

Statin Use and Hypercholesterolemia: Are the Current Guidelines' Recommendations Being Followed?

Renato Jorge Alves^{1,2}

Departamento de Cardiologia na Santa Casa de Misericórdia de São Paulo,¹ São Paulo, SP - Brazil Faculdade de Ciências Médicas, Santa Casa de São Paulo,² São Paulo, SP - Brazil Short Editorial related to the article: Statins Prescriptions and Lipid Levels in a Tertiary Public Hospital

Despite advances in treating cardiovascular diseases, acute myocardial infarction and stroke are still the main causes of death worldwide.¹

The prevention of coronary atherosclerotic disease (CAD), represented by the treatment of low-density lipoprotein cholesterol (LDL-c), is one of the main alternatives for increasing the survival of patients with cardiovascular risk factors. Case-control, observational, and genetic studies confirm the importance of increased cholesterol level as one of the main modifiable risk factors for cardiovascular disease, especially for CAD and ischemic stroke. The reduction in LDL-c throughout life has been associated with a lower risk of developing CAD. There seems to be a causal relationship between LDL-c and CAD, which is continuous and which depends on the magnitude of the reduction in LDL-c.²⁻⁵

After the Japanese biochemist Akira Endo discovered statins in 1976, intervention studies with this drug class changed the CAD prevention concern. Currently, statins (3-hydroxy-3methyl-glutaryl-CoA reductase inhibitors) are recommended by all guidelines as first-line drugs in the pharmacological treatment of hypercholesterolemia for primary and secondary prevention of CAD. This drug class acts by inhibiting cholesterol synthesis, thus increasing expression of receptors, resulting in greater removal of plasmatic LDL.⁶⁻⁸

The most robust meta-analysis on statins evaluated data from 170,000 patients in 26 clinical studies. This publication highlighted the comparison of statins versus placebo and more versus less potent statins. It was observed that, for LDL-c reduction of 1 mmol/L or 40 mg/dL, there was an average reduction of 22% in the main cardiovascular outcomes. The analysis also showed that the greater the reduction in LDL-c, the greater the benefit achieved from the treatment. Large clinical trials with statins have demonstrated that the greater the absolute reduction in LDL-c, the greater the reduction in the relative risk of cardiovascular events.⁵ To date, no threshold has been identified below which lipid-lowering treatment

Keywords

Cardiovascular Diseases; Stroke; Myocardial Infarction; Mortality; Atherosclerosis; Risk Factors; Hydroxymethylglutaryl –CoA Reductase Inhibitors; Hospitalization; Hospitals, Public.

Mailing Address: Renato Jorge Alves •

Irmandade da Santa Casa de Misericórdia de São Paulo - Departamento de Medicina - Rua Cesário Motta Jr., 112. Postal Code 04126-000, São Paulo, SP – Brazil E-mail: renatoalves178@gmail.com

DOI: https://doi.org/10.36660/abc.20210089

would fail to promote cardiovascular benefit; however, very low LDL-c levels were evaluated for a short period of time.⁹⁻¹¹

In the article "Statins Prescriptions and Lipid Levels in a Tertiary Public Hospital"12 the statin prescription is frequent, possibly due to the recognition of dyslipidemia as a relevant cardiovascular risk factor. However, it was performed without a specific LDL-c target, without dose adjustment, and without at least one annual control test, showing that the guidelines' recommendations are not fully considered. Moreover, it showed that the prescription without evaluation of blood cholesterol occurred predominantly in Vascular Surgery and that Cardiology was the specialty with the highest number of statin prescriptions. Despite this, a considerable percentage of individuals have LDL-c above that recommended in primary prevention guidelines. On the order hand, it is interesting to note that compared with the AHA/ACC guideline, the Brazilian guideline seems to classify a larger proportion of primary prevention patients into higher-risk categories, increasing the statin eligibility criteria.¹³ It was also noted that the use of statins by the Public Health System is cost-effective and that, among the treated individuals, 2.4% had LDL-c \geq 190 mg/ dL. This LDL-c level, higher than that registered in the general population, accompanied by a mean age lower than the total sample (55 \pm 15 versus 63 \pm 13 years, p < 0.05), suggests the possibility of the presence of familial hypercholesterolemia in that group. Thus, a more cautious follow-up would be recommended, as there would be a greater cardiovascular risk in this population.^{14,15}

The two statins used in this survey, simvastatin (78%) and atorvastatin (22%), showed that plasma cholesterol and LDL-c concentrations were lower in patients receiving prescriptions from cardiology. Therefore, it would be expected that the achievement of goals recommended in the guidelines, not achieved in a large percentage of patients, should have been more achieved by this specialty.

The results found in this study illustrate the need not only for more accurate laboratory diagnosis, but mainly for more effective lipid-lowering treatment. We have sufficient data on the safety and efficacy of statins, including in acute coronary syndrome.¹⁶

More aggressive lipid-lowering therapy and early diagnosis should be emphasized. Statins continue to be the gold standard in the pharmacological treatment of hypercholesterolemia. However, in addition to enhancing the dosage, new drugs with proven scientific evidence in this therapeutic arsenal, such as ezetimibe and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, have already been shown to reduce cardiovascular risk safely.

