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Application and Research Progress of Moxibustion Therapy in the Care of Patients with Alzheimer's Disease

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Abstract: With the intensification of aging, the number of patients with Alzheimer's disease (AD) in China has increased, which has brought a heavy burden to families and society. However, there is currently a lack of specific curative drugs for AD and commonly used clinical drugs can only relieve symptoms while accompanied by adverse reactions. Traditional Chinese medicine nursing techniques have unique advantages in the treatment of AD. Moxibustion therapy can improve cognitive function and improve living ability by stimulating acupoints with warmth. Therefore, this article summarizes the research progress of moxibustion therapy in the treatment of AD from the understanding of AD in traditional Chinese and Western medicine, an overview of moxibustion therapy, the mechanism of moxibustion therapy in the treatment of AD, and the clinical application of moxibustion therapy in the treatment of AD. It is hoped to provide a reference for the application of moxibustion therapy in AD patients.

Keywords: Alzheimer's disease; Moxibustion therapy; Review

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1. Introduction

According to the 2020 census data, China's population aged 65 and over accounts for 13.5%, making it the country with the largest elderly population. It is estimated that by 2035, the population aged 60 and over will exceed 400 million, accounting for over 30%, indicating that China is about to enter a stage of deep aging [1]. The rapidly aging population has brought increasing attention to issues affecting the elderly, with dementia emerging as a major health and social concern. Now recognized as the seventh leading cause of death, dementia poses a serious threat to the health and quality of life of older adults [2]. Alzheimer's disease (AD) is the main type, accounting for 60%–80% of all types of dementia. Research statistics show that there are about 15.07 million AD patients in China and it is estimated that there will be 28.98 million dementia patients by 2050 [3]. AD patients suffer from

varying degrees of cognitive impairment, which severely affects their daily life and social functioning [4]. The most common causes of death are complications such as lung infections and heart failure, and the risk of wandering and accidents caused by cognitive decline also increases [5]. Additionally, the cost of AD treatment is rising year by year, with an estimated cost of $1,887.18 billion by 2050, posing a heavy burden on families and society [6]. However, there is currently no specific medication for AD, and commonly used clinical medications can only alleviate symptoms but cannot prevent disease progression. Moreover, adverse reactions such as nausea, vomiting, and sleep disorders caused by these medications severely affect patient compliance [7]. In recent years, traditional Chinese medicine nursing techniques have received widespread attention. Studies have shown that moxibustion has a definite effect on dementia recovery through warm stimulation of acupuncture points, which is superior to acupuncture and Western medicine in some ways [8]. This article focuses on the understanding of AD in both Western and traditional Chinese medicine, an overview of moxibustion therapy, the mechanism of moxibustion in treating AD, and clinical application research. It summarizes the research progress of moxibustion therapy in the treatment of AD, providing a basis for clinical healthcare workers in the prevention and treatment of AD.

2. Understanding of Alzheimer's disease in Western and traditional Chinese medicine

Western medicine views Alzheimer's disease as a common degenerative disease of the central nervous system in the elderly, mainly characterized by decreased learning and memory abilities aa well as cognitive dysfunction [9]. The pathogenesis of AD is complex, and the main clinical theories include the β-amyloid (Aβ) cascade hypothesis, Tau protein abnormality hypothesis, inflammation and immune mechanism hypothesis, and neurotransmitter imbalance. AD can be divided into three stages according to disease progression: pre-clinical AD, AD-derived mild cognitive impairment (MCI), and AD-derived dementia [10]. The newly revised AD diagnosis guidelines by the National Institute on Aging and the Alzheimer's Association (NIA-AA) divide AD into four biological stages based on biomarker staging: A, B, C, and D, representing the early, early-stage, mid-stage, and late-stage of the disease, respectively [11].

The clinical symptoms are also staged into 0 to 6 stages based on the severity of cognitive impairment. Stage 0 indicates the presence of pathogenic genes associated with familial Alzheimer's disease (AD) without any core AD biomarkers or clinical symptoms. Stage 1 is characterized by abnormal core biomarkers but no evident symptoms. Stage 2 builds on Stage 1, with patients possibly experiencing subjective cognitive decline and emotional changes. Both Stage 1 and Stage 2 are classified as the pre-clinical stage of AD. Stage 3 represents the pre-dementia stage, marked by mild cognitive impairment (MCI) without impairment of daily living activities. Stages 4, 5, and 6 correspond to mild, moderate, and severe dementia, respectively, reflecting progressive deterioration in cognitive and functional abilities [12]. However, current clinical diagnosis of AD lacks sensitivity in early stages, and the new guidelines are significant in this regard.

