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THE IMPACT OF LIPID- LOWERING THERAPIES ON THE MANAGEMENT OF DYSLIPIDEMIA AND THE PREVENTION OF CARDIOVASCULAR EVENTS

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Abstract: Lipid-lowering therapies, such as PCSK9 inhibitors and bempedoic acid, are essential in the treatment of dyslipidemia, especially for patients who do not reach their LDL-C targets with statins. PCSK9 inhibitors can reduce LDL-C levels by up to 60% and have shown efficacy in preventing cardiovascular events in high-risk populations. However, their high cost limits access, generating debate about cost-effectiveness, especially in developing countries. Bempedoic acid offers an alternative for those who cannot tolerate statins, but its efficacy in cardiovascular events still needs more data. Long-term safety and affordability are key concerns as these therapies evolve.

Keywords: Dyslipidemia. Hypoglycemic agents. Cardiovascular events. Prevention.

INTRODUCTION

Dyslipidemia is one of the main modifiable risk factors for the development of cardiovascular diseases, with elevated low-density lipoprotein cholesterol (LDL-C) being the main therapeutic target¹. Several studies have shown that reducing LDL-C levels is strongly associated with a reduction in the incidence of cardiovascular events, such as myocardial infarction and stroke. Historically, statins have been the cornerstone of dyslipidemia management, showing proven efficacy in reducing cardiovascular morbidity and mortality². However, not all patients achieve adequate LDL-C levels with statins, and some show intolerance to this class of drugs, creating the need for new therapeutic strategies.³

In recent years, state-of-the-art lipid-lowering therapies have emerged, such as proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors and bempedoic acids, which offer new treatment options for patients with dyslipidemia that is difficult to control². PCSK9 inhibitors, by significantly reducing LDL-C levels, have shown potential in preventing cardiovascular events, even in

high-risk individuals or those with familial hypercholesterolemia. As for bempedoic acids, they have emerged as a viable alternative for those who are intolerant of statins, offering an additional reduction in LDL-C with a more tolerable safety profile.¹

These new therapies not only expand the options for managing dyslipidemia, but also have a significant impact on the prevention of cardiovascular disease, one of the leading causes of mortality worldwide. However, their high cost and limited accessibility still represent challenges to be overcome, especially in countries with health systems with limited resources². This study aims to review the impact of these state-of-the-art lipid-lowering therapies on the control of dyslipidemia and their effectiveness in reducing cardiovascular events, as well as discussing their clinical and economic implications in current medical practice.¹

METHODOLOGY

This is an exploratory bibliographic review, organized through an integrative literature review. The collection of scientific data and the systematization of information come from scientific productions published from 2021 to 2024, in Portuguese and English, indexed in the Virtual Health Library (VHL), Scientific Electronic Library Online (SCIELO), Up to Date, PubMed and Google Scholar. The collection of information used in the development of the work was based on the proposed theme, as well as its objectives.

RESULTS AND DISCUSSION

Lipid-lowering therapies have played a crucial role in the management of dyslipidemia and the prevention of cardiovascular events. Reducing LDL-C has been the central focus, since its high levels are strongly associated with atherosclerosis and serious cardiovascular events such as myocardial infarction and stroke⁴. Although statins have historically been the first-line treatment, they have

limitations, particularly in patients who fail to achieve LDL-C targets or who are intolerant of them. The arrival of new therapies, such as PCSK9 inhibitors and bempedoic acid, has brought new perspectives, but has also opened up discussions about their efficacy, cost-effectiveness and accessibility.³

PCSK9 inhibitors, such as alirocumab and evolocumab, have shown impressive efficacy in reducing LDL-C levels, with studies suggesting a reduction of up to 60% in some cases⁵.

