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ADVANCES IN THE TREATMENT OF ALZHEIMER'S DISEASE: CURRENT THERAPIES AND FUTURE PROSPECTS

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Abstract: Alzheimer's disease (AD) is the leading cause of dementia worldwide, characterized by the gradual decline of cognitive functions, with a significant impact on patients' quality of life. Although genetic factors, such as APOE-ε4, and modifiable factors, such as hypertension and obesity, influence the disease, age remains the main risk factor. The pathophysiology of AD involves the accumulation of abnormal proteins and an inflammatory process that results in neuronal damage and loss of cognitive functions. Current treatment is based mainly on pharmacological therapies, such as cholinesterase inhibitors and memantine, and non-pharmacological therapies, such as Cognitive-Behavioral Therapy (CBT). However, these treatments have limitations, and the search for therapeutic alternatives continues. The use of biomarkers, such as tau and Aβ levels, has shown potential for early diagnosis and monitoring disease progression, but disease-modifying therapy is still lacking. Psychological support for patients and caregivers also stands out as essential for improving quality of life and disease management.
Keywords: Alzheimer's disease, Pharmacological therapies, Non-pharmacological therapies, Biomarkers, Early diagnosis, Psychological support, Cognition, Quality of life.

INTRODUCTION

Alzheimer's disease (AD) is the leading cause of dementia worldwide, and its incidence has increased substantially as the elderly population grows. AD is characterized by a gradual decline in cognitive functions, mainly memory, judgment and language, with a direct impact on the functional capacity of affected individuals and their quality of life. Age is the greatest risk factor for developing the disease, although genetic factors, such as the APOE-ε4 genotype, and potentially modifiable conditions, such as hypertension, obesi-

ty and smoking, play a significant role in its manifestation. The amnesic form of the disease, which begins with episodic memory loss, is the most common presentation, but there are also non-amnesic forms, which can begin with behavioral changes or language difficulties, progressing to global cognitive impairment (KNAPSKOG et al., 2021).

The pathophysiology of Alzheimer's disease (AD) has been widely studied, and evidence indicates that neurological deficits begin years before the onset of characteristic clinical symptoms, evolving gradually and progressively. This insidious course often makes early identification of the disease difficult (KNAPSKOG et al., 2021). Studies show that AD compromises four amino neurotransmitter systems related to the N-methyl-D-aspartate (NMDA) receptor: serotoninergic, noradrenergic, histaminergic and cholinergic, the latter being the most affected due to the accumulation of abnormal proteins. The impairment of these systems results in reduced brain plasticity and loss of neurophysiological functions. In addition, the pathogenesis of the disease involves an intense inflammatory process, which contributes to oxidative stress and consequent neuronal damage (BOCWINSKA-KILUK et al., 2023).

Although there are still no treatments capable of modifying the course of the disease, studies show that interventions to reduce modifiable risk factors can prevent or delay up to 40% of dementia cases, which reinforces the importance of preventive measures during middle age. Early diagnosis is crucial to optimizing the therapeutic approach, and the use of biomarkers, combined with up-to--date diagnostic criteria, makes it possible to identify patients with atypical presentations of the disease. Such approaches are essential for appropriate, individualized treatment aimed at improving quality of life and slowing down the progression of AD. (DUBOIS et al., 2023)

Although pharmacological treatment is still limited, there is growing interest in non-pharmacological therapies, such as psychological interventions, which have shown potential to slow down the progression of the disease by focusing on patients' emotional well-being. Recent research highlights the importance of studying the biochemical aspects of AD, since interventions based on this knowledge can help to contain the progression of the disease. However, an effective treatment method that can consistently modify the underlying pathology of the disease has yet to be identified. (BEATA et al., 2023) Advancing the understanding of AD and exploring new therapeutic strategies remain important challenges in clinical practice and scientific research into the disease. (KNAPSKOG et al., 2021)

METHODOLOGY

The methodology adopted in this study consists of a bibliographic review of the most recent therapeutic approaches to the treatment of AD. To select the articles, a search was carried out in the PubMed database using the descriptors "Alzheimer's Disease" and "Treatment", focusing on publications from the last five years, in order to ensure that the information analyzed was the most up-to-date on the subject. The search was carried out in March 2025, and the inclusion criteria included complete articles, in English, dealing with the pharmacological and non-pharmacological treatment of AD, including clinical studies, reviews and reports of randomized controlled trials.