In traditional Chinese medicine, Alzheimer's disease falls under the category of "dementia" or "idiocy". Early records can be found in the "Jingyue Quanshu" by Zhang during the Ming Dynasty, which states that "dementia is related to phlegm-dampness stagnation" while in the "Shishi Milu" by Chen during the Qing Dynasty, points out that "the strongest phlegm-Qi leads to the deepest idiocy" [13]. The location of idiocy is in the brain and is closely related to the dysfunction of the heart, kidneys, liver, and spleen. Its basic pathogenesis is deficiency in origin and excess in superficiality. The syndrome is characterized by kidney essence deficiency, Qi and blood deficiency,

heart and kidney deficiency as the origin, and phlegm-turbidity blocking the orifices, blood stasis blocking the collaterals, and turbid toxin blocking as the superficiality [14].

According to Wei *et al.*, the etiology and pathogenesis of AD are based on kidney deficiency and marrow depletion [15]. On one hand, due to aging and chronic illnesses, vital Qi is depleted, leading to deficiency of Qi, Yin, Yang, essence, and blood in the kidneys, heart, liver, and spleen. This further leads to brain malnutrition and improper functioning of the mind, causing AD. On the other hand, due to the dysfunction of the five internal organs, the brain marrow cannot be properly utilized, and phlegm-turbidity and blood stasis mutually obstruct each other, leading to AD. The syndrome can be generally classified into four types: insufficient endowment, spleen and kidney deficiency, phlegm-turbidity blocking the orifices, and blood stasis internally blocking the collaterals [16]. The treatment principle of traditional Chinese medicine focuses on nourishing deficiency and dissipating stagnation. Since AD may also be associated with personality changes and mental abnormalities, it is also related to "mania" and "confusion" in traditional Chinese medicine [17].

3. Overview of moxibustion therapy

Moxibustion, also known as moxa-burning or moxibustion therapy, is a traditional Chinese medical technique that uses the heat generated from mugwort leaves to stimulate acupuncture points or specific areas of the body. The purpose is to treat, maintain health, and prevent diseases through meridian conduction. The onset of AD is related to "insufficient marrow sea" and "obstruction of the clear orifices", while moxibustion therapy has the effect of dredging meridians, harmonizing Yin and Yang, and awakening the brain. As the saying goes, "What acupuncture cannot do, moxibustion can." Moxibustion is included in acupuncture and moxibustion therapy.

Cai proposed that the treatment of dementia should start from the "spirit-brain-Du meridian-Ren meridian" axis. The Du meridian connects to the heart and kidney meridians, and these four are interconnected to play the role of the seat of the primordial spirit [18]. Research shows that the most commonly used acupuncture points for acupuncture treatment of AD are Baihui and Sishencong. Shenshu is also commonly used. The meridians are mainly the Du meridian and the Foot Shaoyang Gallbladder Meridian. The stimulation sites are mainly concentrated in the head, face, neck, and back regions, focusing on combining local acupuncture points with remote acupuncture points selected along the meridians.

Among them, the use of intersecting acupuncture points is most critical [19]. The commonly used Baihui point is a key point on the Du meridian, which connects the kidneys, marrow, and brain, and can nourish Qi and Yang, awaken the brain and open the orifices; Sishencong, also known as Shencong point, is located on the top of the head and can promote Qi and blood circulation; Shenshu is the back shu point of the kidney, which can nourish kidney essence, generate marrow, and strengthen the brain [20–21].

