



EDITORIAL

A glow in the secondary prevention of cardiovascular disease[☆]



Un resplandor en la prevención secundaria de la enfermedad cardiovascular

J. Pedro-Botet, E. Climent

Lipids and Vascular Risk Unit, Hospital del Mar, Universitat Autònoma de Barcelona, Barcelona, Spain

Received 17 January 2017; accepted 19 January 2017

The main objective of cardiovascular prevention is to reduce morbidity and mortality, improve quality of life and increase longevity with good health. The modification of risk factors is the best standard of quality in clinical practice that an individual doctor can and should do to effectively and plausibly achieve a reduction in the burden of cardiovascular disease. Thus, in countries where there has been a significant reduction in cardiovascular disease, control of blood pressure, control of lipid levels and smoking cessation were the main contributors.¹

An abundance of clinical evidence supports the idea that lipid-lowering therapy in the secondary prevention of cardiovascular disease is one of the most effective strategies. The latest 2016 European guidelines for cardiovascular prevention make it clear that low-density lipoprotein (LDL) cholesterol is a causal factor for atherosclerosis,² and that high cholesterol is a prerequisite for atheromatous plaque formation. Multiple interventional studies in very high-risk patients have shown that achieving LDL cholesterol levels <70 mg/dL or even lower is associated with a decrease in cardiovascular events and a regression of atherosclerosis. In

addition, no subgroup of subjects has been identified that does not benefit from the decrease in concentrations of LDL cholesterol.

However, despite the evidence of the cardiovascular benefits attributed to strict lipid control, the degree of achievement of therapeutic goals in patients with very high cardiovascular risk, such as patients with ischaemic heart disease, is unacceptable and universally low. Thus, in EUROASPIRE IV,³ a cross-sectional study conducted in 78 hospitals in 24 European countries in the period 2012–13, which included patients under 80 years of age with coronary heart disease, only 22% of men and 17% of women achieved the therapeutic goals of LDL cholesterol <70 mg/dL, despite the fact that, overall, 85.7% were treated with statins. Recently, the data of the *Dyslipidaemia International Study* (DYSIS) were published for the period 2013–14.⁴ The results are stratified by country and are obtained from a global registry, so that achievement rates of objectives can be compared within the different national health systems. Overall, of the 41,953 patients at very high risk in this registry, only 21.7% achieved the aforementioned LDL cholesterol goal. It is worth noting that Spain and Greece were the two countries with the worst rates: 10.1% and 9.2%, respectively.

The *Spanish Registry on Lipid Control in Very High-Risk Patients* (REPAR),⁵ which included 1103 patients with stable ischaemic heart disease, showed that 95.3% received lipid-lowering pharmacological treatment, but only 26% achieved strict lipid control.

DOI of original article:

<http://dx.doi.org/10.1016/j.arteri.2017.01.001>

[☆] Please cite this article as: Pedro-Botet J, Climent E. Un resplandor en la prevención secundaria de la enfermedad cardiovascular. Clin Invest Arterioscler. 2017;29:20–21.

In conclusion, and based on the above, we can affirm that with the pharmacological treatment available at the time of the studies, together with the changes in lifestyle, only one in four patients at very high cardiovascular risk achieved the lipid-control objectives recommended by clinical practice guidelines.

In this issue of "CLÍNICA E INVESTIGACIÓN EN ARTERIOSCLEROSIS", an observational study was conducted in Cáceres to learn the degree of lipid control in patients with ischaemic heart disease in this area of health; there are several aspects of this study that we wish to highlight.⁶ First, it included all patients who were admitted to hospital consecutively with a diagnosis of acute and chronic stable heart disease from January 2009 to June 2015 and for whom a recent lipid profile was available. As far as secondary prevention is concerned, there are two different clinical scenarios to positively modify the lipid profile: the immediate post-acute coronary syndrome (ACS) phase and the long-term phase. Therefore, we consider it a success in the design of the LIPICERES study to have included patients with heart disease in an acute phase, since secondary prevention begins from the appearance of the first cardiovascular complication, such as an ACS. It is well established that initiating treatment with high-intensity statins, unless contraindicated, immediately after a cardiovascular event, is the most effective therapy and its impact on morbidity and mortality is not only immediate but also long-term. This validates the axiom applicable to patients at very high cardiovascular risk: "LDL cholesterol, the lower and the sooner the better".

