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USE OF MONOCLONAL ANTIBODIES IN THE TREATMENT OF ALZHEIMER'S DISEASE: LITERATURE REVIEW

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Abstract: Introduction: Alzheimer's disease is a progressive neurodegenerative condition characterized by cognitive decline, functional impairment, and beta-amyloid accumulation in the brain. In recent decades, disease-modifying therapies aimed at amyloid removal have gained prominence, particularly monoclonal antibodies developed to slow the clinical progression of the disease. Recent studies, including narrative reviews, systematic reviews, and meta-analyses, have evaluated the efficacy, safety, and applicability of molecules such as aducanumab, lecanemab, and donanemab, seeking to understand whether reducing amyloid burden translates into significant clinical benefits and what the real impact of these treatments is in practice. **Method:** This study is a narrative review that analyzed the literature on the use of monoclonal antibodies in the treatment of Alzheimer's disease. Articles were selected from the BIREME, PubMed, and Cochrane databases using the keywords "monoclonal antibodies," "treatment," and "Alzheimer's." Inclusion criteria covered articles in English and Portuguese published in the last five years. Studies with unclear methodology or irrelevant to the topic were excluded. A total of five articles were selected and analyzed. **Results and Discussion:** The literature reviewed consistently demonstrates that anti-amyloid monoclonal antibodies can significantly reduce beta-amyloid deposition detected by imaging techniques, with modest but statistically significant effects on slowing cognitive and functional decline. Lecanemab and donanemab show the most robust results, with more reproducible benefits across studies, while aducanumab shows more limited and controversial efficacy. Despite these advances, the clinical effects remain modest and more evident in the early stages of the disease, which limits the universal applicability of these treatments. At the same time, the harms are considerable: events such as ARIA — which can range from asymptomatic findings to severe neurological complications — are frequent and require intensive monitoring. **Conclusion:** Monoclonal antibodies are a significant advance in the search for therapies modifying therapies for Alzheimer's disease, offering measurable clinical benefits and supporting the amyloid hypothesis. However, their effects remain modest, limited mainly to the early stages of the disease, and accompanied by significant risks and practical challenges that hinder their widespread adoption. The literature converges on the idea that, although promising, these treatments do not represent a definitive solution and should be seen as part of a broader therapeutic approach.

INTRODUCTION

The age pyramid in Brazil has undergone significant changes in recent years, highlighting the aging of the population. Along with population aging, the prevalence of senescence-related diseases such as coronary heart disease, neoplasms, musculoskeletal diseases, and dementia is increasing. The incidence of dementia syndromes increases proportionally with age and involves major mental, physical, and psychological disorders (YASSUDA et al., 2009).

Alzheimer's disease (AD) is a progressive and irreversible neurodegenerative disorder of onset insidious onset, which causes loss of and and incapacitation. In general, late-onset AD, with an incidence around 60 years of age, occurs randomly, while early--onset AD, with an incidence around 40 years of age, shows familial inheritance (SMI-

TH, 1999). In general, the first symptom is recent memory loss, while remote memories are preserved until a certain stage of the disease. In addition to other cognitive difficulties, such as attention, verbal fluency, and the ability to make calculations, disorders behavioral , such as aggression, hallucinations, hyperactivity, irritability, and depression (SERENIK; VITAL, 2008).

The most relevant neuropathological characteristics in AD patients are the presence of diffuse cortical atrophy, neurovascular degeneration, neuronal and synaptic losses involving various neurotransmission systems, the presence of extracellular senile plaques composed of filamentous aggregates of β-amyloid (Aβ) protein, and intracellular neurofibrillary masses, formed mainly by tau protein. Although healthy elderly individuals may also have these characteristics, the symptoms are not observed together or with the same intensity as in patients affected by AD (REY et al., 2016).

The treatment of AD involves pharmacological strategies and psychosocial interventions. In the pharmacological field, several psychoactive substances have been proposed to preserve or restore cognition, behavior, and functional abilities in patients with dementia. However, the effects of drugs currently approved for the treatment of AD are limited to slowing the natural progression of the disease, allowing only a temporary improvement in the patient's functional status (FORLENZA; ORESTES, 2005).

METHOD

The study is a narrative review conducted in six stages: selection of the theme and formulation of the research question; establishment of 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 that aims to analyze the existing literature on the benefits of monoclonal antibodies in the treatment of Alzheimer's disease. The research was conducted through the Regional Medical Library (BIREME) using the Virtual Health Library (VHL) and included databases such as PUBMED (National Library of Medicine) and Cochrane.