4. Mechanism of moxibustion therapy in treating AD

4.1. Regulation of related protein expression

The Amyloid-β (Aβ) cascade hypothesis is the most classical theory, which proposes that excessive deposition of Aβ in senile plaques is the initiating factor leading to the pathophysiological changes of Alzheimer's disease (AD) [22]. In AD patients, increased production or decreased clearance of Aβ leads to the formation of plaques with neurotoxic effects on nerve cells, which further triggers neuronal damage and dysfunction, affecting cognitive

function [23]. Additionally, excessive deposition of Aβ promotes the phosphorylation of tau protein, which in turn accelerates the generation of Aβ, forming a vicious cycle that exacerbates AD symptoms [24]. Moxibustion can promote the degradation and clearance of Aβ through warm stimulation. Yu *et al.* performed early intervention treatment with grain-sized moxibustion on bilateral "Heart Shu" and "Kidney Shu" points in APP/PS1 transgenic AD mice [25].

The study showed a significant reduction in the amount of Aβ1-40 deposition, indicating that early intervention with moxibustion can improve cognitive function and delay the progression of AD in mice. Wang applied moxibustion to "Guan Yuan", "Chang Qiang", "Ming Men", and "Bai Hui" points on the Ren and Du meridians in AD rats, finding that moxibustion can improve learning and memory abilities by reducing the expression levels of GSK-3B and phosphorylated tau protein [26]. Ge treated AD patients with moxibustion at "Bai Hui", "Da Zhui", and "Feng Fu" points, discovering that moxibustion can also down-regulate the expression of lncRNA H19 in human plasma exosomes, thereby promoting the clearance of Aβ1-42 and improving cognitive and life abilities [27].

4.2. Regulation of cellular autophagy levels

Abnormal cellular autophagy is closely related to neurodegenerative diseases such as AD. Moderate autophagy can eliminate excessive accumulation of Aβ and tau proteins, while excessive autophagy can damage the stability of lysosomal membranes and accelerate AD-related pathological changes [28]. Zhu team speculated that the decreased memory ability of AD mice is associated with disordered signaling pathways that regulate autophagy in their brains, leading to reduced autophagy levels and capacity, resulting in abnormal accumulation of Aβ in the brain [29]. Moxibustion on the Du meridian can up-regulate cellular autophagy levels and improve neuronal brain damage.

Wu *et al.* applied moxibustion with aconite cake at "Bai Hui", "Feng Fu", and "Da Zhui" points in AD mice [30]. The results showed decreased expression of mTOR, p-mTOR, p70S6K, and p-p70S6K proteins, indicating that moxibustion on the Du meridian acupoints can enhance autophagy in hippocampal tissue cells of AD mice and reduce abnormal accumulation of Aβ in the brain by inhibiting the mTOR/p70S6K signaling pathway. Wang *et al.* treated AD rats with moxa stick moxibustion at "Bai Hui", "Kidney Shu", and "Sanyin Jiao" points [31]. The results showed that moxibustion increased the expression levels of ATG5 and p-AMPK proteins, elevated the LC3B-II/LC3B-I ratio, and decreased the expression levels of P70S6K and p-mTOR in the hippocampus of mice. These findings indicate that moxibustion can modulate the AMPK/mTOR signaling pathway, promote cellular autophagy, inhibit Aβ accumulation in the brain, and enhance cognitive function.

4.3. Protection of neurons and reduction of neuroinflammation

As a chronic neurodegenerative disease, neuroinflammation is also one of the main pathological features of AD. Brain damage caused by neuronal loss can lead to changes such as decreased learning and memory, cognitive dysfunction, and emotional abnormalities [32]. Microglia (Mi), as inherent immune cells of the nervous system, have phagocytic and preventive functions, and their activation is essential for neurogenesis, angiogenesis, and maintaining brain development [33]. Activated Mi can differentiate into pro-inflammatory M1 and anti-inflammatory M2 types.

In the early stages of AD, the M2 type enhances phagocytosis to eliminate Aβ and p-Tau. But in later stages, excessive activation of the M1 type produces large amounts of pro-inflammatory factors, leading to the accumulation of Aβ and p-Tau [34]. Therefore, promoting the activation of M2-type microglia and inhibiting

excessive activation of the M1 type are focal points for the prevention and treatment of AD. Li *et al.* performed gentle moxibustion on "Bai Hui" and "Yong Quan" points in AD mice [35]. The results showed that moxibustion can up-regulate the IL-33/ST2 signaling pathway, promote the polarization of microglia towards the M2 direction, reduce the pathological deposition of Aβ and p-Tau, and improve the spatial learning and memory abilities of AD mice.

