Revista Portuguesa de Cardiologia 41 (2022) 131–133

Revista Portuguesa de
Cardiologia
Portuguese Journal of Cardiology
www.revportcardiol.org

EDITORIAL COMMENT

Management of dyslipidemia in diabetic patients: More than atheroma – The key things to understand in order to avoid a bittersweet taste

Tratamento da dislipidemia em doentes diabéticos: mais do que ateroma - Os aspetos chave a compreender para evitar o sabor agridoce

Alberto Mello e Silva [a,b]

[a] *Sociedade Portuguesa de Aterosclerose, Portugal*
[b] *Grupo Luz Saúde, Portugal*

Available online 23 November 2021

Preventing cardiovascular disease by promoting ideal cardiovascular health requires shifting the focus from treating disease after it develops to preventing cardiovascular events before they happen by slowing the progression of atherosclerosis. One of the most important biomedical success stories of the past half-century in the USA has been a 50% reduction in cardiovascular mortality.[1]

Achieving and maintaining optimal lipid levels is necessary to achieve ideal cardiovascular health. This goal will require patient-tailored strategies combining multiple approaches that can help to overcome a crucial barrier to long-term adherence due to the asymptomatic nature of cardiovascular risk factors, particularly dyslipidemia in diabetic patients.

In this issue of the *Journal*, Débora Fonseca and colleagues[2] report a quality improvement study aimed at health care professionals that included patients with diabetes and dyslipidemia. Twenty-seven general practitioners from three primary care units were enrolled.

The study was well designed and had a representative sample of diabetic patients with dyslipidemia. Quality standards were defined for each of the criteria evaluated (target LDL-c level achieved, change in lipid-lowering therapy at the time of consultation when LDL-C above the target level was determined, and scheduling of a reassessment consultation within three months and monitoring of lipid parameters if target LDL-C level was not achieved) in two time periods – July 1 to December 31, 2017 (329 patients) and January 1 to June 30, 2019 (333 patients).

Comparing the first and second assessments, 14.6% vs. 22.2% (p=0.016) of the patients, respectively, achieved the target LDL-C value of <70 mg/dl. Of those who did not meet the target level, 11.0% vs. 13.6% (p=0.395) had their pharmacological therapy changed and 4.6% vs. 3.3% (p=0.448) had their lipid profile reassessed within three months.

Overall, 50.2% of the patients received medium-intensity therapy with 20-40 mg simvastatin, the most commonly prescribed statin. Non-statin therapy was being prescribed in 10.4% and 16.8%, respectively, at the first and second assessments. There was no reference to combination therapy. In conclusion, control of dyslipidemia in patients with diabetes in those three primary care units at two assessments in 2017 and 2019 confirms that lipid-lowering therapy (LLT) prescription improved only slightly, while attainment of adequate lipid control rates remained unsatisfactory in terms of LDL-C goals achieved. Additionally, the prescription rates for combination LLT could not be analyzed in this study.

As acknowledged by the authors, it is essential to increase the literacy of physicians and to encourage the search for the best possible lipid control in patients with diabetes, in order

E-mail address: amelloesilva@gmail.com

https://doi.org/10.1016/j.repc.2021.10.005

to reduce cardiovascular risk, as well as to raise awareness among patients to increase adherence to therapy.

There are many reasons for these results. Conventional risk factors are fixed, but modifiable risk factors, such as cholesterol level, can be reduced in order to improve patients' outcomes, but this depends on the patient engaging and continuing to make lifestyle changes or indeed to take medication. Unfortunately, many patients do not accomplish this task.

One explanation is a lack of adequate patient-provider communication and indeed failure to understand the importance of shared decision-making. The clinician and the patient make decisions together using the best available evidence, with the patient being encouraged to consider available screening, treatment, or management options, and the likely benefits and harms of each.

Another important point is the need to know what patients' priorities are. The physician's priorities are not necessarily those of the patient.

Patients with dyslipidemia are often being treated for primary prevention, and sometimes for secondary prevention. This means that they do not immediately feel unwell as a result of their condition. They are given medication that at best is not going to make them feel any different, and at worst might result in side effects. It is important to underline the huge benefits of helping patients understand the importance of engaging with treatment and of continuing to take their medication appropriately. Pharmacotherapy is prescribed not to achieve a 'good' lipid analysis but because doctors believe that treatment targets and goals for cardiovascular disease prevention mean a lower likelihood of a person experiencing a fatal or non-fatal atherosclerotic cardiovascular event over a defined period of time.

Last but not least, there are some constraints and barriers to overcome in the management of patients with chronic disease, for example diabetic patients with dyslipidemia: structural barriers, such as time constraints; organizational factors, such as the need for communication with other health professionals; and patient-related factors, such as educational level, family and social environment, and socioeconomic status.

