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STATIN USE FOR PRIMARY PREVENTION IN THE ELDERLY WITHOUT ESTABLISHED CARDIOVASCULAR DISEASE: A LITERATURE REVIEW

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Abstract: Introduction: Statins, discovered in the 1970s by Akira Endo, revolutionized the treatment of cardiovascular diseases by inhibiting the enzyme HMG-CoA reductase, reducing LDL cholesterol levels. Its use has been consolidated in both primary and secondary prevention of cardiovascular events, and its pleiotropic effects, such as anti-inflammatory action and stabilization of atherosclerotic plaques, extend its clinical benefit. Despite its efficacy, its use in the elderly is still surrounded by doubts, especially regarding safety, adverse effects and real benefit in patients with greater frailty or multiple comorbidities. **Method:** A narrative literature review was carried out using the Virtual Health Library (VHL) and PUBMED databases. The descriptors "statin", "elderly", "primary prevention" and "cardiovascular disease" were used without initial restrictions. After applying inclusion criteria (full articles, free of charge, published in the last five years, in English or Portuguese) and exclusion criteria (undated articles, editorials, letters, PowerPoint presentations and unclear methodology), six articles were selected for analysis and synthesis. **Results and Discussion:** Analysis of the studies revealed that although the elderly are at increased risk of cardiovascular events, they often receive less treatment due to fear of adverse effects and doubts about the efficacy of statins in this age group. Recent literature shows that, with adequate monitoring , statins are also safe and effective in the elderly, with benefits observed in reducing heart attacks and mortality, even in people over 75. However, adverse effects such as muscle symptoms and liver changes, although generally mild, reinforce the need for individual assessment. Guidelines are still inconsistent for older people over 75, especially the very frail, making a personalized approach essential. **Conclusion:** The review shows that the use of statins for primary prevention in the elderly can bring benefits, but their indication should be cautious and individualized. More robust evidence is still needed to confirm their efficacy and safety in this group. Therefore, the use of statins is only recommended in patients with moderate to long life expectancy, taking into account comorbidities, frailty and patient preferences, always with careful medical monitoring.

INTRODUCTION

The discovery of statins began in the 1970s with Japanese biochemist Akira Endo, who, inspired by fungi and the need to combat heart disease caused by high cholesterol, searched for natural inhibitors of the enzyme HMG--CoA reductase, key in the synthesis of cholesterol. After analyzing thousands of strains of fungi, Endo isolated mevastatin (compactin) from *Penicillium citrinum*, demonstrating its effectiveness in reducing cholesterol in animal and human studies. Despite initial obstacles, such as Sankyo stopping the tests, the research paved the way for the development of other statins, such as Merck's lovastatin, approved in 1987, revolutionizing the treatment of cardiovascular diseases (AKIRA ENDO, 2010).

Statins are widely recognized for their effectiveness in preventing cardiovascular disease, both in primary and secondary prevention contexts. Clinical studies show that these drugs significantly reduce the risk of myocardial infarction, stroke and death from cardiovascular causes. In addition to lowering LDL-cholesterol levels, statins have pleiotropic effects, such as stabilizing atherosclerotic plaques and reducing inflammatory processes in the vascular endothelium. International guidelines recommend their use for adults with cardiovascular risk factors, even in the absence of previous events, due to their proven clinical benefit.

The main adverse events associated with the use of these drugs are myalgias, hepatotoxicity and drug interactions. Despite these

effects, serious complications are rare, which shows that statins are safe and effective interventions in reducing cardiovascular events in different populations (SANTIAGO, 2011).

METHOD

The study is a narrative review carried out in six stages: selection of the topic and elaboration of the research question; establishment of the inclusion and exclusion criteria for the search; evaluation and critical analysis of the included studies; analysis and synthesis of the included studies with interpretation of the results; and presentation of the review.

This article is a narrative review which aims to analyze the existing literature on the use of statins as primary prevention in elderly people without established cardiovascular disease. The search was conducted through the Regional Library of Medicine (BIREME) using the Virtual Health Library (VHL) and included databases such as PUBMED (National Library of Medicine).