Additionally, studies have found that there is continuous and widespread astrocyte activation in the early stages of AD. Astrocytes can degrade Aβ and play dual roles in neurotoxicity and neuroprotection [36]. Tang *et al.* combined acupuncture and gentle moxibustion at "Bai Hui" and "Kidney Shu" points in AD rats [37]. They found that the edema around neuronal cytoplasm and astrocytes was reduced, mitochondrial swelling was alleviated, and there were no significant abnormalities in the endoplasmic reticulum and ribosomes of neurons. It was concluded that acupuncture combined with moxibustion helps to improve astrocyte damage induced by Aβ 1-42 in AD rats. Moxibustion regulates glial cell function and reduces neuroinflammation.

5. Clinical application research of moxibustion therapy in the treatment of AD

Moxibustion therapy, with its effects of warming meridians, harmonizing Qi and blood, resolving stagnation, and dissipating nodules, is widely used in the treatment of AD. In clinical applications, there are various moxibustion methods, including traditional moxibustion (such as direct moxibustion and indirect moxibustion), gentle moxibustion, heat-sensitive moxibustion, thunder-fire moxibustion, etc. Different moxibustion methods have varying efficacy in treating AD.

5.1. Different methods of moxibustion therapy

Zhu *et al.* treated patients with mild cognitive impairment with moxibustion at "Bai Hui", "Da Zhui", "Shen Ting", and "Shen Dao" points on the Governor Vessel meridian, in addition to the Western medicine control group (oral nimodipine tablets) [38]. The patients' Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), and Activities of Daily Living (ADL) scores all showed significant improvement and were better than the control group. It was concluded that moxibustion at these points on the Governor Vessel meridian has unique advantages in improving cognitive function in patients with mild cognitive impairment, even better than drug treatment. Therefore, moxibustion therapy can effectively improve cognitive function and enhance the quality of life for AD patients.

Direct moxibustion involves placing a moxa cone on the skin surface of the acupuncture point. Pressure moxibustion belongs to direct moxibustion without scarring. Yang *et al.* applied pressure moxibustion at the Bai Hui point for patients with mild to moderate AD and the results showed that pressure moxibustion could improve the cognitive function and daily self-care ability of these patients [39]. Indirect moxibustion uses a medium for heat conduction, which can exert the pharmacological effects of the medium while reducing burning sensation. Shen *et al.* selected main points such as "Shen Ting", "He Gu", and "Shen Men", and combined them with medicinal cakes made of aconite, ephedra, and cinnamon for indirect moxibustion at the Bai Hui point in the treatment of senile dementia [40]. They found that the patients' MMSE scores and clinical symptoms improved.

Gentle moxibustion is a commonly used method. Su *et al.* applied gentle moxibustion at "Bai Hui", "Da Zhui", "Ming Men", and "Zhi Yang" points for AD patients, in addition to the western medicine control group (oral donepezil hydrochloride) [41]. After three months of intervention, the results showed that the total effective

rate of the treatment group was higher than that of the control group and the MMSE score of the treatment group was better than that of the control group ($P < 0.01$), indicating that gentle moxibustion can improve the cognitive function of AD patients. Heat-sensitive moxibustion involves using the method of gentle moxibustion to perform suspended moxibustion on the heat-sensitive points of the human body. Yue applied heat-sensitive moxibustion at the "Da Zhui" point for AD rats and found that their spatial ability and memory ability improved, which was related to its ability to effectively improve brain tissue damage and necrosis and reduce inflammatory cell infiltration [42]. Heat-sensitive moxibustion is widely used in the treatment of many chronic diseases and studies have shown that it is more effective than traditional moxibustion in some diseases [43].

Thunder-fire moxibustion involves using moxa sticks made of Chinese herbal powder and mugwort floss to perform moxibustion on acupuncture points. Wei *et al.* selected points such as "Shen Que", "Zhong Wan", "Yong Quan", and "Bai Hui" for thunder-fire moxibustion in patients with early-stage senile dementia, with each intervention lasting 20 minutes and a total of 12 weeks of intervention [44]. The results showed that the intervention group was superior to the control group in terms of MMSE, ADL and Global Deterioration Scale (GDS) scores ($P < 0.05$), indicating that the addition of thunder-fire moxibustion to conventional therapy can effectively slow down the progression of dementia.

