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The Study of Public Health Policies for Alzheimer's Disease Based on the Pathogenesis

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Abstract:

In the current social context, the increasing aging population has led to a rising incidence of Alzheimer's disease (AD). Today's research primarily focuses on the development of new drugs for AD, exploration of its causes, and the formulation of reasonable policies for AD patients. As of now, there is still no curative drug available for AD. This article mainly analyzes the pathogenesis of AD, discussing its causes, symptoms, diagnostic methods, corresponding public strategies, measures, and care aspects, providing insights for the development of public health policies related to AD. Through this article, people can gain a better understanding of the mechanisms and pathology of AD, as well as the methods and policies for addressing it, while also recognizing the importance of improving public health policies for AD. It offers a general research direction for future studies, particularly concerning unresolved issues related to AD medications. It is hoped that future research will make further progress in developing new drugs specifically for AD.

Keywords: Alzheimer's disease; pathogenesis; public health policy.

1. Introduction

Alzheimer's disease (AD), commonly referred to as senile dementia, is a prevalent degenerative neurological disorder among the elderly population. It denotes a persistent impairment of neurologic function and activity, characterized by distinctive pathological features such as β-amyloid protein deposition and neurofibrillary tangles. In China, the prevalence of dementia has shown a significant increase with age: 8.26% among those aged 75 and above, rising to 11.4% among those aged 80 and above. Women are more affected by dementia than men, with females over 60 years old experiencing dementia at rates typically 2 to 3 times higher than their male counterparts. Globally, the World Health Organization (WHO) estimates that by 2020, the population aged 60 and above will reach 1 billion, and by 2050, it will double to 2.1 billion, with two-thirds residing in low- and middle-income countries. During the same period, the population aged 80 and above is expected to double to 426 million. These statistics underscore the urgent need for improved medical interventions

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and the implementation of relevant public health policies.
While effective treatments for AD remain elusive, ongoing research continues to yield new advancements in this field. Recent Aβ-immunotherapy trials have provided the first definitive evidence that eliminating aggregated Aβ from the brains of symptomatic patients can slow the progression of AD. Although the clinical benefits observed in these trials have been modest, they underscore the necessity for a more profound comprehension of disease mechanisms and the importance of early intervention in the pathogenic cascade. [1] Beyond Aβ immunotherapy, nanoparticles (NPs) offer promising support in drug delivery. NPs, sized between 1-100 nm, possess several advantages including enhanced biocompatibility, extended half-life, the capacity to transport large molecules, the ability to cross the blood-brain barrier (BBB) to reach the central nervous system, and superior targeting capabilities. Furthermore, NPs showcase excellent diagnostic potential. Multifunctional NPs can integrate diagnostic, targeting, and therapeutic advantages, offering a holistic approach to disease management. [2]
This paper will conduct some research on the pathology, mechanism, diagnosis and treatment of AD, and spread it to public health policies for AD. The aim is to popularize knowledge about AD, let more people understand it, and propose some suggestions for public health policies, urging the implementation of government policies and creating a better environment for all Alzheimer‘s patients and their caregivers.

2. Pathogenesis of Alzheimer’s Disease

Up to now, it is still unclear how AD develops, and its causes are diverse and interrelated, involving multiple levels. Among all the hypotheses related to the pathogenesis of AD, the following hypotheses are widely accepted:

2.1 Hypothesis of β-amyloid Protein Cascade

The cascade hypothesis of β - amyloid protein (A-β) is currently the most popular theory in the pathogenesis of AD. The reason for this is that soluble peptides produced by the continuous hydrolysis of A-β precursor protein (APP) by two secreted enzymes aggregate and precipitate in the cytoplasmic matrix, and such soluble oligomers are believed to be the main culprit of neurotoxicity and ultimately cognitive dysfunction. Research has shown that A-β oligomers can be divided into various forms, among which dodecamers have been found to be one of the oligomers that can significantly affect brain function.
ApoE plays an important role in the occurrence and development of AD. The apolipoprotein E (ApoE) ε 4 gene is currently the only recognized AD risk gene. The frequency of carrying the APOE ε 4 allele in sporadic AD patients is 40%. People carrying one APOE ε 4 allele have a 3-4 times higher risk of AD than non APOE ε 4 individuals, while those carrying two APOE ε 4 alleles have a 12 times higher risk of AD than non APOE ε 4 individuals.

