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DIAGNOSIS AND TREATMENT OF ALZHEIMER'S DISEASE: A REVIEW ARTICLE

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ABSTRACT

Alzheimer's disease is most common cause of dementia in all over country, day by day these disease are grow because of the aging world population. Diagnosis is based on clinical criteria such as impairment of memory and other cognitive function. This disease is not based on laboratory tests. Alzheimer's disease not completely cures by medicines but some option may reduce its symptom and improve the quality of life there by help the patient to some extent. Treatment is currently targeted on symptomatic therapy, although trials are underway that aim to reduce the burden of pathology within the brain. The main goal of these projects to know the Risk factor, sign, and symptoms stages of the Alzheimer disease, treatment and provide the safe and supportive environment to the Alzheimer's disease patient

INTRODUCTION

Alzheimer's disease is the most prevalent neuro degenerative disorder and the most common cause of dementia. In India ,more than 4 million people have suffering from dementia. And in Worldwide, at least 44 million people are living with dementia. Alzheimer's is more likely in women. Because of women live longer than men on average, and older age is the greatest risk factor for Alzheimer's. Various factors are responsible for development of Alzheimer's disease such as Environmental factor, vascular factor, and psychical factor. There are three main stages of the disease. each with its own challenges and symptoms. By identifying the current stage of the disease, physicians can predict the symptoms can see in the future and possible courses of treatment. For cure the Alzheimer's disease, physicians can ask to the patient about his previous history should include information about mental state assessment should include validate cognitive function test and physical examination they include neurological condition. Assessment of dementia involves a two –step process. Firstly, it is important to distinguish dementia syndromes from other condition that can mimic them, such as depression, delirium and mild cognitive impairment. The pre dementia stage is often unreliably distinguished from normal aging or stress –related issues. One of the first signs is the deterioration of episodic memory, and other aspects such as executive, verbal and visuos patial functions are slightly impaired at most. The cause of Alzheimer's disease is poorly understood. About 70% of the risk is beloved to be inherited from a person's parents with many genes usually involved. Other risk factor includes a history of head injuries, depression, and hypertension. The disease process is associated with plaques and neurofibrillary tangles in the brain. No treatment stop or reverse it's progression, though some may temporarily improve symptoms. Affected people increasingly rely on other for assistance, often placing a burden on the caregiver. The pressures can include social, psychological, physical, and economic elements. Exercise programs may be beneficial with respect to activities of daily living and can potentially improve outcomes. Behavioral problems or psychosis due to dementia are often treated with antipsychotics, but this is not usually recommended, as there with little benefit with an increased risk of early death.

Risk factor

1) **Age:** The single greatest risk factor for developing Alzheimer's disease is age, one of the non-modifiable risk factor. Most causes of Alzheimer's diseases are seen in older

adults, ages are 65 years or above. Between the ages of 65 and 74, approximately 5% of people have Alzheimer's disease. For those over 85, the risk increases to 50%. Various studies show that aging can impair the body's self-repair mechanism, including in the brain. And, many of the cardiovascular risk factors increase with age, such as high blood pressure, heart disease, and high cholesterol.

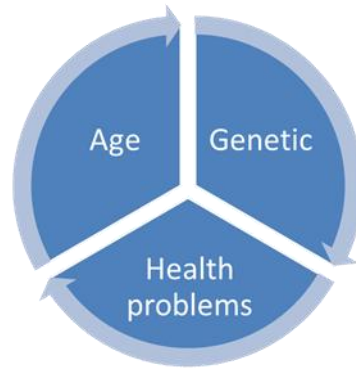


Fig. 1: Risk factor

2) Genetics:

In Alzheimer's disease, there is no appearance of a genetic pattern of inheritance. A connection has been found between age of one called Apo lipoprotein E (ApoE) and the development of Alzheimer's disease. This gene is supposed to be responsible for the protein that carries cholesterol in the blood vessels. One form of the gene, ApoE4, has been shown to increase the chances of developing of the disease to a greater extent. However, the ApoE2 form protect from the disease. In the cases occurring before age 65, a mutation of chromosomes can be responsible. This rare form of the disease is called familial Alzheimer's disease and it affects less than 10 % of Alzheimer's disease patients. It is observed to be caused by mutation on chromosomes 1, 14 and 21. If one mutation on chromosome are inherited, the persons have 50% risk of developing Alzheimer's disease.