Each of the moxibustion methods mentioned above has its advantages and disadvantages. Direct moxibustion provides strong thermal stimulation but can easily cause burns, so the skin needs to be closely observed during the operation. Pressure moxibustion is less likely to leave scars but provides weaker stimulation, which may have limited effects on severe patients. The pressure applied during moxibustion needs to be controlled. Indirect moxibustion can exert the pharmacological effects of the medium, but there are various medium options and the preparation is complex. Nursing staff need to select a suitable medium for the patient based on their illness and physical condition to prevent adverse reactions such as allergies. Attention should be paid to the temperature and fit of the medium during operation. Gentle moxibustion is simple to operate and easy to accept, while heat-sensitive moxibustion provides stronger stimulation and better efficacy than gentle moxibustion and traditional moxibustion.

However, there is limited research on it, and it requires high precision in locating heat-sensitive points and suspended moxibustion skills for the operator. Thunder-fire moxibustion combines Chinese herbs and mugwort floss, resulting in strong medicinal power and rapid firepower but posing significant safety hazards [45]. Regardless of the moxibustion method used, the specific situation of the patient should be considered during operation to select the appropriate moxibustion method, accurately locate the acupuncture points, perform precise moxibustion, closely observe the patient's response, and adjust the moxibustion plan in a timely manner to ensure the effectiveness and safety of moxibustion.

5.2. Application of combined moxibustion therapy

Traditional Chinese medicine emphasizes holistic and comprehensive care. Clinically, scholars have adopted a combination of moxibustion and other methods to treat Alzheimer's disease (AD). Tang *et al.* found that the MMSE scores of patients with mild to moderate AD significantly improved after treatment with moxibustion combined with traditional Chinese medicine [46]. This suggests that the organic combination of internal and external therapies in traditional Chinese medicine can increase the effectiveness of AD treatment.

Zhu treated 80 patients with dementia using scalp acupuncture combined with moxibustion at acupoints on the limbs [47]. After three months of treatment, the total effective rate of the dementia rating scale (CRD) score

reached 95.0%. Su used acupuncture combined with moxibustion at back Shu points for patients with senile dementia of spleen and kidney deficiency syndrome [48]. After intervention, the patients' MMSE, ADL, and SDSD scores were significantly improved, indicating that acupuncture combined with moxibustion can improve patients' cognitive and life abilities and is superior to traditional acupuncture.

He *et al.* believed that AD is closely related to the olfactory system and aromatherapy can act on the brain through the olfactory pathway to improve cognition [49]. The aromatic smoke generated by moxibustion can regulate the body through multiple pathways. Therefore, it is inferred that moxibustion combined with aromatherapy may be effective in preventing and treating AD. Zhang implemented a combination of Chinese medicine nursing, including circular moxibustion, acupoint massage, Ba Duan Jin exercises, dietary nursing, and emotional nursing for 60 AD patients based on routine nursing [50]. The results showed that the effective rate of ADL scores in the observation group was 80.0%, while the control group was 53.3%. The total effective rate of MMSE scores in the observation group reached 76.7%, while the control group was 20.0%. There were significant differences between the two groups. These studies show that moxibustion combined therapy has a synergistic effect and can improve the clinical application effect of AD.

6. Conclusion

In summary, AD has become one of the most serious diseases threatening humans in the 21st century. Taking effective measures to improve the quality of life of AD patients and enabling them to spend their later years in peace has gradually become a top priority today. In recent years, the government has increased its emphasis on and support for traditional Chinese medicine, and Chinese medicine nursing has also been recognized by people. As an important part of traditional Chinese medicine nursing, moxibustion therapy has demonstrated unique advantages in the treatment of AD due to its convenient treatment, high safety, small side effects, and significant efficacy. However, current research is mostly focused on animal studies, with few studies on human populations. Most studies have small sample sizes and lack large-scale, multi-center, randomized controlled clinical studies, which limits the persuasiveness of the research results. In addition, different studies have inconsistent operating standards for acupuncture methods, acupoint selection, and moxibustion control, which reduces comparability to some extent. Therefore, it is necessary to further deepen the research on the mechanism of AD, establish relatively unified operating standards, and better provide health services for AD patients in the future.

Disclosure statement

The authors declare no conflict of interest.

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