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Research Article

Achievement of LDL-Cholesterol Targets in a Reference Service of the Brazilian Public Health System

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Abstract

Introduction: Guidelines recommend that physicians reduce levels of low-density lipoprotein cholesterol (LDL-c) in patients with high cardiovascular risk. However, the achievement of these targets is low. It is paramount to know the success rate of lipid control to improve therapy and reduce cardiovascular events.

Objective: To assess the efficacy of lipid-lowering therapy in the achievement of LDL-c goals for each cardiovascular risk group in public outpatient ambulatory in Brazil.

Methods: Cross-sectional, observational, retrospective study in the Cardiology outpatient clinic of a referral hospital in Brazil. We included all patients with a history of dyslipidemia who were attended between May and June 2022. We excluded patients who had their first consultation at the time of recruitment. Data were obtained from medical records and the success rates for LDL-c goals were analyzed across cardiovascular risk groups. Statistical analyses were made by Pearson's chi-square test, unpaired Student's T-test and ANOVA One-Way test. Differences among groups were considered to be statistically significant if p-values were lower than .05.

Results: We included 431 patients; 207 (48.0%) were classified as very high risk, 159 (36.9%) as high risk, 46 (10.7%) as intermediate risk and 19 (4.4%) as low risk. 82.8% received statins, 30.4% received high-intensity statin therapy (HIST), 6.7% received ezetimibe and none received PCSK9 inhibitor. The LDL-c goal had been reached in different proportions among risk groups: 15.9% of very high risk patients, 31.4% of high risk patients, 54.3% of intermediate risk patients and 73.7% of low risk patients (p=.0001 for comparison among groups).

Conclusions: Our study showed poor success rates in achieving LDL-c goals, with the lowest success rate in the very-high risk group, despite the more frequent use of HIST and ezetimibe. These results demonstrate challenges in achieving LDL-c targets in real world.

Keywords

Cholesterol, LDL; Coronary Disease; Hypercholesterolemia; Public Health System.

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Introduction

Cardiovascular disease is the major cause of death in the world; surprisingly, approximately 75% of these deaths could have been prevented by controlling risk factors [1-3]. In Brazil, cardiovascular disease represents the first cause of death, especially coronary artery disease [4,5]. Among other risk factors, the prevalence of dyslipidemia is high, reaching 18.6% to 32.7% of the population [5].

It is well known that low density lipoprotein (LDL) is the major component of non-high density lipoprotein (N-HDL) cholesterol, which has almost a log linear association with the incidence of cardiovascular diseases, increasing two times the risk for each millimole per litre unit increase of N-HDL [6-9]. Furthermore, other studies demonstrate that a reduction of 39 mg/dl in LDL cholesterol (LDL-c) represents a reduction of 22.0% in relative risk for atherosclerotic cardiovascular disease [8,10]. From the strong evidence of cardiovascular benefit in lowering LDL-c, the new guidelines adopt very low goals of LDL-c levels for patients at highest risk [11-13]. Thus, aggressive lowering LDL-c therapy is a safe strategy to reduce cardiovascular risk and prevent deaths for cardiovascular events [8]. Despite the current recommendations to achieve very low LDL-c levels, reaching these targets is still a challenge. Few studies have evaluated the efficacy in reaching LDL-c targets and they all showed low prevalence of patients within the goals [14-16]. It is important to know the success rate of achievement of LDL-c target in our population to improve lipid-lowering therapy and reduce cardiovascular events. This study aims to analyze the efficacy of lipid-lowering therapy in the achievement of LDL-c goals for each cardiovascular risk group in a public Brazilian outpatient ambulatory.

Methods

Study Design

Cross-sectional, observational, retrospective study conducted in the outpatient Cardiology clinic of a tertiary referral hospital in Brazil. The data were obtained from medical records.

Population

We analyzed all the patients that were attended between May and June 2022. The inclusion criteria were having a previous diagnosis of dyslipidemia. Patients who had their first medical appointment in the months of recruitment were excluded.

Analyzed Variables

The variables analyzed were age, first LDL-c level, last LDL-c level, number of previous medical appointments in the institution, comorbidities, the presence of atherosclerotic disease and current lipid-lowering treatment. The comorbidities analyzed were hypertension, diabetes mellitus and chronic kidney disease. These data were obtained from previous diagnosis described on medical records. The presence of atherosclerotic disease was divided in previous acute myocardial infarction, chronic coronary artery disease with previous revascularization, chronic coronary artery disease above 50.0% stenosis without previous revascularization, stroke or transient ischemic attack, carotid artery disease above 50.0% stenosis and peripheral artery disease above 50.0% stenosis, also based on previous medical records. The current treatment was divided in statin, ezetimibe and PCSK9 inhibitor. The statin group included the use of simvastatin, pitavastatin, atorvastatin and rosuvastatin. High-intensity statin therapy (HIST) was defined as the current prescription and use of atorvastatin in a dose of at least 40 mg or rosuvastatin in a dose of at least 20 mg.