2.2 Tau Protein Hypothesis

Neurofibrillar tangles are one of the two major pathological manifestations of AD, mainly composed of hyperphosphorylated tau protein. The content of hyperphosphorylated tau protein is significantly increased in AD patients. Overphosphorylation of tau protein leads to normal microtubule depolymerization, and abnormally hyperphosphorylated tau protein can also self aggregate into neurofibrillary tangles, subsequently causing dendritic microtubule loss, synaptic dysfunction, and cell death. The tau protein can also be released by neurons into the extracellular space and subsequently taken up by neighboring neurons. This process can lead to abnormal phosphorylation of tau protein in other neurons, facilitating its spread between cells and highlighting tau’s significant role in AD progression. According to the amyloid cascade hypothesis, tau protein acts as a downstream effect of Aβ toxicity. Numerous in vitro studies have demonstrated that Aβ can trigger excessive phosphorylation of tau protein.

3. Diagnosis of AD

Currently, the only definitive method to diagnose AD is through a post-mortem examination of brain tissue, which can confirm the presence of AD or other forms of dementia [3]. However, this approach is not feasible while the patient is alive. Thus, the diagnosis of AD necessitates both clinical and pathological evidence. Consequently, a prenatal diagnosis can only indicate a ‘possible AD’ rather than a definitive one. There are currently three commonly used diagnostic criteria for AD: DSM-IV-R criteria developed by the National Psychiatric Association in 1994. Diagnostic criteria of the WHO International Classification of Diseases (ICD-10) in 1992. National Institute of Neurology, Language Disorders, and Stroke AD and Roll over Disease (NINCDS-ADRDA) criteria.
1) Electroencephalograms can show normal or non-specific diffuse slow waves, with slower alpha wave rhythms and lower wave amplitudes, and even disappear in severe disease. Generally speaking, there is a correlation between the degree of EEG changes and the degree of intellectual impairment in patients.
2) CT head CT mainly shows brain atrophy. The gray matter of the brain generally shrinks, manifested as an increase and deepening of sulci in both hemispheres, widening of brain fissures, and atrophy of the temporal

lobe (mainly the middle temporal gyrus), manifested as an increase and deepening of sulci in the temporal lobe, narrowing of the middle temporal gyrus, widening of the suprasellar and annular ventricles, enlargement of the temporal horn of the lateral ventricle, and white matter atrophy mainly manifested by enlargement of the third ventricle and the body of the lateral ventricle.

3) Magnetic resonance imaging (MRI) offers unparalleled soft tissue contrast resolution among medical imaging techniques, enabling precise differentiation of gray and white matter within the brain. It is notably effective in illustrating brain atrophy or ventricular enlargement with greater sensitivity and clarity than computed tomography (CT). MRI's capability to measure the volumes of critical brain structures, such as the temporal lobe, hippocampus, and amygdala, holds significant potential for the early diagnosis of AD.

4. Treatments for AD

AD is the most prevalent neurodegenerative disorder globally and regrettably remains without an effective cure. However, various medications can help mitigate memory symptoms and other cognitive impairments associated with AD. Below are the primary types of drugs currently used in AD treatment.

4.1 Acetylcholinesterase inhibitors (AchEIs)

Due to the deficit in cholinergic neurotransmission seen in AD, cholinesterase inhibitors are deployed as first-line treatments. These agents help by retaining acetylcholine, a chemical messenger that is often depleted in AD patients. Clinical benefits include improved cognition, functional stabilization, and moderated behavioral symptoms. Most patients experience a degree of symptomatic relief. These medications are available both orally and as transdermal patches. Common AchEIs include Aricept, Adlarity, Razadyne, and Exelon patches. While these drugs can significantly improve quality of life, they come with potential side effects such as diarrhea, nausea, loss of appetite, and sleep disturbances [4]. Patients with certain heart conditions like arrhythmia may face more severe risks.

4.2 Namenda

Memantine is utilized for patients with moderate-to-severe AD. It functions as an NMDA receptor antagonist, protecting neurons from excessive glutamate, a neurotransmitter that can cause significant neuronal damage when present in high concentrations. Memantine is often combined with AchEIs to provide a more comprehensive treatment strategy [5]. It slows symptom progression and is particularly beneficial for maintaining daily functions. Common side effects are relatively rare but can include dizziness and confusion.