The exclusion criteria involved disregarding articles that did not meet the inclusion requirements, such as those that were not available in the PubMed database, as well as studies in languages other than English, articles that addressed only aspects unrelated to the treatment of AD or that were outside the five-year time frame. In addition, studies with

patient samples that did not represent cases of AD or that did not directly address current therapies or future treatment prospects were excluded.

The articles were selected by reading the title and abstract, following a criterion of relevance to the proposed topic. The full articles were then analyzed to ensure that the information was relevant to the discussion of Alzheimer's disease treatment. The entire search and selection process strictly followed the principles of transparency and reproducibility, allowing other researchers to replicate the methodology and the inclusion and exclusion criteria. The analysis and synthesis of the data found was carried out critically, with the aim of providing a current overview of the treatment of AD, highlighting both pharmacological therapies and new emerging therapeutic perspectives.

RESULTS AND DISCUSSION

The treatment of AD encompasses various therapeutic approaches, both pharmacological and non-pharmacological, with the aim of relieving symptoms and improving patients' quality of life. The symptomatic treatment currently available in the West includes two main groups of drugs: cholinesterase inhibitors and memantine. Cholinesterase inhibitors, such as rivastigmine, donepezil and galantamine, have shown clinical efficacy in early and moderate stages of AD, stabilizing or reducing changes in cognition, behaviour and general function. However, these drugs have common side effects, such as diarrhea, nausea, vomiting, dizziness and difficulty sleeping, and caution is needed in patients with cardiac disorders due to the risk of bradycardia. In cases of more advanced AD, when cholinesterase inhibitors are not effective or tolerated, memantine can be introduced as a therapeutic option, acting as an NMDA receptor antagonist and modulating the effects of glutamate. Although effective, the combination of both drugs is only recommended in exceptional cases, as indicated by national dementia guidelines (KNAPSKOG et al., 2021).

Non-pharmacological therapies play a fundamental role in the management of various clinical conditions. Among them, Cognitive--Behavioral Therapy (CBT) stands out as one of the most widely used. This approach aims to integrate the patient's daily life into the therapeutic process, promoting their physical and mental permanence in the present. The effectiveness of CBT stems from its ability to stimulate different brain areas in an integrated way, activating memories associated with the five senses. To do this, simple resources are used, such as notes scattered around the room, photographs, olfactory stimuli (smells and perfumes), music, variations in texture, among others. In addition, this intervention can be applied in different contexts, as long as the patient has some previous familiarity with the place, which contributes to their adaptation and engagement in the treatment. (BOCWINSKA-KILUK et al., 2023)

However, the effectiveness of these treatments remains limited, especially in advanced stages of the disease, and there is no robust evidence to prove their ability to slow the progression of dementia or treat mild cognitive impairment. In addition, the response to treatments can vary between patients, and side effects often compromise adherence to the therapeutic regimen, requiring constant adjustments to the approach. In this context, the search for more effective and long-lasting therapeutic alternatives remains an area of intense research. Biomarkers, such as tau and Aβ levels in cerebrospinal fluid (CSF), have shown promise for early diagnosis and for assessing disease progression, although biomarker-based therapeutic solutions that can significantly alter the course of AD are still lacking (DUBOIS et al., 2023).

From a psychological point of view, AD brings significant challenges for both patients and their caregivers. Early detection of the disease, although crucial, can generate psychological complications, as patients often face an exacerbation of emotional symptoms, such as depression, anxiety and social withdrawal, soon after diagnosis. Studies indicate that a considerable number of patients show signs of depression and suicidal thoughts up to two years before diagnosis, and symptoms such as hallucinations, paranoia and delusions develop rapidly after the diagnosis is confirmed. Patients' emotional response to the progressive loss of cognitive and functional abilities can be accentuated by the lack of effective treatment, which makes psychological support crucial. In addition, the impact of the disease on caregivers, who often deal with emotional exhaustion, also needs to be recognized, as caregiving dynamics can affect both the patient's and the caregiver's quality of life. (BEATA et al., 2023) Psychological support, therefore, is an essential part of AD management, and health policies should consider implementing support programs for both patients and caregivers.