Comparisons

All the patients included were categorized in a cardiovascular risk group - low risk, intermediate risk, high risk or very high risk - using the Global Risk Score based on the Update of Brazilian Dyslipidemia and Atherosclerosis Prevention Guideline, published in 2017 [12]. The data were analyzed to compare the proportion of patients who met the LDL-c target in each cardiovascular risk group.

Statistical Analysis

Statistical analysis was made by the use of Pearson's chi-square test, Student's T-test and ANOVA One-Way test, using the Statistical Package for the Social Sciences (SPSS) version 23.0. The sample size to reach the target alpha 5% and beta 20% was 387, for a 10% difference on the success rate among at least two of the four risk groups. Differences among groups were considered to be statistically significant if p-values were lower than .05.

Ethical Aspects

This study was approved by the ethics research committee of the institution under the number 3.041.855. All ethical principles regarding studies involving humans were followed, according to the Declaration of Helsinki.

Results

We included 432 patients; one was excluded because of missing essential data to stratify cardiovascular risk. Hence, results are described for the remaining 431 participants. Mean age was 64.2 ± 18 years; 177 (41.1%) patients were female and 254 (58.9%) patients were male. In the overall cohort, 90 (20.9%) participants had previous acute myocardial infarction, 76 (17.6%) had chronic coronary artery disease with previous revascularization, 13 (3.0%) had chronic coronary artery disease above 50.0% stenosis without previous revascularization, 27 (6.2%) had stroke or transient ischemic attack, two (0.4%) had carotid artery disease above 50.0% stenosis and two (0.4%) had peripheral artery disease above 50.0% stenosis. 226 (52.4%) of participants did not have previous atherosclerotic disease. The prevalences of the other comorbidities

are summarized in table 1.

207 patients (48.0%) were classified as very high risk, 159 (36.9%) as high risk, 46 (10.7%) as intermediate risk and 19 (4.4%) as low risk. As current lipid-lowering treatment, 357 (82.8%) received statins, 131 (30.4%) received HIST, 29 (6.7%) received ezetimibe and none received PCSK9 inhibitor. The distribution of the current treatment for each cardiovascular risk group is demonstrated in table 2.

The average number of medical appointments before inclusion in the study was 3.92 and the mean number was 2 appointments. The mean value of LDL-c level at the time of the first appointment, available in 298 (69.1%) patients, was 97.4 mg/dl. The mean value of the last LDL-c level was 87.2 mg/dl. Only 122 participants (28.3%) reached the LDL-c target according to the recommendation of his or her risk group. Table 3 compares first LDL-c, last LDL-c, variation in LDL-c, number of medical appointments and rate of achievement of LDL-c goal for each cardiovascular risk group.

Discussion

In this cohort, we found that less than one third of the outpatients reached LDL-c targets. The achievement of LDL-c goals was inversely proportional to the cardiovascular risk. Despite the increased HIST and ezetimibe use in the very high risk group, only 15.9% reached the LDL-c target. This group also had higher prevalence of comorbidities and was more elderly. A multinational study that involved countries in Africa, Asia, Eastern Europe, Latin America and Middle East had similar findings. The proportion of patients who achieved LDL-c goals in the very high risk group was 32.1% and it was the lowest among other groups; only 25.0% of participants were receiving HIST. In our study, 30.4% were receiving HIST. They also found that overweight or obesity, high blood pressure, neurocognitive disorder and current smoking were associated with not achieving LDL-c goal. As in our study, the very high-risk group tended to be older and have more comorbidities. It is possible that these conditions may contribute to the low achievement of LDL-c goal in our population, although a causal relationship was not assessed in our study [16]. Despite the apparent concordance in these results, that study used the 2011 European Society of Cardiology Guideline targets [17], in which the goal for very high-risk group was less than 70 mg/ml. Therefore, the achievement of LDL-c target could have been even worse if compared to the new guidelines target of less than 50 mg/ml used in our study [16].

Table 1: Age and prevalence of cardiovascular risk factors in each cardiovascular risk group.

Clinical characteristic	Low risk (n = 19)	Intermediary risk (n=46)	High risk (n = 159)	Very high risk (n = 207)	Total
Age, mean ± SD	39 ± 16	53 ± 12	66 ± 11	67 ± 12	64 ± 14
Hypertension, n (%)	14 (73.7)	29 (63.0)	146 (91.8)	193 (93.2)	379 (87.7)
Diabetes mellitus, n (%)	11 (57.9)	1 (2.2)	61 (38.3)	99 (47.8)	161 (37.2)
Chronic kidney disease, n (%)	0 (0.0)	0 (0.0)	25 (15.7)	43 (20.7)	68 (15.7)

SD = standard-deviation.

Table 2: Use of lipid-lowering medical therapy in each cardiovascular risk group.

Medical therapy	Low risk (n = 19)	Intermediary risk (n=46)	High risk (n = 159)	Very high risk (n = 207)	P
Statin, n (%)	4 (21.0)	23 (50.0)	129 (81.1)	201 (97.1)	.0001
HIST, n (%)	0 (0.0)	2 (4.3)	36 (22.6)	93 (44.9)	.0001
Ezetimibe, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	28 (13.5)	.001

HIST = High-intensity statin therapy.

