



ALZHEIMER'S DISEASE: A LITERATURE REVIEW

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ABSTRACT

Many older people forget someone's name or misplace things from time to time. This kind of forgetfulness is normal. But, forgetting how to get home, getting confused in places a person knows well, or asking questions over and over can be signs of a more serious problem. The person may have Alzheimer's disease. Alzheimer disease (AD) is the most common form of dementia and possibly contributes to 60-70% of

cases. Alzheimer's disease takes a stronger toll on women than men. More women than men develop the disease, and women are more likely than men to be informal caregivers for someone with Alzheimer's disease or dementia. There is an urgent need for both early diagnoses with specific markers as well as effective therapies that could be taken at the different stage of the disease.

KEYWORDS: Alzheimer's disease, caregivers, dementia, women.

INTRODUCTION

Dementia is a syndrome characterized by disturbance of multiple brain functions, including memory, thinking, orientation, comprehension, calculation, learning capacity, language, and judgement. Consciousness is not clouded. The impairments of cognitive function are commonly accompanied, and occasionally preceded, by deterioration in emotional control, social behaviour, or motivation.^[1,2]

Physicians diagnose dementia by performing a careful medical, neurological and neuropsychological examination. They first exclude medical conditions that can cause

delirium. Delirium is a state of confusion that often arises abruptly and may accompany such disorders as infections, impaired nutrition, head trauma or other potentially manageable medical or neurological diseases. Delirium is distinguished from dementia because delirious patients have impaired attention and alertness which contributes to the impaired thinking. Demented patients, by contrast, are alert and aware, except at the very late stages of the disease. Dementia is typically documented by poorer than expected performance on neuropsychological tests which assess memory, general knowledge, language, abstract reasoning and the ability to perform certain tasks of minimal skill, including dressing and simple drawing tasks.

Many older people forget someone's name or misplace things from time to time. This kind of forgetfulness is normal. But, forgetting how to get home, getting confused in places a person knows well, or asking questions over and over can be signs of a more serious problem. The person may have **Alzheimer's disease**. It is a disease of the brain that begins slowly and gets worse over time.

Alzheimer disease (AD) is the most common form of dementia and possibly contributes to 60-70% of cases. Other types of dementias include vascular dementia, dementia with Lewy bodies, and a group of diseases that contribute to frontotemporal dementia. The boundaries between subtypes are indistinct and mixed forms often co-exist.^[3] AD causes severe suffering for patients, including progressive functional impairment, loss of independence, emotional distress, and behavioral symptoms. Families and caregivers often experience emotional and financial stress.

The disease may cause a person to become confused, get lost in familiar places, misplace things or have trouble with language. The major risk factor for AD is age, with the prevalence doubling every 5 years after the age of 65. Most estimates of the prevalence of AD in the United States are about 2.3 million for individuals over age 70, but some estimates are as high as 5.3 million individuals over the age of 65. The number of individuals with mild cognitive impairment exceeds the number with AD.

These individuals have mild impairment in cognition or daily functions that does not meet the threshold for a diagnosis of dementia, but they are at increased risk for development of AD, which makes them a prime target for intervention protocols. Studies of selected risk or protective factors for cognitive decline and AD have been published, but it is not clear

whether the results of these previous studies are of sufficient strength to warrant specific recommendations for behavioral, lifestyle, or pharmaceutical interventions/modifications targeted to these endpoints.

As the population ages, Alzheimer disease is becoming more of a medical, social and public health concern. It is a dementing disorder that causes severe and permanent loss of intellectual function. Patients with Alzheimer disease begin having forgetfulness, then progress to having irreversible loss of memory and other previously well-learned skills. Within a few years, some patients may be totally incapable of even the most basic self-care, imposing a great burden on their families and communities.

AD should be differentiated from normal age-related decline in cognitive function, which is more gradual and associated with less disability. Disease often starts with mild symptoms and ends with severe brain damage. People with dementia lose their abilities at different rates.^[4-8]

Types of Alzheimer Disease: Early-onset Familial and Late-onset Sporadic

Alzheimer disease is generally diagnosed after the age of 65 years, when it is referred to as late-onset Alzheimer disease. The condition affects 5% of the population aged over 65 years and more than 20% of the population over 85 years. Only 10% of all persons diagnosed with Alzheimer disease develop symptoms before the age of 65 years. They are said to have early-onset Alzheimer disease, and approximately 10% of these early-onset cases have a familial form of the condition, which is transmitted as an autosomal dominant trait. Mutations in three genes – amyloid precursor protein, presenilin-1 and presenilin-2 – cause the majority of cases of familial Alzheimer disease. However, the vast majority of cases are not clearly transmitted as inherited traits. Most early- and late-onset cases generally occur sporadically or with familial clustering that has no clear mendelian inheritance pattern. Other than the difference in the age of onset, early-onset familial Alzheimer disease and the late-onset sporadic type are difficult to distinguish clinically and pathologically. Therefore, the appearance of Alzheimer disease may represent a common pathway of neurodegeneration, which can be initiated by one of several distinct factors, including single gene mutations or a combination of genetic and environmental effects.

