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EDITORIAL

No-HDL-cholesterol as risk marker and therapeutic goal☆

Colesterol no-HDL como marcador de riesgo y objetivo terapéutico

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Pharmacological and non-pharmacological interventions aimed at reducing plasma concentrations of LDL are part of the first line of attack in the battle to prevent cardiovascular disease. In fact, reducing LDL has become a priority, both in primary and secondary prevention.

However, other lipoproteins also have a well-known role in vascular risk, with the most characteristic examples being the increase in triglyceride-rich lipoproteins or the decrease in high-density lipoproteins.[1] For that reason, as recommended in some of the Clinical Practice Guidelines most commonly used to manage dyslipidaemia, these lipoproteins and their plasma expression (concentration of triglycerides and HDL cholesterol [HDL-C]) sometimes become secondary therapeutic objectives.

Taking into account the different atherogenic or antiatherogenic roles played by the different lipoprotein families, non-HDL-C (total cholesterol minus HDL-C) can provide a measurement in the balance of atherogenic lipoproteins, as it essentially represents the cholesterol bound to any class of atherogenic lipoproteins: LDL, IDL and VLDL, and even the cholesterol bound to lipoprotein(a) ([Lp(a)].[2]

Under these conditions, non-HDL-C is a very important element which enables us to assess cardiovascular risk, particularly in clinical situations where simply measuring LDL may underestimate the concentrations of atherogenic cholesterol, because levels of the other lipoproteins families that also contain cholesterol may be very high. This is the case in diabetes mellitus, metabolic syndrome and visceral obesity. We need to stress how simple it is to use this measurement in routine clinical practice; it is easy to calculate as it is not influenced by the other lipid determinations. Yet its correlation with apoB makes it a marker of choice.[3]

In this issue of the journal *Clínica e Investigación en Arteriosclerosis*, the Albacete Vascular Diseases Group (*Grupo de Enfermedades Vasculares de Albacete*, GEVA) has published a study assessing non-HDL-C as a predictor of non-fatal cardiovascular events in a prospective population-based cohort.[4] According to the authors, the aim of the study was to assess the predictive capacity of non-HDL-C, but also to compare it with that of LDL-C. They included about 1200 individuals, and the results show that, after adjustment, for each increase of 30 mg/dl in non-HDL-C, the incidence of new non-fatal cardiovascular events increased by 31% (HR: 1.31, 95% CI: 1.06–1.61; $p = 0.018$). The 10.7-year follow-up is quite noteworthy. The significance of LDL-C was lower. Consequently, the results showed that in a population including individuals with high triglycerides (especially patients with metabolic syndrome, visceral obesity, prediabetes or diabetes), non-HDL-C has the greatest predictive power, supporting the idea that it should also be used as a therapeutic target.[5,6]

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Having become an excellent indicator of the totality of atherogenic cholesterol, non-HDL-C is also a primary therapeutic target, particularly in individuals with atherogenic dyslipidaemia. Maintaining that this parameter is underused despite being easy to determine and the fact that no fasting is required beforehand, the expert recommendations[7] establish the use of non-HDL-C as a therapeutic target (+0.8 mmol/l, or the equivalent: +30 mg/dl) over LDL as target. In fact, according to clinical practice guideline recommendations and the results from various clinical trials and population-based and genetic epidemiological studies, in very high-risk individuals, optimal LDL-C is below 70 mg/dl and optimal non-HDL-C, below 100 mg/dl, while in high-risk individuals, optimal levels are 100 mg/dl and 130 mg/dl, respectively.

In summary, the combination of different lipid abnormalities, known as atherogenic dyslipidaemia (elevation of baseline and postprandial triglycerides), low HDL, and small and dense LDL particles, situations in which non-HDL-C is a good marker, also shows us that it may be a good secondary therapeutic target. This is particularly important in situations such as diabetes mellitus, in which, despite treatment with statins (even at high doses and associated with ezetimibe or a PCSK inhibitor), the residual risk is clinically significant.

The advantage of using non-HDL-C is that, as has been shown, it can be a better marker of cardiovascular risk, this being accounted for by the atherogenic role of the other triglyceride-rich lipoproteins. Consequently, use of non-HDL-C in clinical practice also helps us to identify patients who might benefit from a reduction in the residual risk of lipid origin with the use of a more specific treatment such as the combination of statin and fenofibrate.

References

1. The Emerging Risk Factors Collaboration. Major lipids, apolipoproteins, and risk of vascular disease. JAMA. 2009;302:1993–2000.
2. Millan J, Hernandez Mijares A, Ascaso J, Blasco M, Brea A, Diaz A, et al., Grupo de Trabajo sobre Dislipemia Aterogénica. Sociedad Española de Arteriosclerosis. La auténtica dimensión del colesterol-no-HDL: colesterol aterogénico. Clin Invest Arterioscl. 2016;28:265–70.
3. Boekholdt SM, Arsenault BJ, Mora S, Pedersen TR, LaRosa JC, Nestel PJ, et al. Association of LDL cholesterol, non-HDL-cholesterol, and apolipoprotein B levels with risk of cardiovascular events among patients treated with statins: a meta-analysis. JAMA. 2012;307:1302–9.
4. Carbayo Herencia JA, Simarro Rueda M, Palazón Bru A, Molina Escribano F, Ponce Garcia I, Artigao Ródenas LM, et al., en nombre del Grupo de Enfermedades Vasculares de Albacete (GEVA). Valoración del colesterol no HDL como predictor de episodios cardiovasculares no mortales en una cohorte prospectiva de origen poblacional. Clin Invest Arterioscler. 2018;30:64–71.
5. Ascaso JF, Carmena R. Importancia de la dislipidemia en la enfermedad cardiovascular: un punto de vista. Clin Invest Arterioscler. 2015;27:301–8.
6. Ascaso JF, Millan J, Hernandez Mijares A, Blasco M, Brea A, Diaz A, et al., Grupo de Trabajo sobre Dislipemia Aterogénica de la SEA. Documento de Consenso sobre el manejo de dislipemia aterogénica de la Sociedad Española de Arteriosclerosis. Clin Invest Arterioscler. 2017;29:86–91.
7. Grupo de Trabajo de Dislipemia Aterogénica de la Sociedad Española de Arteriosclerosis, Grupo Europeo de Expertos. Recomendaciones prácticas para el manejo del riesgo cardiovascular asociado a la dislipemia aterogénica, con especial atención al riesgo residual. Adaptación española de un Consenso Europeo de Expertos. Clin Invest Arterioscler. 2017;29:168–77.