The main outcome of the LIPICERES study was that one in every two patients with heart disease achieved the objectives of lipid control in LDL cholesterol, an extremely positive and encouraging finding compared with previous studies.³⁻⁵ In addition, there was a progressive increase in the percentage of patients with LDL cholesterol in objectives in the period from 2013-14 to 2015, going from 42.8% to 55.9%, respectively. Without intending to make a simplistic reading of these promising results, given that there are many possible determinants, we consider that the message of a conceptual change from a high-intensity statin therapy to a high-intensity hypocholesterolaemic therapy⁷ is being received by the professionals involved in cardiovascular prevention. This aspect has recently been endorsed by a meta-analysis and systematic review by Silverman et al.,⁸ which showed that statins and other drugs, such as ezetimibe and anti-PCSK9 monoclonal antibodies, which act through the upregulation of LDL-receptor expression, are associated with similar reductions of risk of severe cardiovascular events by similar percentage reduction in LDL. We must remember that with the co-administration treatment of a high-intensity statin and ezetimibe the maximum effect of LDL cholesterol reduction is 60%, and if we add as a third drug a PCSK9 inhibitor we can achieve a reduction of 84%.⁹

Another aspect to be highlighted in the LIPICERES study is that 59.3% of patients older than 75 years had LDL cholesterol <70 mg, compared with 49% of those younger than 75 years. The increase in the population of elderly patients, together with better primary prevention strategies, has increased the importance of secondary prevention of cardiovascular disease¹⁰ and has in some way called into question certain unscientifically proven states of opinion

that proposed the suppression of hypolipidaemic treatment in this specific population.

We consider that the extraordinary improvement reflected by the results of the LIPICERES study, compared with the previous experiences, is excellent news for patients, health professionals and health institutions, because it establishes that strict lipid control in secondary prevention is clearly feasible. Undoubtedly, the correct planning of the hypocholesterolaemic pharmacological strategy in patients with very high cardiovascular risk, with a greater use of co-administration treatments, is the way forward.

References

- Blankenberg S, Zeller T, Saarela O, Havulinna AS, Kee F, Tunstall-Pedoe H, et al. Contribution of 30 biomarkers to 10-year cardiovascular risk estimation in 2 populations cohorts. The MONICA, risk, genetics, archiving, and monograph (MONOGRAM) biomarker project. *Circulation*. 2010;121:2388-97.
- Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Atherosclerosis*. 2016;252:207-74.
- Kotseva K, Wood D, De Bacquer D, De Backer G, Rydén L, Jennings C, et al. EUROASPIRE Investigators. EUROASPIRE IV: A European Society of Cardiology survey on the lifestyle, risk factor and therapeutic management of coronary patients from 24 European countries. *Eur J Prev Cardiol*. 2016;23:636-48.
- Gitt AK, Lautsch D, Ferrieres J, Kastelein J, Drexel H, Horack M, et al. Contemporary data on low-density lipoprotein cholesterol target value attainment and distance to target in a cohort of 57,885 statin-treated patients by country and region across the world. *Data Brief*. 2016;9:616-20.
- Galve E, Cordero A, Cequier A, Ruiz E, González-Juanatey JR. Degree of lipid control in patients with coronary heart disease and measures adopted by physicians. REPAR Study. *Rev Esp Cardiol (Engl Ed)*. 2016;69:931-8.
- Gómez-Barrado J, Ortiz C, Gómez-Turégano M, Gómez-Turegano P, Garcipérez-de-Vargas FJ, Sánchez-Calderón P. Control lipídico en pacientes con enfermedad coronaria del área de salud de Cáceres (España): estudio LIPICERES. *Clin Invest Arterioscler*. 2016, <http://dx.doi.org/10.1016/j.arteri.2016.09.003>.
- Masana L, Pedro-Botet J, Civeira F. IMPROVE-IT clinical implications. Should the "high-intensity cholesterol-lowering therapy" strategy replace the "high-intensity statin therapy"? *Atherosclerosis*. 2015;240:161-2.
- Silverman MG, Ference BA, Im K, Wiviott SD, Giugliano RP, Grundy SM, Braunwald E, et al. Association between lowering LDL-C and cardiovascular risk reduction among different therapeutic interventions: a systematic review and meta-analysis. *JAMA*. 2016;316:1289-97.
- Masana L, Ibarretxe D, Plana N. Maximum low-density lipoprotein cholesterol lowering capacity achievable with drug combinations. When 50 plus 20 equals 60. *Rev Esp Cardiol (Engl Ed)*. 2016;69:342-3.
- Pedro-Botet J, Climent E, Chillarón JJ, Toro R, Benaiges D, Flores-Le Roux JA. Statins for primary cardiovascular prevention in the elderly. *J Geriatr Cardiol*. 2015;12:431-8.