4.3 Leqembi and Kisunla

The FDA has approved Leqembi and Kisunla for individuals with mild AD or mild cognitive impairment due to AD. Clinical trials have shown that these drugs can decelerate cognitive and functional decline in the early stages of AD by inhibiting the formation of amyloid plaques in the brain. Despite their benefits, these treatments come with risks [6,7]. For instance, while most adverse reactions to lecanemab (an active ingredient) are asymptomatic, some patients can experience severe or even fatal microhemorrhages and rare macrohemorrhages. Those on anticoagulants are especially at risk and should avoid these medications until more interaction data becomes available [8].

5. Public Policies to Address Alzheimer's Disease

With advancements in national policies, China has made notable progress in the prevention and control of AD. The "Policy Recommendations" document provides a comprehensive overview of the current state of AD, offering detailed data and summarizing challenges faced in efforts to combat this disease. The policy highlights strategies for early diagnosis, effective treatment plans, and long-term care solutions, reinforcing the importance of government support in tackling AD.

Firstly, as the most common cause of dementia, the disease burden and social issues caused by AD are becoming increasingly prominent. According to projections, the number of elderly people over 80 in China will reach 130 million by 2050, quadrupling the number of elderly people in 2020. The increasing number of elderly individuals will further escalate the number of AD patients.

Secondly, the burden on society and families is growing. Patients with AD often require treatment and care for several years, sometimes even decades, resulting in enormous costs borne by families and society. Data show that the cost of long-term care is mostly shouldered by families alone; caregivers typically need to sacrifice about 47 hours of work each week (equivalent to six working days) to look after patients, leading to significant direct and indirect costs such as lost working hours. The unique "421" family structure in China has caused increasing pressure on family members, who often feel overwhelmed and are negatively affected in terms of their willingness to work and have children.

It is noteworthy that the current diagnosis rates for pa-

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tients with mild and severe dementia in our country are only 14% and 34%, respectively, with 49% of cases misdiagnosed as natural aging, missing the early intervention period.

At the same time, treatment for the disease has numerous unmet needs. Currently, only five drugs have been approved to treat AD in China, and these drugs can only short-term control the symptoms without slowing disease progression. The long-term lack of drugs targeting clear pathological mechanisms makes it difficult to effectively treat and manage the disease. The clinical setting continues to face objective issues such as "scarcity of precise diagnostic and treatment methods, and lack of doctors and medicines," severely hindering the prevention and control of AD.

During this period, the social security mechanism needs to be further improved. Currently, outside of a few pilot cities, there are no relevant systems in place to support the costs of patients' medication and daily care. Relevant social organizations also face a series of problems, including limited professional capabilities, narrow coverage, and uneven development of elderly care services.

To this end, the "Policy Recommendations" put forward five suggestions to help improve China's prevention and control system for AD. These include formulating a national strategy and action plan for AD that aligns with China's national conditions; promoting early screening and diagnosis of the disease to capture the golden window period; clarifying diagnostic and treatment standards to enhance medical quality; promoting the research and market launch of drugs targeting specific pathological mechanisms; and establishing a comprehensive social security ecosystem to alleviate the living pressures on patients and families.

The social work community is actively seeking progress in the face of this dilemma [9]. Furthermore, it is suggested that community-based early screening for AD be included in the annual health check-ups for individuals over 55 years old; in workplaces, it could be considered to add AD screening during annual check-ups for individuals over 40. Effective AD care necessitates timely diagnosis and a multidisciplinary management approach. The evaluation process includes taking a detailed history from both the patient and caregivers, reviewing symptoms and functional status, and conducting comprehensive examinations and tests (including laboratory tests and neuroimaging). This thorough assessment helps to identify the level of impairment, characterize the cognitive-behavioral syndrome, and determine the underlying cause [10].

6. Conclusion

The article begins by discussing the pathogenesis of AD, including its causes, symptoms, diagnostic methods, corresponding public strategies, measures, and care. This article provides a better understanding of the mechanisms and pathology of AD, as well as the methods and policies for addressing it. It also highlights the urgent need for improved public health policies related to AD. Additionally, the article provides feasible references for the development of reasonable public policies in future research. Due to the limitations of the article, it does not delve deeply into the pathology of AD, and the diagnostic and treatment methods discussed are not comprehensive. It is hoped that future research will focus on the development of medications for treating AD, leading to the design of more complete public policies that genuinely address the needs of every AD patient.

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