3) Health Problems:

It is observed that there is a strong link between cardiovascular health and brain health of an Alzheimer's patient. Having heart disease, high blood pressure or high cholesterol can increase the risk of developing Alzheimer's disease to a greater extent. This is caused by damage to blood vessels in the brain, resulting in the less blood flow and possible drastic brain tissue death. Type 2 diabetes may also increase the risk for

Alzheimer's disease. Inefficiency of insulin to convert blood sugar to energy may cause higher levels of sugar in the brain, causing severe harm to the entire body. Symptoms such as forgetfulness and confusion are mild during the early stages of the disease as is observed in almost every case, but they gradually worsen as the disease progresses and damage to the brain becomes more severe and prominent. Some people with AD also have severe depression and do not know how to cope with a loss of cognitive and basic function. The symptoms of depression can be similar to the general symptoms of AD as seen many cases. This can make it difficult to determine whether your loved one is experiencing depression or just the normal symptoms of AD which is normally difficult to understand. Treatment option for depression in people with AD including attending support groups and speaking with a therapist to make him understand your condition. Getting regular exercise and participating in activities can also improve their mental outlook. In some cases, a doctor may recommend antidepressants to get relief from depression. AD can also affect balance and coordination of the body to a greater extent.

4. Stages of Alzheimer's disease:

Effect of ageing on memory but not AD

1. Forgetting things Occasionally
2. Misplacing items sometimes
3. Minor short term memory loss
4. Not remembering exact details

Early stage Alzheimer's:

1. Not remembering episodes of forgetfulness
2. Forgets names of family or friends
3. Changes may only be noticed by close friends or relatives
4. Some confusion in situation outside the familiar

Middle stage Alzheimer's:

1. Greater difficulty remembering recently learned information
2. Deepening confusion in many circumstances
3. Problems with sleep
4. Trouble determining their location

Late stage Alzheimer's:

Poor ability to think, Problems speaking, Repeats same conversation, More abusive, anxious, or paranoid.

5. Signs and symptoms:

Pre-dementia:

The first symptoms are often mistakenly attributed to ageing or stress. Detailed neuropsychological testing can reveal mild cognitive difficulties up to eight years before a person fulfils the clinical criteria for diagnosis of AD. These early symptoms can affect the most complex activities of daily living. The most noticeable deficit is short term memory loss, which shows up as difficulty in remembering recently learned facts and inability to acquire new information. Subtle problems with the executive function of attentiveness, planning, flexibility, and abstract thinking, or impairments in semantic memory can also be symptomatic of the early stages of AD. Apathy can be observed at this stage, and remains the most persistent neuropsychiatric symptom throughout the course of the of subtle memory difficulties are also common. The preclinical stage of the disease has also been termed mild cognitive impairment. This is often found to be a transitional stage between normal ageing and dementia.

Early:

In people with AD, the increasing impairment of learning and memory eventually leads to a definitive diagnosis. In a small %, difficulties with language, executive function, perception (agnosia), or execution of movements (apraxia) are more prominent than memory problems. AD does not affect all memory capacities equally. Older memories of the person's life (episodic memory), facts learned (semantic memory), and implicit memory (the memory of the body on how to do things, such as using a fork to eat or how to drink from a glass) are affected to a lesser degree than new facts or memories.

Language problems are mainly characterised by a shrinking vocabulary and decreased word fluency, leading to a general impoverishment of oral and written language. In this stage, the person with Alzheimer's is usually capable of communicating basic ideas adequately. While performing fine motor tasks such as writing, drawing or dressing, certain movement coordination and planning difficulties (apraxia) may be present, but they are commonly unnoticed. As the disease progresses, people with AD can often continue to perform many tasks independently, but need assistance or supervision with the most cognitively demanding activities.

Moderate:

Progressive deterioration eventually hinders independence. With subjects being unable to perform most common activities of daily living Speech difficulties become evident due to an inability to recall vocabulary. Which leads to frequent incorrect word substitution (paraphasias). Reading and writing skills are also progressively lost. Complex motor sequences become less coordinated as time passes and AD progresses, so the risk of falling increases. During this phase. Memory problems worsen, and the person may fail to close relatives. Long-term memory, which was previously intact, becomes impaired.

Behavioural and neuropsychiatric changes become more prevalent, common manifestations are wandering, irritability and labile affect, leading to crying, outbursts of unpremeditated aggression, or resistance to care giving. Sun downing can also appear. Approximately 30% of people with AD develop illusionary misidentification and other delusional symptoms. Subject also loses insight of their disease process and limitations (anosognosia). Urinary incontinence can develop. These symptoms create stress for relatives and carers, which can be reduced by moving the person from home care to other long-time care facilities.

Advanced

During the final stages, the patient is complete dependent upon caregivers Language is reduced to simple phrases or even single words, eventually leading to complete loss of speech. Despite the loss of verbal language abilities, people can often understand and return emotional signals, Although aggressiveness can still be present, extreme apathy even the simplest tasks independently; muscle mass and mobility deteriorates to the point where they bedridden and unable to feed themselves. The cause of death is usually an external factor, such as infection of pressure ulcers or pneumonia, not the disease itself. The cause for most Alzheimer's cases is still mostly unknown except for 1% to 5% of cases where genetic differences have been identified.