Using the keywords "statin", "elderly", "primary prevention" and "cardiovascular disease" without restricting any criteria, 83 articles were found. When conducting the search, the inclusion criteria were: English and Portuguese languages, published in the last 5 years, complete and free articles and the exclusion criteria were: publications in PowerPoint (PPT), those without a date, editorials, letters to the reader, letters to the editor without case reports, articles with unclear methodology and publications that did not fit the desired focus. After applying the inclusion and exclusion criteria, 77 articles were excluded.

After excluding the aforementioned publications, we selected 6 scientific articles for analysis. Based on this selection, we classified, compiled and directed the articles according to the objectives of the final article. Subsequently, we synthesized the results found, taking into account the similarity of content.

RESULTS AND DISCUSSION

This article sought to analyze the literature's approach to the real evidence on the use of statins as primary prevention in elderly patients without established cardiovascular disease. Through a careful survey of the literature on the subject, it was possible to note that although the elderly have a high risk of cardiovascular events, they tend to receive less treatment for fears of adverse effects and uncertainty about efficacy. Recent studies, including meta-analyses, suggest that statins are just as safe and effective in this age group as in younger people, as long as they are used with proper monitoring. It is important to emphasize that advanced age alone should not be a barrier to the use of statins - the real limit would be the "futility" of treatment in very frail patients with low life expectancy, in whom the risks may outweigh the benefits (PERNA, 2021).

Among the adverse effects of statins were a modest increase in self-reported muscle symptoms, liver changes, mild kidney impairment and eye issues, but no significant increase in cases of diabetes or confirmed muscle disorders. Despite these adverse events, the benefits of statins in terms of reducing major cardiovascular events far outweighed the risks, confirming that the benefit-harm balance remains favorable, which does not justify the fear of prescribing statins in the elderly (Ting Cai et al., 2021).

In 2022, Maria Bergami et. al, investigated the effects of statin use on the primary prevention of cardiovascular events in elderly men and women with no previous history of cardiovascular disease. The results showed that the use of these drugs was associated with a significant reduction in the occurrence of ST--segment elevation myocardial infarction, as well as lower mortality after these events, both in individuals aged between 65 and 75 and those over 76. These benefits were observed

regardless of the presence of hyperlipidemia, although the effects were slightly less pronounced in younger women within the age range studied.

Wettermark et al. evaluated statin use in individuals aged 75-84 and concluded that, in general, doctors take cardiovascular risk into account when starting statin therapy in the elderly population, adhering well to the guidelines. Even so, there is evidence of under--treatment in older people at higher risk (especially women and ≥ 85 years) and possible overuse in low-risk individuals. These findings highlight the need for clinical adjustments to ensure that the benefit of statins is maximized in those who really need them, avoiding both the disadvantage of undertreatment and the unnecessary costs and side effects of overuse.

However, Nanna et. al point out that, up to the age of 75, data from meta-analyses and clinical trials show consistent benefits in reducing cardiovascular events. However, for individuals over this age, the evidence is limited and controversial, reflecting inconsistent guidelines on starting statins in this population, and more robust information is needed on efficacy and safety in this specific population. Thus, they emphasize the importance of an individualized approach, incorporating factors such as comorbidities, life expectancy, frailty and patient preferences.

Finally, according to Cobos et al, despite robust evidence in middle-aged adults, the efficacy of statins in primary prevention in the elderly is less clear due to changes in metabolism, polypharmacy, frailty, and a lower relative risk of cardiovascular events after the age of 70. Important concerns, such as myositis, increased risk of falls and possible adverse cognitive effects, are highlighted as factors that could compromise safety in this age group. On the other hand, the review recognizes that the prevention of serious atherosclerotic diseases can preserve the functionality and independence of elderly people with established cardiovascular diseases. Thus, like other studies cited, the authors conclude that the decision must be individualized, with a careful assessment of the balance between risk/benefit, taking into account comorbidities, life expectancy and frailty.

CONCLUSION

This literature review highlights the benefits and limitations of using statins in the elderly as primary prevention. The benefits are still questionable, as more robust evidence is still needed on the efficacy and safety of using these drugs in this population.

Therefore, the evidence currently available suggests that the benefits of the medication only begin to manifest after a few years of continued use, which reinforces the recommendation to consider this therapy only in individuals with moderate to long life expectancy and that before prescribing, the doctor should make a critical, careful and individualized assessment for each patient about the real benefit and possible risks.

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