Table 3: Comparison of achievement of low-density lipoprotein targets in each cardiovascular risk group.

LDL-c levels and number of medical appointments	Low risk (n = 19)	Intermediary risk (n=46)	High risk (n = 159)	Very high risk (n = 207)	P
First LDL-c, mean ± SD	114.2 ± 29	102.4 ± 31	98.6 ± 21	90.1 ± 25	.002
Last LDL-c, mean ± SD	102.8 ± 26	100.3 ± 32	93.1 ± 34	78.6 ± 32	.001
Change in LDL-c, mean ± SD	-11.4 ± 9.9	-2.1 ± 2.0	-5.5 ± 5.6	-11.5 ± 12.8	.05
Medical appointments, mean ± SD	5.3 ± 5	3.3 ± 3	3.1 ± 2	2.9 ± 3	.89
LDL-c target achieved, n (%)	14 (73.7)	25 (54.3)	50 (31.4)	33 (15.9)	.0001

LDL-c = Low-density lipoprotein cholesterol level; SD = standard-deviation.

The DA VINCI study, designed to provide contemporary information regarding LDL-c goal attainment, enrolled 5,888 patients across 18 European countries [17]. As in our study, goal attainment was higher among individuals at lower cardiovascular risk and lower among those at higher risk. Only 54% of patients achieved their risk-based 2016 LDL-c goal, and only 18% of very high-risk patients achieved LDL-c goals of <55 mg/ml as recommended by the 2019 European Society of Cardiology Guidelines [18]. The authors concluded that there is a gap between guideline recommendations for achieving LDL-c goals and their implementation in clinical care, and that non-statin therapy will probably need to be added for patients at highest risk.

In Brazil, the ELSA-Brasil cohort study showed that 45.5% of the population had high LDL-c levels. Among these subjects, 42.3% were using lipid-lowering therapy and 58.3% reached the targets, almost two times the proportion found in our study. The pattern of LDL-c targets according to risk groups was very similar to ours, with the lowest achievement of LDL-c goal in the very high risk group (10.0%). Once again, our study used lower LDL-c targets, as established in the new guidelines, and ELSA-Brasil population had more than half of the subjects with high educational level and health insurance, which may contribute to a higher achievement of LDL-c target as socioeconomic conditions have an inverse association with LDL-c levels [5,19,20]. Studies developed in the cities of São Paulo, Curitiba and Aranpongas also had similar results, with low achievement of LDL-c goals especially for the very high risk group (11.1%, 7.4% and 10.0% respectively). All these three studies had population characteristics and LDL-c target similar to our study [21-24].

In real world conditions, the achievement of LDL-c goal is low not only in our study, but also in other regions in Brazil and in other countries. This failure may be related to several factors, such as: lack of medical education, therapeutic inertia, lack of patients' comprehension about the risks and the importance of intensive treatment, and poor treatment adherence. This last issue may occur mainly due to side effects of statins or financial difficulties to purchase medication [15,25]. In present days, in the Brazilian public health system, the availability of HIST is limited for bureaucratic issues and PCSK9 inhibitor is unavailable in most health facilities. Although this study is relevant for showing real world challenges on lipid-lowering therapy, it has important limitations. One is that the whole treatment period was not assessed, although we may infer from the number of medical appointments that the subjects were using lipid-lowering therapy for at least three months, which is sufficient time for consistent LDL-c lowering. Besides, we did not analyze socioeconomic factors that are closely related to poor therapeutic adherence. Even though, it is known that patients in Brazilian Unified Health System often have poor socioeconomic conditions, which offers another challenge in the achievement of LDL-c targets. Lastly, the findings of this single-center cohort cannot be extrapolated to other regions or institutions, since practices may differ considerably. However, consistent and repeated results of poor rates of success on lipid-lowering therapy raise awareness and claim for medical staff to improve practices.

Conclusions

Our study showed low rates of achievement of LDL-c goal even in a tertiary referral institution in Brazil. The achievement of LDL-c targets behaved inversely proportional to the cardiovascular risk group, with the lowest success rate in the very high risk group, despite the more frequent use of HIST and ezetimibe. These results demonstrate a great challenge in achieving LDL-c targets in real life and unexplained clinical inertia that demands immediate action.

Authors' Contributions

Pedro Henrique Paiva Faria Faleiro, Carolina Bravim Ferraço Vetorazi, Ana Beatriz Parma Marçal, Priscila Cabral Gomes Coelho Lima, Nickolas Fraga Perin da Cruz, Layla Pasolini Lott, Valentin Trevizani Neto and Eduardo Gomes Vieira were responsible for collecting, analyzing and organizing data from the study participants. Glícia Chierici Baptista was responsible for writing and reviewing this manuscript and for creating the tables and figures. Roberto Ramos Barbosa and Luiz Fernando Machado Barbosa were responsible for the conception of the study, for the statistical analysis and for reviewing this manuscript. Guilherme Freitas Fernandes de Oliveira, Lucas Crespo de Barros, Larissa Novaes Paganini, Lucas Martins Frizzera, Renato Giestas Serpa and Osmar Araujo Calil were responsible for reviewing this manuscript. All authors agreed to the publication of this study.

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