Pathophysiology

The pathophysiology of AD is related to the injury and death of neurons, initiating in the hippocampus brain region that is involved with memory and learning, then atrophy affects the

entire brain.^[7] Amyloid beta, also written A β , is a short peptide that is an abnormal proteolytic byproduct of the transmembrane protein amyloid precursor protein (APP), whose function is unclear but thought to be involved in neuronal development. Amyloid beta monomers are soluble and contain short regions of beta sheet at sufficiently high concentration, they undergo a dramatic conformational change to form a beta sheet-rich tertiary structure that aggregates to form amyloid fibrils. These fibrils deposit outside neurons in dense formations known as senile plaques or neuritic plaques, in less dense aggregates as diffuse plaques, and sometimes in the walls of small blood vessels in the brain in a process called amyloid angiopathy or congophilic angiopathy. In Alzheimer disease abnormal aggregation of the tau protein, a microtubule-associated protein expressed in neurons is also observed. Tau protein acts to stabilize microtubules in the cell cytoskeleton. Like most microtubule-associated proteins, tau is normally regulated by phosphorylation. In AD patients, hyperphosphorylated tau P-tau accumulates as paired helical filaments that in turn aggregate into masses inside nerve cell bodies known as neurofibrillary tangles and as dystrophic neurites associated with amyloid plaques.^[9]

Diagnosis

A diagnosis of Alzheimer's disease is most commonly made by an individual's primary care physician. The physician obtains a medical and family history, including psychiatric history and history of cognitive and behavioral changes. The physician also asks a family member or other person close to the individual to provide input. In addition, the physician conducts cognitive tests and physical and neurologic examinations and may request that the individual undergo magnetic resonance imaging (MRI) scans. MRI scans can help identify brain changes, such as the presence of a tumor or evidence of a stroke that could explain the individual's symptoms.

Treatment of Alzheimer's Disease

Pharmacologic Treatment

Pharmacologic treatments are treatments in which medication is administered to slow or stop an illness or treat its symptoms. None of the treatments available today for Alzheimer's disease slows or stops the malfunction and death of neurons in the brain that cause Alzheimer's symptoms and eventually make the disease fatal. However, dozens of drugs and therapies aimed at slowing or stopping neuronal malfunction and death are being studied by scientists around the world. Five drugs have been approved by the U.S. Food and Drug

Administration that temporarily improve symptoms of Alzheimer's disease by increasing the amount of chemicals called neurotransmitters in the brain. The effectiveness of these drugs varies from person to person. Despite the lack of disease-modifying therapies, studies have consistently shown that active management of Alzheimer's and other dementias can improve quality of life through all stages of the disease for individuals with dementia and their caregivers.^[10-12]

Active management includes (1) appropriate use of available treatment options, (2) effective management of coexisting conditions, (3) coordination of care among physicians, other health care professionals and lay caregivers, (4) participation in activities and/or adult day care programs and (5) taking part in support groups and supportive services.

Non-Pharmacologic Therapy

Non-pharmacologic therapies are those that employ approaches other than medication, such as physical therapy and reminiscence therapy (therapy in which photos and other familiar items may be used to elicit recall). As with pharmacologic therapies, non-pharmacologic therapies have not been shown to alter the course of Alzheimer's disease. Rather than altering the disease course, non-pharmacologic therapies are often used with the goal of maintaining cognitive function or helping the brain compensate for impairments. Non-pharmacologic therapies are also used with the goals of improving quality of life or reducing behavioral symptoms such as depression, apathy, wandering, sleep disturbances, agitation and aggression. A wide range of non-pharmacologic interventions have been proposed or studied. The Cochrane Database of Systematic Reviews of published articles on non-pharmacologic therapies found that few have sufficient evidence supporting their effectiveness.^[13] Of the 25 categories of non-pharmacologic therapies reviewed in the Cochrane Database, only cognitive stimulation had findings that suggested a beneficial effect. A different systematic review found that there were too few high-quality studies to show that non-pharmacologic therapy for dementia was effective. However, of the high-quality studies reviewed, cognitive training, cognitive stimulation and training in activities of daily living appeared most successful in reaching the aims of the interventions.^[14] A metaanalysis, which combines results from many studies, found the most successful non-pharmacological interventions for neuropsychiatric symptoms of dementia were multicomponent, tailored to the needs of the caregiver and person with dementia, and delivered at home with periodic follow-up.^[15]

CONCLUSION

Due to the ageing of the world population the number of patients with Alzheimer disease will rise significantly. If no treatment is available, this will be a major health issue with enormous financial burdens to health care systems. Thus, there is an urgent need for both early diagnosis with specific markers as well as effective therapies that could be taken at the different stage of the disease.

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