Genetic:

The genetic heritability of Alzheimer's disease (and memory components thereof), based on reviews of twin and family studies, ranges from 49% to 79% Around 0.1% of the cases are familial forms of autosomal (not sex-linked) dominant inheritance, which have an onset before age 65, This form of the disease is known as early onset familial Alzheimer's disease. Most of autosomal dominant familial AD can be attributed to

mutations in the one of the three genes: those encoding Amyloid precursor protein (APP) and presenilins 1 and 2. Most mutations in the APP and presenilin genes increase the production of a small protein called A β 42, which is the main component of senile plaques. Some of the mutation merely alters the ratio between A β 42 and the other major forms –particularly A β 42, without increasing A β 42 levels. Two other genes associated with autosomal dominant Alzheimer’s disease are ABCA7 and SORL1.

Most cases of Alzheimer’s disease do not exhibit autosomatic - dominant inheritance and are termed sporadic AD, in which environmental and genetic differences may act as risk factors. The best known genetic risk factor is the inheritance of the ϵ 4 allele of the apolipoprotein E (APOE). Between 40 and 80% of people with AD possess at least one APOE ϵ 4 allele.

Cholinergic hypothesis

The oldest, on which most currently available drug therapies are based, is the cholinergic hypotheses, which propose that AD is caused by reduced synthesis of the neurotransmitter acetylcholine. The cholinergic hypothesis has not maintained widespread support, largely because medications intended to treat acetylcholine deficiency have not been very effective.

Amyloid hypothesis

In 2009, this theory was updated, suggesting that a close relatives of the beta-Amyloid protein, and not necessary the beta-Amyloid itself may be a major culprit in the disease. The theory holds that an Amyloid-related mechanism that prunes neuronal connection in the brain in the fast –growth phase of early life may be triggered by ageing –related processes in later life to cause Amyloid and is cleaved from APP by one of the same enzymes N-APP triggers the self-destruct pathway by binding regions to a neuronal receptor called death receptor (DR6,also known as TNFRSF21)-DR6 is highly expressed in the human brain regions most affected by Alzheimer’s, so it is possible that the N – APP/DR6 pathway might be hijacked in the ageing brain to cause damage. In this model, beta – Amyloid plays a complementary role, by depressing synaptic function. In early 2017, a trial of verubecestat, which inhibits the beta-secretases protein responsible for creating beta-Amyloid protein was discontinued as an independent panel found virtually no chance of finding a positive clinical effect. In 2018 -2019, The so-called Amyloid

hypothesis, that the accumulation and deposition of oligomeric or fibrillar amyloid β (A β) peptide is the primary causes Alzheimer's diseases.

6. Diagnosis

A diagnosis of Alzheimer's disease is based on medical history, history from relatives, and behavioural observation. The presence of characteristic neurological and neuropsychological features and the absence of alternative conditions is supportive.

Laboratory and imaging tests can rule out other potential causes or help the doctor better characterize the disease causing dementia relatively high accuracy whether Alzheimer's disease or another condition is the cause. Alzheimer's disease can be diagnosed with complete certainty after death, when microscopic examination of the brain reveals the characteristic plaques and tangles.

Tests

1. A diagnostic work –up would likely include the following tests :
2. Physical and neurological exam
3. Your doctor will perform a physical exam and likely assess overall neurological health by testing the following :
4. Reflexes
5. Muscle tone and strength
6. Ability to get up from a chair and walk across the room
7. Sense of sight and hearing
8. Coordination
9. Balance

Lab tests:

Blood tests may helpful to know the potential causes of memory loss confusion such as a Longer forms of neuropsychological testing may provide additional details about mental function compared with people of a similar age and education level. These tests are also important for establishing a point to track the progression of symptoms in the future. of the brain are now used chiefly to pinpoint visible abnormalities related to conditions other than Alzheimer's disease –such as strokes, trauma or tumors –that may cause cognitive change. New imaging application – currently used primarily in major medical centres or in clinical trials – may enable doctors to detect specific brain changes caused by Alzheimer: Magnetic resonance imaging (MRI).MRI uses radio waves and a

strong magnetic field to produce detailed images of the brain. MRI scan are used primarily to rule out other condition.

Computerized tomography (CT)

ACT scan, an specialized X-ray technology. Produced cross-section images (slices) of brain strokes & head injuries

Imaging of disease processes can be performed with positron emission tomography (PET). During a PETs can, low-level radioactive tracer is injected into the blood to reveal a particular feature in the brain. PET imaging may include the following:

Fluorodeoxyglucose (FDG) PET scan show areas of the brain in which nutrients are poorly metabolized. Identifying patterns of degeneration – areas of low metabolism – can help distinguish between Alzheimer's disease and other type of dementia.

