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Editorial

Atherogenic Dyslipidemia as a Marker of Cardiometabolic Risk

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Editorial

Current scientific evidence indicates the association between the elevation of triglycerides (TG), the decrease the High Density Lipoprotein Cholesterol HDLC and the increase in cardiovascular risk [1]. The analysis arising from major intervention studies demonstrates that both in acute coronary syndrome as well as in chronic ischemic cardiovascular diseases, the hypertriglyceridemia (HTG) and the decreased concentration of HDLC is accompanied by a high cardiovascular risk even in populations with recommended LDLC levels according to the guidelines [2-5]. Nevertheless, there is a certain controversy surrounding the suitability of deeming such lipid markers therapeutic objectives [6].

From the physiopathology point of view of the vascular atherosclerosis injury has been widely demonstrated that the remaining particles, rich in TG, may directly contribute to the formation and the progression of atheromatous plaque [7]. Meanwhile the HDLC particles in addition to the role in the reverse transport of cholesterol, demonstrate a wide spectrum of potentially useful biological activities such as those of antiatherosclerotics [8]. In fact, they are both two key elements with a phenotype of small and dense Low Density Lipoprotein (LDL) that constitutes the atherogenic triad characteristic associated with a high cardio metabolic risk.

The association of both disorders is very common, above all in patients with metabolic disorders that are accompanied by high cardiovascular risk in such a way that a variable percentage of between 30- 60% of patients with high risk may show a dyslipidemia with an increase of TG and/or decrease in HDLC [9-11]. In the PROCAM study, the prevalence of this dyslipidemia was double in patients with previous myocardial infarction with respect to those without such circumstances [12]. In the Spanish study, the DYSIS, approximately half of the high risk patients with statins presented said disorder [13].

The Panel of Experts of the European Society of Arteriosclerosis considers that the abnormality associated with the increase of cardiovascular risk is precisely, the association between both disorders: an increase of TG and a decrease of HDLC serum levels, while it is still controversial whether there is an association between the isolated elevation of TG or the isolated decrease of HDLC [14].

Antlerogenic Dyslipidemia

The combination of an increase of TG and a decrease of HDLC is associated with cardiovascular diseases and with a high prevalence in high-risk populations. It is also the lipid profile more frequently found among young people [15, 16], especially in those adolescents who are overweight [17] or who have a metabolic syndrome [18]. According to our results, among the Canadian population, having high TG with low HDLC was associated with mellitus diabetes, sedentarism, obesity, HTA and tobaccoism in comparison with those that had low TG and high HDLC .

Therefore, both dyslipidemic components are relevant criteria for the diagnosis of metabolic syndrome and a reference for the cardiovascular risk associated with it among the general population. In the DARIO study performed on the general Spanish population, the metabolic syndrome prevalence was 31%. It was the greatest coronary risk among women and persons with metabolic syndrome [19]. In the MESYAS study the metabolic syndrome is related to coronary disease and both the independent association of HTG (odds ratio: 3.39) as well as the isolated decrease in HDLC (odds ratio 2.35) is significant [20]. Moreover, in patients with mellitus type 2 diabetes both the HTG as well as the decrease in HDLC are predictor factors regardless of coronary disease, and the combination of both is a good predictor of atherosclerotic disease evaluated by means of the intima-average thickness [21,22]. It is known that among diabetic patients the TG is two to three times more frequent that in non-diabetics and at the same time, the total cholesterol/HDLC or LDLC/HDLC proportion (accompanying characteristic of HTG) is found to be higher in these patients, both facts of which express the atherogenic dyslipemia accompanying diabetics. A recent study

has indicated that approximately 60% of patients with HTG have an increase of the LDLC/ HDLC [23] quotient and in another study the TG/HDLC ratio identified insulin resistance in non-obese, non-diabetic Asian adults [24].