Real-world data show that poor LDL-C goal attainment is an issue across all categories of high-risk and very-high-risk patients. Similar studies in Portugal and other European countries[3,4] have shown comparably poor lipid control in patients at high and very high risk. Limited uptake of high-intensity statin therapy, and underuse of combination therapy (such as statins plus ezetimibe), on top of suboptimal treatment adherence is a major issue, for various reasons including adverse effects (whether perceived or real), and clinician inertia.

In 2016, in mainland Portugal, 15 123 deaths were attributable to atherosclerosis, accounting for 14.3% of overall mortality. Disability-adjusted life years totaled 260 943, 75% due to premature death (196 438 years of life lost) and 25% due to disability (64 505 years lived with disability).[5] Atherosclerosis imposes a high disease burden on society. A large part of this burden would be avoidable if effective, evidence-based and cost-effective interventions were implemented targeting known risk factors, such as dyslipidemia, from prevention to treatment.

Achieving this goal will require continuous efforts and policies that set out to improve health interventions on a population level, monitoring interventions until cardiovascular disease no longer represents an important cause of morbidity or death.

Concerning dyslipidemia, we need to recognize that while the standard drugs we have, statins, are extremely efficacious for many patients, they are not always well tolerated. Furthermore, diabetic patients with dyslipidemia are frequently at high or very high risk for cardiovascular disease, with LDL-C targets unattainable with statin monotherapy. High- and very-high-risk patients[6] can be prescribed upfront LLT combination treatment of a statin and a non-statin drug such as ezetimibe, an oral selective cholesterol absorption inhibitor interacting with Niemann-Pick C1-like 1 (NPC1L1). Other non-statin drugs for combination treatment with a statin are available, including evolocumab and alirocumab, proprotein convertase subtilisin/kexin type 9 (PCSK9) monoclonal antibodies that target LDL receptors by preventing them from binding to PCSK9, thereby interrupting LDL receptor degradation and increasing clearance of LDL-C from the bloodstream; bempedoic acid (not yet available in Portugal), an oral prodrug that undergoes liver-specific activation to inhibit adenosine triphosphate-citrate lyase, an important enzyme in the cholesterol biosynthesis pathway directly upstream of HMG-CoA reductase; and inclisiran (also not yet available in Portugal), a small interfering RNA that inhibits the synthesis of PCSK9. These combinations should improve adherence and help accomplish lipid targets.[6–8]

Gaps between clinical guidelines and clinical practice for lipid management across Europe persist and will be exacerbated by the 2019 guidelines. Even with optimized statins, greater use of non-statin LLT is likely to be needed to reduce these gaps for patients at highest risk.

The past half-century of progress in alleviating the burden of cardiovascular disease gives us great optimism as we look ahead to emerging opportunities to further enhance cardiovascular health.

Until then, we cannot afford not to take full advantage of the right tools to achieve our goals, since they have been shown to reduce morbidity and mortality due to cardiovascular disease. Otherwise the success story will be incomplete and a bittersweet taste will persist.

Conflicts of interest

Dr. Alberto Mello e Silva has received consultancy and speaker fees from Bayer, Daiichi-Sankyo, Menarini, Mylan, Novartis, Servier and Tecnimede.

References

1. Gibbons GH, Christine E, Seidman CE, et al. Conquering atherosclerotic cardiovascular disease – 50 years of progress. N Engl J Med. 2021;384:785–8.
2. Fonseca DA, Lamas JPS, Duarte LL. Abordagem Terapêutica da Dislipidemia em Doentes Diabéticos – A realidade das USF. Rev Port Cardiol. 2022;40.
3. Silva PM, Aguiar C, Morais J. Suboptimal lipid levels in clinical practice among Portuguese adults with dyslipidemia under lipid-

lowering therapy: data from the DISGEN-LIPID study. Rev Port Cardiol. 2019;38:559–69.
4. Ray KK, Molemans B, Schoonen WM, et al. DA VINCI study. EU-wide cross-sectional observational study of lipid-modifying therapy use in secondary and primary care: the DA VINCI study. Eur J Prev Cardiol. 2020;28:1279–89.
5. Costa J, Alarcão J, Araújo F, et al. The burden of atherosclerosis in Portugal. Eur Heart J Qual Care Clin Outcomes. 2020;7:154–62.
6. Averna M, Banach M, Bruckert E, et al. Practical guidance for combination lipid-modifying therapy in high- and very-high-risk patients: a statement from a European Atherosclerosis Society Task Force. Atherosclerosis. 2021;325:99–109.
7. Mach F, Baigent C, Catapano AL, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J. 2019:1–78.
8. Ray KK, Corral P, Morales E, Nicholls SJ. Pharmacological lipid-modification therapies for prevention of ischaemic heart disease: current and future options. Lancet. 2019;394:697–708.