In addition, data shows that these drugs are able to reduce cardiovascular events in high-risk patients, such as those with familial hypercholesterolemia or who have suffered previous events. However, the accessibility of these treatments is a crucial point. The high cost of PCSK9 inhibitors has limited their use in many health systems, especially in countries with fewer resources. While some experts argue that the cardiovascular benefit justifies the cost, there are concerns about their viability for widespread use³.

Another important advance in the treatment of dyslipidemia is bempedoic acid, a non-statin therapy that is gaining popularity. It is especially useful for patients who are intolerant of statins, offering additional LDL-C reduction with an acceptable safety profile⁶. Studies have shown that bempedoic acid reduces LDL-C levels by around 17-28%, which, although not as significant as PCSK9 inhibitors, is a valuable alternative in specific contexts.⁷

However, critics argue that its impact on reducing cardiovascular events still needs more robust long-term data. In the long term, its true effectiveness compared to more established therapies such as statins and PCSK9 inhibitors is still under debate.²

From the point of view of primary prevention of cardiovascular disease, the role of the latest generation of lipid-lowering therapies also raises questions. While statins are widely accepted as first-line treatment, especially in patients at high risk of cardiovascular events,

the use of PCSK9 inhibitors and bempedoic acid in primary prevention is less clear. There is evidence to suggest that PCSK9 inhibitors may benefit extremely high-risk individuals, but the benefits in moderate-risk populations are still controversial¹. In addition, the debate about the high cost of these therapies for use in primary prevention compared to statins remains a critical issue³.

In secondary prevention, however, there is a stronger consensus on the benefit of new lipid-lowering therapies. Patients who have already suffered cardiovascular events and fail to achieve LDL-C targets with statins and ezetimibe often benefit significantly from PCSK9 inhibitors⁹. The additional reduction in cardiovascular events in this population justifies, in many cases, the high cost of therapies⁴. However, some argue that the inclusion of low-risk patients in clinical trials can inflate the results and lead to more optimistic conclusions about the efficacy of these therapies than would be observed in routine clinical practice.⁵

Another point of discussion involves the long-term safety of these new therapies. Although initial studies of PCSK9 inhibitors and bempedoic acid have shown favorable safety profiles, with few serious side effects, the absence of very long-term safety data raises concerns. For example, there are fears about potential unknown effects that may arise with the continued use of these therapies over decades, especially considering that some of these drugs affect biological pathways that are not fully understood⁴.

Statins, on the other hand, have a well-documented history of safety and efficacy, which still positions them as the most reliable treatment.¹

Finally, the debate on the cost-effectiveness of these new therapies is fundamental. In countries with public health systems or limited resources, the feasibility of using PCSK9 inhibitors, for example, may be compromised due to high costs. Although the clinical bene-

fits are indisputable in high-risk populations, health economics needs to consider the financial impact of these therapies, especially when alternatives such as statins and ezetimibe are widely available and offer substantial benefits at lower costs⁶. This issue becomes even more pressing in countries with fewer resources, where inequalities in access to advanced therapies can exacerbate health disparities⁷.

Therefore, although state-of-the-art lipid-lowering therapies have undoubtedly expanded treatment options for patients with dyslipidemia, their impact on clinical practice should be assessed with caution⁸. The balance between efficacy, safety, accessibility and cost-effectiveness remains a challenge for health professionals and health policy managers. As more data emerges, these treatments are likely to take on an increasingly important role, but it will still take a concerted effort to ensure that these advances are available to the majority of patients who need them.²

CONCLUSION

Ethical and legal challenges in medical practice represent a dynamic and multifaceted scenario that requires constant reflection on the part of health professionals³. From issues related to informed consent and the fair distribution of resources to complex dilemmas about the end of life and technological development, medical practice is intrinsically linked to decisions that have significant ethical and legal implications.⁵

Therefore, it is essential that doctors commit themselves to the highest ethical standards, seek constant updates on legal issues and, above all, put the best interests of patients at the center of their decisions, thus promoting a clinical practice that prioritizes quality, safety and respect for the rights and dignity of each individual served.

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