



EDITORIAL

Severe hypertriglyceridemias: What is necessary and what is sufficient[☆]

Hipertrigliceridemias graves: lo necesario y lo suficiente

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Severe hypertriglyceridemia is known as the elevation of plasma triglyceride levels over 1000 mg/dL.¹ This is an arbitrary cut-off point based on the relation to an increased risk of pancreatitis,^{2,3} although the association with atherosclerotic cardiovascular disease is already present at levels above 100–150 mg/dL.⁴ Fortunately, and in general terms, this relationship is neither necessary nor sufficient for the development of both complications, although minimising its impact is currently a challenge for researchers and clinicians.⁵

It is assumed that for the evolution of the human species it has been necessary—but probably not sufficient—to develop a lipid transport system (source of energy and essential molecules) made up of “modern” subcellular structures not present in all vertebrates and which are the so-called triglyceride-rich lipoproteins (TRLs).⁶ These lipoproteins are organised into 2 pathways, the exogenous (after food intake) and the endogenous pathway, and have chylomicrons originally as protagonists—not present

in fasting—and very low-density lipoproteins, respectively. To maintain normotriglyceridemia, we require a balance between the synthesis and catabolism of these lipoproteins that is mainly controlled by lipoprotein lipase and other enzyme systems. The loss of this balance determines the appearance of hypertriglyceridemia, while the saturation of the lipolytic rate of the plasma is sufficient for this to worsen, when fasting chylomicronemia may appear.⁶

During phylogenetic development, the biomolecular substrate of this enzymatic network (lipases and others) accumulates variants that impact, to varying extents, on the efficiency of these metabolic pathways.^{7–9} Some do so definitively, and their presence is sufficient to cause chylomicronemia, as is the case of the biallelic pathogenic variants present in familial chylomicronemia (FC). In most cases, however, there are underlying variants that have a low impact on the metabolism of TRLs, variants that are necessary, but not sufficient, to cause chylomicronemia, since the concurrence of other factors is required to saturate the system (gene-environment interaction); this is the case of multifactorial chylomicronemia syndrome (MCS). All the above justifies the fact that intervening on the diet is necessary in both cases, and sufficient to control chylomicronemia in MCS¹⁰ but not in the chronic phase, where classic lipid-lowering agents are not effective either, making the search for new treatment targets necessary.¹¹

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Undoubtedly, we are facing an aspect of lipidology in constant change, still with many uncertainties remaining, as well as unmet needs, for which reason we consider that a monographic paper like this one is necessary and pertinent, as it addresses the most relevant advances and the state of the art in this area. We are aware that it will not be sufficient, however we hope that it will be useful for researchers and clinicians in improving care for people with severe hypertriglyceridemia.

Declaration of competing interest

The authors declare that they have no conflict of interest.

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