In short, the HTG is a commonly secondary lipid anomaly to a spectrum of clinical situations that are accompanied by a high risk associated with metabolic factors, very particularly those characterized by insulin resistance. In clinical practice the occurrence of HTG and low HDLC is especially frequent in those circumstances in which there is a context of underlying insulin resistance [25] and in fact the TG/HDLC index has been recommended as a biological marker of insulin resistance [26] and in such cases it is frequently found to comprise a constellation of risk linked to small and dense LDL, constituting a lipid profile with special atherogenic power. Therefore, the HTG + low HDLC comprises the association known as metabolic syndrome [27-29], that has been demonstrated an association with a risk 5 times greater than type 2 mellitus diabetes and 2 times for cardiovascular illness [30,31]. In our study the presence of the HTG binome with low HDLC was statistically significant in patients with type 2 mellitus diabetes and/or metabolic syndrome.

Likewise, HTG may increase the vascular risk either directly or indirectly, in this case through changes in the composition, size or concentration of other lipoproteins, particularly the HDLC. It has been indicated that the association of HTG with cardiovascular disease is modulated through HDLC concentration due on one side to the influence that lipoproteins rich in TG have in the conditioning metabolism of the concentration and composition of the HDLC [32] and on the other, due to the phonotypical heterogeneity of previously mentioned association, genetically conditioned [33]. In addition the composition and quality of the HDLC particle governs certain enzymatic activities of the TG concentrations such as the hepatic lipase, lipolytic enzyme which contributes to the regulation of the plasmatic levels of TG the hepatic release of which is regulated by the HDLC [34]. In this manner, changes in HDLC may inhibit the release and activation of the hepatic lipase and, affect the TG plasmatic level. In the same way, the relationship of TG and HDLC is performed through the enzymatic activity of the cholesterol ester transfer protein that transfers cholesterol from the HDLC molecule to the vey-low density lipid in order to enrich cholesterol in its metabolic route to LDLC. In presence of a resistance to insulin, the activity of the lipoprotein lipase is deteriorated while the activity of the hepatic lipase is increased [35].

These facts justify that HTG by itself or by its association with low HDLC has an impact on vascular pathology a despite of the concentrations of LDLC [36].

All the aforementioned, while being able to provide orientation in regard to therapeutic needs, may also indicate new therapeutic targets for the standardization of the hypertriglyceridemia – low HDLC binome through an increase of hepatic lipase and CEPT inhibition. As of the present time, modifications in lifestyle, physical exercise, abstinence from tobacco and pharmaceuticals such as fibrates, niacin and omega-3 fatty acids are the most effective means for correcting isolated hypertriglyceridemia or that related to low HDLC [37] and in this manner, correct atherogenic dyslipemia that is characteristically found in metabolic risk situations such as mellitus type 2 diabetes or metabolic syndrome, conferring an excess of risk and a non-LDLC dependent residual risk [38].

Triglycerides represent one component of a heterogeneous pool of triglyceride-rich lipoproteins. The reliance on triglycerides or triglyceride-rich lipoproteins as cardiovascular disease risk biomarkers prompted investigations into therapies that lower plasma triglycerides as a means to reduce cardiovascular diseases events. Genetic studies identified triglyceride-rich lipoproteins components and pathways involved in their synthesis and metabolism dislipemia. Our study reveals how there is a wide margin of improvement in the use of pharmaceuticals with clinical benefit in these patients, and whether we need to address with greater impetus the pharmacological treatment of atherogenic dislipemia.

In this sense, we must highlight Mendelian randomization studies in which known genetic mutations lead to the elevation or fall in plasmatic levels of lipoproteins rich in triglycerides that are in accordance with the size and increase vs. decrease direction of the risk of cardiovascular disease [39]. Mendelian randomization data strongly suggest HTG causes atherosclerotic cardiovascular disease, and so TG level-lowering treatment in HTG is now more strongly recommended to address the residual atherosclerotic cardiovascular disease risk than has been published in the guidelines.

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