Short Editorial

References

- Smith SC Jr, Collins A, Ferrari R, Holmes DR Jr, Logstrup S, McGhie DV, Ralston J, Sacco RL, Stam H, Taubert K, Wood DA, Zoghbi WA; World Heart Federation; American Heart Association; American College of Cardiology Foundation; European Heart Network; European Society of Cardiology. Our time: a call to save preventable death from cardiovascular disease (heart disease and stroke). J Am Coll Cardiol. 2012;60(22):2343-8.
- Management of the long-term intervention with pravastatin in ischaemic disease (LIPID) study after the scandinavian simvastatin survival study (4S) Andrew M. Tonkin AM. Am J Cardiol. 1995; 28;76(9):107C-112C.
- 3. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al; INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet. 2004;364(9438):937-52.
- Ference BA, Yoo W, Alesh I, Mahajan N, Mirowska KK, Mewada A, et al. Effect of long-term exposure to lower low-density lipoprotein cholesterol beginning early in life on the risk of coronary heart disease: a Mendelian randomization analysis. J Am Coll Cardiol. 2012;60(25):2631-9.
- Baigent C, Blackwell L, Emberson J, Holland LE, Reith C, Bhala N, et al; Cholesterol Treatment Trialists' (CTT) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. Lancet. 2010;376(9753):1670-81.
- 6. Faludi AA, Izar MCO, Saraiva JFK, Chacra APM, Bianco HT, Afiune AN, Bertolami A, Pereira AC, Lottenberg AM, Sposito AC, Chagas ACP, Casella AF, Simao AF, Alencar ACF, Caramelli B, Magalhaes CC, Negrao CE, Ferreira C, Scherr C, Feio CMA, Kovacs C, Araujo DB, Magnoni D, Calderaro D, Gualandro DM, Mello EPJ, Alexandre ERG, Sato EI, Moriguchi EH, Rached FH, Santos FCD, Cesena FHY, Fonseca FAH, Fonseca H, Xavier HT, Mota ICP, Giuliano ICB, Issa JS, Diament J, Pesquero JB, Santos JED, Faria JRN, Melo JXF, Kato JT, Torres KP, Bertolami MC, Assad MHV, Miname MH, Scartezini M, Forti NA, Coelho OR, Maranhao RC, Santos RDDF, Alves RJ, Cassani RL, Betti RTB, Carvalho T, Martinez T, Giraldez VZR and Salgado WE. Atualização da Diretriz Brasileira de Dislipidemias e Prevenção da Aterosclerose – 2017. Arq Bras Cardiol. 2017;109(1):1-76.
- Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/ APhA/ ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart

Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018;73(24):e285-e350.

- ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS, European Heart Journal (2019) 00, 1-78.
- 9. Cannon CP, Blazing MA, Giugliano RP, McCagg A, White JA, Theroux P, et al; IMPROVE-IT Investigators. Ezetimibe added to statin therapy after acute coronary syndromes. N Engl J Med. 2015;372(25):2387-97.
- Sabatine MS, Giugliano RP, Keech AC, Honarpour N, Wiviott SD, Murphy SA, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. N Engl J Med. 2017;376(18):1713-22.
- 11. Schwartz GG, Bessac L, Berdan LG, Bhatt DL, Bittner V, Diaz R, et al. Effect of alirocumab, a monoclonal antibody to PCSK9, on long-term cardiovascular outcomesfollowing acute coronary syndromes: rationale and design of the ODYSSEY outcomes trial. Am Heart J. 2014 Nov;168(5):682-9.
- Schmidt A, Moreira HT, Volpe GJ, Foschini VB, Lascala TF, Romano MMD, et al. Perfil de Prescrição de Estatinas e de Níveis Lipêmicos em Ambulatórios de Hospital Terciário Público. Arq Bras Cardiol. 2021; 116(4):736-741.
- Cesena FHY, Valente VA, Santos RD, Bittencourt MS. Cardiovascular Risk and Statin Eligibility in Primary Prevention: A Comparison between the Brazilian and the AHA/ACC Guidelines. Arq Bras Cardiol. 2020 Sep;115(3):440-449.
- Santos RD, Gagliardi AC, Xavier HT, Casella Filho A, Araújo DB, Cesena FY, Alves RJ et al. Sociedade Brasileira de Cardiologia. I Diretriz Brasileira de Hipercolesterolemia Familiar (HF). Arq Bras Cardiol. 2012;99(2 Supl. 2):1-28.
- 15. Ribeiro RA, Duncan BB, Ziegelmann PK, Stella SF, Vieira JL, Restelatto LM and Polanczyk CA. Cost-effectiveness of high, moderate and low-dose statins in the prevention of vascular events in the Brazilian public health system. Arq bras cardiol. 2015;104:32-44.
- Schubert J, Lindahl B, Melhus H, Renlund H, Leosdottir M, Yari A, Ueda P, James S, Reading SR, Dluzniewski PJ, Hamer AW, Jernberg T, Hagström E.. Low-density lipoprotein cholesterol reduction and statin intensity in myocardial infarction patients and major adverse outcomes: a Swedish nationwide cohort study. Eur Heart J. 2021;42(3):243-252.

 \odot