Amyloid PET imaging can measure the burden of Amyloid deposits in the brain. This imaging is primarily used in research but may be used if a person has unusual or very early onset of dementia symptoms.

Tau Pet imaging, which measures the burden of neurofibrillary tangles in the brain, is only used in research.

In special circumstances such as rapidly progressive dementia or very early onset dementia, other tests may be used to measure abnormal beta-amyloid or tau in the cerebrospinal fluid.

7. Treatment

Drugs

Current Alzheimer's medication can help for a time with memory symptoms and other cognitive changes. Two types of drugs are currently used to treat cognitive symptoms



Figure 1: Site of action Of AD drug

Cholinesterase inhibitors:

These drugs work by boosting levels of cell-to-cell communication by preserving a chemical messenger that is depleted in the brain by Alzheimer's disease. The improvement is modest. Cholinesterase inhibitors may also improve neuropsychiatric symptoms, such as agitation or depression. Commonly prescribed cholinesterase inhibitors include donepezil (Aricept), galantsmine (Razadyne) and rivastigmine (Exeion)

The main side effects of these drugs include diarrhea, nausea, loss of appetite and sleep disturbances. In people with cardiac conduction disorders, serious side effects may include cardiac arrhythmia.

Memantine (Namenda)

This drug works in another brain cell communication network and slows the progression of symptoms with moderate to severe Alzheimer's disease. It's sometimes used in combination with a cholinesterase inhibitor. Relatively rare side effects include dizziness and confusion.

Sometimes other medication such as antidepressants may be prescribed to help control the behavioral symptoms associated with Alzheimer's disease.

Creating a safe and supportive environment

Adapting the living situation to the needs of a person with Alzheimer's disease is an important part of any treatment plan. For someone with Alzheimer's, establishing and

strengthening routine habits and minimizing memory – demanding tasks can make life much easier .

You can take these steps to support a person’s sense of well-being and continued ability to function:

1. Always keep keys, wallet, mobile phones and other valuable in the same place at home, so they don’t become lost.
2. Keep medication in a secure location. Use a daily checklist to keep track of dosages
3. Arranges for finances to be on automatic payment and automatic deposit.
4. Carry a mobile phone with location capability so that a caregiver can track its location. Program important phone numbers into the phone.
5. Make sure regular appointments are on the same day at the same time as much as possible.
6. Use a calendar or whiteboard in the home to track daily schedules. Build the habit of checking off completed items.
7. Remove excess furniture clutter and throw rugs.
8. Install sturdy handrails on stairways and in bathrooms.
9. Ensure that shoes and slippers are comfortable and provide good traction.
10. Reduce the number of mirrors .People with Alzheimer’s may find images in mirrors confusing or frightening
11. Make sure that the person with Alzheimer’s carries identification or wears a medical alert bracelet.
12. Keep photographs and other meaningful objects around the house.

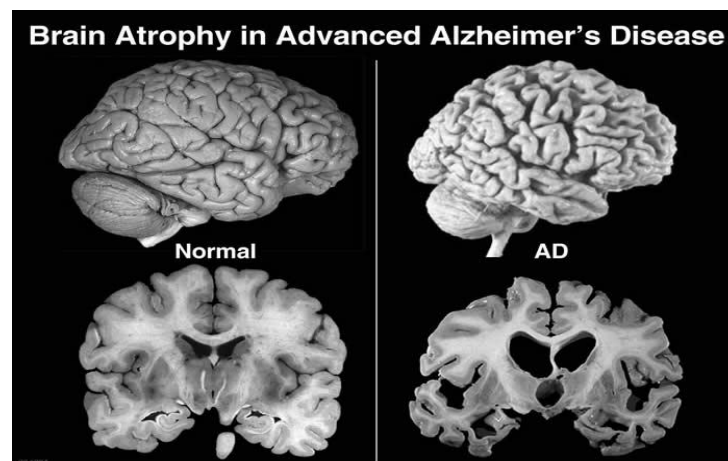


Fig. 2: Comparison of normal brain and AD suffering Patient Brain

CONCLUSION:

In this article, Alzheimer disease and its diagnosis and treatment briefly discussed. There are four stages of Alzheimer's disease in series i.e, predementia, mild, moderate and severe. Various risks factors like age, genetics, health problems etc. Computed tomography, positron emission tomography, Brain imaging, Amyloid PET imaging, Tau Pet imaging, Fluoro deoxyglucose (FDG) PET and Magnetic resonance imaging are the techniques available for detection of Alzheimer's disease in patients. The cause of Alzheimer's disease can be explained on Amyloid hypothesis and cholinergic hypothesis. Cholinesterase inhibitors and memantine these two drugs are used for the treatment of Alzheimer's disease. And also create the safe and supportive environment for the Alzheimer's disease patients.

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