Using the keywords "monoclonal antibodies," "treatment," and "Alzheimer's," without any restrictions, 974 articles were found in the following databases: PubMed (n=973) and Cochrane (n=1). When conducting the search, the inclusion criteria were: languages in English and Portuguese, 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, 968 articles were excluded.

After excluding the aforementioned publications, we selected five scientific articles for analysis. Based on this selection, we classified, compiled, and directed the articles according to the objectives of constructing 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 actual evidence on the use of monoclonal antibodies in the treatment of Alzheimer's disease. Through a careful review of the literature on the subject, it is observed that anti-amyloid monoclonal antibodies represent an important advance in the treatment of Alzheimer's disease, as they demonstrate a consistent ability to reduce the burden of cerebral beta-amyloid and slow clinical progression, albeit modestly. However, the results of clinical trials show significant variations between molecules, with more robust benefits for lecanemab and donanemab, while other antibodies have limited efficacy. (CUMMINGS et al., 2024).

Based on the review presented by Vitek et al., 2024, it can be observed that lecanemab has stood out as one of the most promising disease-modifying therapies for Alzheimer's disease. The studies analyzed demonstrate that the drug consistently reduces cerebral amyloid burden and is associated with a modest but clinically relevant delay in the progression of cognitive and functional symptoms. However, clinical trials also reveal important limitations: although its efficacy is more consistent than that of previous antibodies, the benefits remain relatively small and concentrated in the early stages of the disease. Thus, although lecanemab represents a significant advance in Alzheimer's therapy, the evidence suggests that it is not a definitive solution, reinforcing the need for complementary strategies and broader therapeutic approaches to more effectively modify the course of the disease.

As mentioned, FDA-approved anti-beta-amyloid monoclonal antibodies represent a milestone in Alzheimer's disease-modifying therapy. However, the meta-analysis by WU et al., 2023, also reveals important limitations: the benefits observed, although significant, are modest and tend to be restricted to the early stages of the disease, which highlights the need for early diagnosis and careful selection of patients. In addition, adverse events such as ARIA (Amyloid-Related Imaging Abnormalities) remain a limiting factor, requiring rigorous monitoring and continuous follow-up, especially in individuals with a genetic predisposition. Thus, Wu et al. reinforce that, although anti-amyloid antibodies advance the understanding and management of Alzheimer's disease, they do not yet constitute a definitive solution, reinforcing the urgency of complementary therapeutic strategies, pharmacological combinations, and approaches that also consider inflammatory, synaptic, and tau-pathological aspects of the disease. On the other hand, the possible harms of these therapies must be carefully observed. The most relevant adverse event identified is ARIA, which encompasses cerebral edema and microhemorrhages or siderosis, with a high incidence in several trials, especially among carriers of the APOE4 allele. Although some cases are asymptomatic, many can progress to headache, confusion, seizures, and, in severe situations, substantial neurological risk. In addition, antibodies can cause infusion reactions, vascular events, and an overall increase in therapy-related hospitalizations. The harms tend to be more frequent and potentially more serious than the benefits provided, which should make researchers and prescribers question whether, in the real clinical context, the routine use of these drugs is justified for all patients. Thus, Ebell et al., 2024, argue that although there are measurable benefits, the associated risks are significant and may outweigh the advantages, reinforcing the need for extre-

me caution, rigorous selection of treatment candidates, and intensive monitoring throughout the period of use.

To reiterate, monoclonal antibodies that modify Alzheimer's disease represent an important advance because they act directly to reduce the burden of cerebral beta-amyloid and provide a measurable, albeit modest, slowdown in cognitive and functional progression, especially in the early stages of the disease. However, these benefits coexist with significant limitations, including a high incidence of ARIA — varying from asymptomatic asymptomatic to severe neurological events — in addition to infusion reactions, the need for intensive monitoring, high costs, and the requirement for specialized infrastructure for administration and follow-up. Thus, although these antibodies offer an intervention that goes beyond the merely symptomatic nature of traditional treatments, the risk-benefit ratio is still a matter of debate, and their clinical applicability must be carefully weighed against the potential harms and practical barriers associated with their use (XIAOMING QI et al., 2024).

CONCLUSION

This literature review reinforces that although monoclonal antibodies offer possible hope for modifying the course of Alzheimer's disease, the potential harms of the therapy must be considered, and therefore, prescribing the drug to all Alzheimer's patients is not justified.

Therefore, the evidence suggests that amyloid removal may have a measurable clinical impact, but the evidence also indicates that this strategy alone is not sufficient to broadly modify the course of the disease, pointing to the need for more integrated and multifactorial therapeutic approaches.

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