2.50 years ($p = 0.011$).
Conclusions: In our reference population with FH, it was found that there was an increased risk of suffering a cardiovascular event in male patients, with a family history of premature CVD, diabetics, and in those in whom lipid lowering treatment was started after 40 years of age.

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PALABRAS CLAVE
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Factores de riesgo cardiovascular;
Enfermedad cardiovascular

Hipercolesterolemia familiar: experiencia en la Unidad de Lípidos de Álava

Resumen
Introducción: La hipercolesterolemia familiar (HF) es el trastorno genético autosómico dominante más frecuentemente asociado a enfermedad cardiovascular (ECV) prematura.
Material y métodos: Estudio observacional, retrospectivo, para determinar las características clínicas, los parámetros analíticos y los factores de riesgo cardiovascular de 133 pacientes con diagnóstico genético confirmado de HF en seguimiento en la Unidad de Lípidos de Álava.
Resultados: El 8,30% de los pacientes ha presentado ECV (en el 100% de los casos cardiopatía isquémica [cI]). El 40,60% alcanza el objetivo de cLDL: el 45,50% en prevención primaria y el 27,30% en prevención secundaria. El 81,80% de los pacientes con CI son varones. El *odds ratio* (OR) de presentar CI en los varones frente a las mujeres es 4,97 (1,03−23,93; $p = 0,03$). El OR de presentar CI en los pacientes con historia familiar de ECV prematura es 6,86 (1,32−35,67; $p = 0,02$). Encontramos una asociación estadísticamente significativa entre fumar y el riesgo de ECV ($p = 0,005$) y también entre tener diabetes y el riesgo de ECV ($p = 0,0001$). Si el tratamiento con estatinas se inicia antes de los 40 años, el OR de presentar CI es 6,40 (1,53−26,50; $p = 0,009$). El tiempo medio desde el diagnóstico hasta el evento en el grupo de exfumadores es $10,80 \pm 5,80$ años y en el grupo de no fumadores es $17,50 \pm 2,50$ años ($p = 0,01$).
Conclusiones: En nuestra población de referencia con HF, encontramos un mayor riesgo de presentar un evento cardiovascular en los pacientes varones, con antecedentes familiares de ECV prematura, diabéticos y en los que se ha iniciado el tratamiento hipolipidemiante después de los 40 años de edad.

Introduction

Familial hypercholesterolaemia (FH) causes elevated LDL cholesterol (LDL-C) concentrations from birth, and is consequently the autosomal dominant genetic disorder most commonly associated with premature cardiovascular disease (CVD). In the Caucasian population, estimates generally place the rate of heterozygous FH at 1/500 and homozygous FH at 1/1,000,000.[1] However, the Copenhagen General Population Study found that the prevalence of confirmed or probable FH, defined as a score >5 according to the Dutch Lipid Clinic Network (DLCN) criteria, was 1/200.[2] In Spain, the estimated prevalence of FH standardised by age and gender is 1/192 individuals for the heterozygous phenotype and 1/425,774 for the homozygous phenotype.[3]

In heterozygous patients, the mutated gene is the LDL receptor (*LDLR*) gene in over 90% of cases, the *APOB* gene in approximately 5% and the proprotein convertase subtilisin/kexin type 9 (*PCSK9*) gene in approximately 1%.[4] Patients with FH have a 3- to 13-fold higher risk of premature CVD than individuals without FH.[2,5] In patients with heterozygous FH who do not receive lipid-lowering treatment, coronary disease typically develops before the age of 55 (males) or 60 (females), while homozygous patients will develop coronary disease before the age of 20 if they do not receive treatment.[5]

The SAFEHEART (Spanish Familial Hypercholesterolaemia) cohort study estimated that the prevalence of diabetes among patients with FH is 3.20%, 14.40% among those with hypertension (HTN) and 26.40% among those who are active smokers. Moreover, 9.40% of these patients have developed premature CVD.[6]

The aims of this study were to identify the clinical characteristics of patients with FH, determine the degree of lipid control and analyse the main cardiovascular risk factors (CVRF) among patients undergoing follow-up by the Lipid Clinic at Hospital Universitario Araba.

Materials and methods

Study design and population

This was a retrospective, observational study of 133 patients with a genetically confirmed diagnosis of FH undergoing follow-up by the Lipid Clinic at Hospital Universitario Araba. The study began including patients in 2001 (the year in which the Lipid Unit was accredited by the *Sociedad Española de Arterioesclerosis* [Spanish Atherosclerosis Society]) and continued until the last patients were included in June 2017. Both index cases and family cases were included. All patients were over the age of 18, except for two cases of recently diagnosed family members (aged 11 and 13, respectively).

Study variables

Demographic data were collected (age, gender, age at diagnosis of FH, age when lipid-lowering therapy was started, etc.), as well as physical examination data (weight, height, presence of corneal arcus and tendinous xanthomas, etc.) and analytical test data (total cholesterol [TC], LDL-C, HDL-C, TG, Lp[a], etc.). In the statistical analysis of the lipid profile data, the two patients aged under 18 and the patient with a diagnosis of homozygous FH were excluded to