Analysis on the Pathogenesis and Nursing of Alzheimer's Disease

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ABSTRACT: Alzheimer's disease is a neurodegenerative disease that occurs mainly in the elderly population, and as medical advances and human lifespan grows, the impact of Alzheimer's disease on the quality of human life is gradually expanding. This paper mainly discusses the Pathogenesis and the patients' nursing issues of Alzheimer's disease, hoping to help people understand more about the Alzheimer's disease and get to grips with the treatment and care available to alleviate the impact of Alzheimer's disease on patients' life.

1. INTRODUCTION

Alzheimer's disease (AD) is a degenerative neurological disease characterized by the impairment of cognitive skills, memory, learning ability, and the impact of AD is also gradually increasing, with statistics now showing that around 50 million people worldwide have Alzheimer's disease or other similar symptoms, also affecting over 35 million people worldwide [1]. Research has not yet identified the specific principles of the disease but has identified a part of the pathogenesis. Among these, the main roles are played by extracellular deposits of β-amyloid protein (Aβ) forming senile plaque (SP) and neurofibrillary tangles (NFTs) caused by highly phosphorylated aggregates of Tau protein [2]. This paper aims to raise awareness of Alzheimer's disease, so that early recognition and appropriate treatment can be provided to reduce the impact of Alzheimer's disease on life and to understand how to effectively care for the disease after its onset.

2. PATHOGENESIS OF ALZHEIMER'S DISEASE

2.1. Alzheimer's disease and Aβ

Studies have indicated that Aβ, which is formed by the hydrolysis of amyloid precursor protein (APP), is one of the major causes of Alzheimer's disease. With the deposition of Aβ, neurons are destroyed, resulting in memory and cognitive impairment, it will disrupt intracellular Ca2+ homeostasis, promoting the formation of free radicals, disrupting neuronal loops, enhancing inflammatory responses caused by inflammatory cytokines, causing chronic inflammation to act at various stages of AD, leading to neuronal cell death, and so on. As

a result, removing Aβ deposition is a key technique in the prevention and treatment of Alzheimer's disease.

2.2. Alzheimer's disease and Tau protein

Tau protein hyperphosphorylation, in addition to Aβ buildup, is a key component in Alzheimer's disease. Tau protein is a microtubule-associated protein that detaches from microtubules and aggregates, resulting in cognitive deficits in Alzheimer's disease [3].

2.3. Alzheimer's disease and the inflammatory response

The inflammatory response, which is primarily mediated by microglia and astrocytes, is one of the body's defense mechanisms. The inflammatory response maintains nerve homeostasis by eliminating chemicals from the nervous system that could injure nerve cells as quickly as possible. However, it has been discovered that a prolonged inflammatory response can produce neuronal damage as a result of the release of inflammatory agents and oxidative reactive substances from microglia, which affects the clearance of Aβ, resulting in neuronal damage [4]. As a result, finding a remedy to uncover the reason of abnormal microglia activation and a technique to suppress the microglia is one of the top therapy priorities for Alzheimer's disease.

3. TREATMENT FOR ALZHEIMER'S DISEASE

At present, there is no cure for Alzheimer's disease and only certain treatments can be used to slow down the process. The reasons for the difficulty in treating Alzheimer's disease are that the pathogenesis is not understood, damaged neurons are difficult to restore or regenerate, and the current drugs are based on a partial

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mechanism, whereas Alzheimer's disease is caused by a combination of factors.

3.1. Cholinergic drugs

Acetylcholine (ACh) is an excitatory neurotransmitter that is important for brain activity, and its levels have been found to influence AD in studies of AD. Most of the drugs currently used to treat AD are based on this mechanism, galantamine, rivastigmine, tacrine, and donepezil [5]. These drugs are cholinesterase inhibitors, which work by inhibiting acetylcholinesterase to reduce acetylcholine hydrolysis, thereby increasing acetylcholine levels and enhancing neurotransmission, ultimately helping patients to slow the onset of AD and improve their cognitive performance.

3.2. Aβ Drug Research

As research has progressed, the accumulation of A is now considered to be one of the most important pathological symptoms of AD and, as a result, research into drugs in this area is widespread, although still inconclusive, with current research falling into three main directions.

3.2.1 Inhibition of Aβ production

Inhibition of Aβ production is mainly through inhibition of β- and γ-secretase activity, however, due to the potential for most of these drugs to be ineffective or potentially dangerous, this aspect of the study is usually discontinued before or during clinical trials. For example, Merck's Verubacestat, which was the first β-secretase inhibitor to enter clinical phase III, however, after a period of trials, it was found to be less effective in Alzheimer's disease and was discontinued in 2017 [6]. Elenbecestat, a BACE-1 inhibitor developed by Eisai, is primarily used for the prevention of Alzheimer's disease and the treatment of pre-AD, and had entered Phase III clinical trials, but the development of the product was subsequently halted as a result of a safety review conducted by the Data Safety Monitoring Board [7].