With regard to biomarkers, research has advanced significantly, with emphasis on CSF biomarkers, which allow the early detection of Aβ and tau peptides, indicating neuronal death. These biomarkers can provide valuable information on the pathology of AD, especially in its atypical forms, and are more effective than neuroimaging biomarkers in the early stages of the disease. (DUBOIS et al., 2023) Although these biomarkers have not yet been widely incorporated into clinical practice, they offer a promising vision for the early diagnosis and monitoring of the progression of AD.

The diagnosis of AD was for a long time based solely on clinical criteria; however, with advances in the study of biomarkers, these are now recognized by current guidelines as an important diagnostic aid. The "ATN" research by the National Institute on Aging and Alzheimer's Association (NIA-AA) proposes a neuropathological diagnosis of AD, regardless of the presence of cognitive symptoms, based on three main findings: amyloid abnormalities (A), alterations in the tau protein (T) and evidence of neurodegeneration (N). However, the research concludes that although it is possible to visualize the presence of AD pathology in the brain, this alone is not sufficient for the diagnosis of the clinical pathological syndrome of the disease, which implies that these guidelines should be used for research purposes, and not for clinical diagnosis. Therefore, although biomarkers are not conclusive for the diagnosis of AD, they are valuable tools for supplementing the patient's assessment and confirming the diagnostic hypothesis.

Positive amyloid PET scans, although relevant, are not necessarily associated with the presence of the disease in the brain, since up to 35% of patients with a clinical diagnosis of AD show negative results in this test. On the other hand, when positive, amyloid PET indicates a high risk of developing the disease and suggests faster progression. It is estimated that between 44% and 74% of patients without a diagnosis of AD, but with a positive PET scan, will develop the disease throughout their lives. In this context, the importance of clinical assessment in conjunction with biomarkers is clear, since a diagnosis based solely on these tests can be harmful to the patient, who may never manifest the disease.

Therefore, the therapeutic approach to Alzheimer's disease remains challenging, with limited progress in the pharmacological options available and the need to improve psychological support for both patients and caregivers. Advances in biomarkers open up new possibilities for early diagnosis and potentially more effective treatments in the future, but there is still much to be done to optimize therapeutic options and improve the quality of life of those affected by the disease.

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CONCLUSION

The treatment of Alzheimer's disease still presents significant challenges, with pharmacological therapies limited in their ability to modify the course of the disease. Current therapeutic approaches, both pharmacological and non-pharmacological, aim to alleviate symptoms and improve patients' quality of life, but the effectiveness of these interventions is restricted, especially in advanced stages of the disease. Research into biomarkers offers new perspectives for the early diagnosis and monitoring of the progression of AD, although there is still a need to develop more effective treatments to slow down or modify the course of the disease. In addition, psychological support for both patients and their caregivers is fundamental to the management of AD, and health policies should incorporate these needs into treatment. Therefore, although progress has been made in understanding and diagnosing AD, the search for therapies that modify the underlying pathology remains a priority in research and clinical practice.

REFERENCES

BEATA, B.-K. et al. Alzheimer's Disease—Biochemical and Psychological Background for Diagnosis and Treatment. **International Journal of Molecular Sciences**, v. 24, n. 2, p. 1059, 5 jan. 2023.

DUBOIS, B. et al. Biomarkers in Alzheimer's disease: role in early and differential diagnosis and recognition of atypical variants. **Alzheimer's Research & Therapy**, v. 15, n. 1, p. 175, 13 out. 2023.

KNAPSKOG, A.-B. et al. Alzheimers sykdom – diagnostikk og behandling. **Tidsskrift for Den norske legeforening**, 2021.