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EDITORIAL

Familial hypercholesterolaemia in childhood: Success starts here☆

Hipercolesterolemia familiar en la infancia. El éxito comienza aquí

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Heterozygous familial hypercholesterolaemia (HeFH), the most common monogenic metabolic disease, affects 1/300–1/500 people. At present, the prognosis of individuals with this disease is good, having been radically improved by lipid-lowering treatment.[1] The prevalence of coronary heart disease in individuals with HeFH has decreased from more than 50% in middle age to nearly equivalent to that of the general population.[2]

Recent data from different countries, including Spain, indicate that cardiovascular risk in middle-aged individuals with HeFH on prolonged treatment with lipid-lowering medication does not exceed 1% annually.[3,4] In a Dutch FH registry, the prevalence of cardiovascular disease in families with HeFH, the incidence of cardiovascular disease was not significantly different in affected versus unaffected persons.[5] This was unthinkable 20 years ago.[6] It should generate a strong sense of satisfaction regarding the prognosis of this disease.

However, all that glitters is not gold. Most of these data come from units specialising in lipid metabolism. They are not representative of the overall population with HeFH. For treatment to work, patients must take it, and for patients to take it, they have to be diagnosed with HeFH and prescribed suitable treatment. Researchers from Hospital Universitario Puerta de Hierro in Madrid, Spain, have found that approximately 9% of cases of acute coronary syndrome before age 65 and LDL cholesterol $\geq$160 mg/dl continue to occur in individuals with HeFH. This figure is ten times higher than that expected[7] and is senseless in a disease that has an effective preventive treatment. Recent data from the Spanish Arteriosclerosis Association (*Sociedad Española de Arteriosclerosis, SEA*) Dyslipidaemia Registry indicate that more than 50% of events in individuals with HeFH occurred before they started taking lipid-lowering treatment and that among those who were on treatment, the vast majority had been taking it for less than five years.[8] This means that individuals with HeFH are either not treated or start lipid-lowering treatment too late.[9] An initial conclusion we can draw from this evidence is that we need to diagnose affected individuals early. Childhood and adolescence are a good time to do this.

Diagnosis at an early age brings tremendous advantages.[10] It can be done in the context of a family unit, which is beneficial because in most cases other family members are affected. This normalises the situation; the child does not see the condition as unusual, and adapts very easily to the slight limitations the disease imposes. Lifestyle habits, whether healthy or harmful, are largely acquired in the first few decades of life. An early diagnosis can therefore make it easier to introduce healthy changes. Lipid-lowering drugs are very well tolerated, especially

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at young ages. Therefore, if children and adolescents are taught to be disciplined about taking medication, then they are less likely to stop treatment later on in life.

However, diagnosis in children and adolescents should not be stigmatising and does have limitations.[11] We as healthcare professionals should not give them the impression that they are ''sick''. We should not subject them to unnecessary frequent check-ups, pointless dramatics and derogatory labels that encourage them to view their disease and by extension their treatment in a negative light. It is one thing to know the risks of the disease. It is quite another to be constantly reminded about them.

In the current issue of *Clínica e Investigación en Arteriosclerosis*, the prestigious Hospital Universitari Sant Joan group in Reus, Spain, presented the results of the DECOPIN study.[12] Dr Nuria Plana et al. demonstrated that diagnosis of HeFH at young ages is simple, efficient and cost-effective. They showed that strategies based on direct cascade, i.e. screening of first- and second-degree relatives for HeFH, or inverse cascade, i.e. screening of the parents of a child with suspected HeFH due to opportunistic detection in childhood/youth, are capable of improving diagnosis in many cases on an individual or family level. In addition, cholesterol levels exceeding 245 mg/dl and LDL cholesterol levels exceeding 170 mg/dl, especially with ApoB/ApoA1 ratios over 0.82, should cause the clinician to suspect HeFH in those under the age of 18. The DECOPIN study should be applied to Spain. The SEA and paediatric associations should establish a protocol based on the knowledge derived from the DECOPIN study to facilitate early diagnosis of HF in Spain and make life easier for this population.

The Reus group is to lead a project on HeFH in children/adolescents in the SEA Dyslipidaemia Registry,[13] with the aim of enhancing insight into the reality faced by this population and improving their day-to-day clinical management.

However, appropriate diagnosis is not enough. Adherence to proper treatment is another prerequisite for success. We need to facilitate treatment, minimise check-ups, encourage treatment adherence and combat counterproductive information. Here is an anecdote of a recent happening that all of us have experienced. A young patient with HeFH was being treated with the maximum dose of a powerful statin plus ezetimibe. He was asymptomatic. His examination was normal, and his laboratory results were within target ranges. He wanted to stop taking his medication. Why? Because every time he picked up his prescription, his pharmacist asked him if he was suffering from any pain or felt weak and if he was feeling alright. The pharmacist alarmed him about the supposed side effects of statins. He was scared. This patient was very likely to develop side effects due to the nocebo effect and stop taking his medication. This is a day-to-day occurrence for us, and it is unacceptable. We need to fight much harder against biased information, most of which is rooted in ulterior motives. It harms our patients, as the benefit of the treatment cannot be denied.[14]

Spain is a leader in diagnosis and healthcare organisation with respect to HeFH in adults.[15] We have come a long way, and we have to keep going. To quote Winston Churchill, ''Now this is not the end. It is not even the beginning of the end. But it is, perhaps, the end of the beginning''. We have to keep going until all our fellow citizens with HeFH have been properly diagnosed and are properly treated. To get there, we need early diagnosis.

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