3.2.2. Aβ antibody

This method involves the body acquiring the ability to clear Aβ by certain means, one being active immunotherapy, where the body can clear Aβ itself by inoculating it with Aβ antigens, however, this method can also cause the body to attack undeposited Aβ, leading to a direct attack on the brain and causing adverse reactions. Most studies using this approach have therefore been discontinued. Another type of passive immunotherapy, in which Aβ is cleared by injection of human-derived Aβ antibodies, allows the amount of Aβ cleared to be controlled, thus avoiding overly severe immunological consequences. There are already 4 drugs in development in this area: gantenerumab, crenezumab, ponezumab, and GSK933776A [8].

3.2.3. Aβ receptor antagonists

This approach avoids damage to nerve cells by binding to the receptor and preventing it from binding to too much Aβ. There are already drugs in phase III clinical trials: Soli's TTP-488 for mild AD, a RAGE receptor antagonist, prevents the neurotoxicity caused by RAGE-Aβ interactions [9].

3.3. Tau protein drug research

Another hallmark pathological feature of AD is Tau protein hyperphosphorylation, which plays an important role in microtubule stability. Tau protein is a microtubule-associated protein that normally binds to microtubules and enhances microtubule stability. When Tau is hyperphosphorylated, it detaches from microtubules and aggregates, forming NFTs, which can lead to cognitive deficits in AD and microtubule instability. The main drugs available in this area are reduction of tau hyperphosphorylation, inhibition of tau aggregation, microtubule stabilization, and immunotherapy.

The drug is based on the mechanism of inhibition of tau protein aggregation and was suspended in preliminary experiments due to the insignificant effects and adverse reactions, but in subsequent studies, a lower level of LMTX was used and effective results were obtained. The drug was granted FDA status for the treatment of frontotemporal dementia with the drug LMTX for rare diseases in 2019 [10].

Drugs based on different principles are still being researched, such as ACI-35, which is in Phase I clinical trials and is being evaluated by Janssen, and is based mostly on the immunological principle, which works by making the body actively immune to eliminate isoforms of the Tau protein [11].

3.4. Drugs related to inflammatory response

Inhibiting the inflammatory response caused by aberrant microglia activation could be useful in the treatment of Alzheimer's disease. Nonsteroidal anti-inflammatory medicines (NSAIDs), a type of anti-inflammatory drug, have been demonstrated to be more successful in the treatment of Alzheimer's disease (AD), however they have drawbacks in that they are only beneficial until the patient exhibits cognitive impairment [8]. As a result, anti-inflammation medications are being developed for different phases of Alzheimer's disease. Chiesi, for example, is working on Itanapraced, a medicine that modulates microglia, lowering inflammation and increasing patient cognition. It is currently in Phase II clinical trials [12].

Furthermore, it has been shown that, in addition to the inflammatory response in the brain, long-term peripheral inflammation has a role in the development of Alzheimer's disease, suggesting that research into the therapy of peripheral inflammation could help with the treatment of AD [13].

4. HEALTHCARE METHODS

There is currently no cure for Alzheimer's disease, so caring for the patient is part of the daily routine. AD care is therefore extremely important, and there is also experimental evidence that effective care can have some alleviating effect on the symptoms of Alzheimer's disease.

Affectionate care combined with psychological care is an effective method of care, using the creation of patient files and taking part in courses or videos to help patients and families understand the condition so that patients and families have a better understanding of the condition and can take appropriate care. At the same time, active attention is paid to the patient's psychology to reduce anxiety about the illness and to maintain a good state of mind. For this type of care, a study found that comparing the observation group with the control group. The health status of the observation group was higher than that of the control group ((P values were < 0.05) (See Table 1), so this nursing method is effective for AD patients and can help relieve symptoms and improve the quality of life of patients [14].

Table 1. Comparison of health status scores between the two1 groups (x ± s, points)[14]

Group	n	Physiological level	Spiritual level	Social functions	Emotional
Observation group	45	93. 32 ± 1. 55	95. 81 ± 1. 75	93. 22 ± 1. 79	95. 81 ± 1. 65
Control group	45	74. 17 ± 1. 88	72. 65 ± 1. 14	74. 65 ± 1. 65	72. 32 ± 1. 68
T-value		52. 722	74. 387	51. 170	64. 069
P-value		< 0. 001	< 0. 001	< 0. 001	< 0. 001

5. CONCLUSION

This paper focuses on the pathogenesis, the current progress in Alzheimer's disease and the care that patients need to help patients and their families understand and care for AD. Because the mechanisms of Alzheimer's disease are complex and research is complicated, this paper only describes a portion of the disease, and research will need to be expanded. In the study of AD, it is now known that the disease is formed by a combination of many complex mechanisms, but in the current research process, it is often studied on a single pathway, probably because the current research progress does not understand how these pathological mechanisms and interactions form AD, but multi-target drug research may also be a research direction, and for the role of drug research, also could verify whether some pathological symptoms are the underlying cause of Alzheimer's disease occurrence.

AUTHORS' CONTRIBUTIONS

This paper is independently completed by Yuehan Wang.

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