ISSN- 2230-7346
Journal of Global Trends in Pharmaceutical Sciences

BASICS OF ALZHEIMER'S DISEASE AND DEMENTIA

Goday Swapna*, M. Mahitha, P. Teja sree

Department of pharmaceutical Analysis, Nirmala College of pharmacy, Atmakuru, Mangalagiri, A.P, India-522503

* Correspoding author E-mail: mahithamedepalli@gmail.com

ARTICLE INFO

Key words:
Alzheimer's disease, neuro degeneration, disease-modifying therapy, chaperons, heat shock proteins.

Access this article online
Website:
https://www.jgtps.com/
Quick Response Code:

ABSTRACT

Alzheimer's disease (AD) is a disorder that causes degeneration of the cells in the brainand it is the main cause of dementia, which is characterized by a decline Independence in an individual's daily activities. AD is considered a multi factorial disease. Two main hypotheses have been proposed as the cause of AD. The cholinergic hypothesis and the amyloid hypothesis. In addition, several risk factors have been implicated in this disease, including aging, genetic factors, head trauma, vascular disease, infections, and environmental factors. Currently, there are only two classes of drugs approved for the treatment of AD, including cholinesterase enzyme inhibitors and N-methyl-d-aspartic acid (NMDA) antagonists, which are not associated with AD symptoms or disease. Prevent. Today, research is focused on understanding the pathology of AD by targeting multiple mechanisms such as alteration of AD course. This review describes the drugs currently available and future theories for the development of new treatments for AD, including disease-modifying therapies (DMTs), chaperones, and natural products.

INTRODUCTION

Alzheimer's disease is the most common type of dementia and can be defined as a slowly progressive neurodegenerative disease characterized by neuritic plaques and neuro fibrillary tangles 1) the accumulation of amyloid beta peptide (A β)in the most affected areas of the brain, the medial temporal lobe and neocortical structures [1] . Alois Alzheimer noticed the presence of amyloid plaques and a massive loss of his neurons when he examined the brain of the first patient who had suffered memory loss and personality changes in his before he died. He described the condition as a serious disease of the cerebral cortex.. Emil Kraepelin first named this clinical picture in hisof the 8th edition of the Handbook of Psychiatry [2,3]. The progressive loss of cognitive function can be caused by brain disorders Such as Alzheimer's disease (AD) or by other factors such as intoxication, infection, brain oxygenation or nutritional deficiencies, pulmonary and circulatory abnormalities that lead to vitamin depletion. there is a possibility. B12 deficiency, tumors, etc. [4,5] Currently, there are approximately 50 million people with AD worldwide, and this number is expected to double every five years to,152 million by 2050. expected. The burden of Alzheimer's disease affects individuals, their families and economies, with an estimated global cost of 4,444 US$1 trillion annually. There is currently no cure for Alzheimer's disease, but there are treatments that only improve symptoms [6,7] . The purpose of this review article is to briefly describe the diagnosis, pathology, causes, and current treatments of AD and to identify compounds that may prevent or treat AD by targeting

multiple pathogenic mechanisms. The emphasis is on recent developments. B. Aggregation and mis folding of A β and Tau, inflammation, oxidative damage, etc.

DIAGNOSTIC CRITERIA FOR ALZHEIMER'S DISEASE

Patients with suspected AD undergo several tests, including neurological examination, neuronal magnetic resonance imaging (MRI), clinical tests such as vitamin B12, and other tests, in addition to the patient's medical and family history. [8] . Vitamin (Vit.) B12 deficiency has long been associated with increased risk of neurological problems and Alzheimer's disease, according to several studies. A specific marker of Vit.B12 deficiency is elevated homocysteine levels, which can lead to brain damage due tooxidative stress, increased calcium influx, and apoptosis. Diagnosis of Vit. B12 deficiency can be determined by measuring serum Vit. B12 levels and blood count and serum homocysteine level tests [9,10] .

In 1984, the National Institute of Neurological Disorders and Communication Disorders (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA)established a working group to establish clinical diagnostic criteria for Alzheimer's disease(NINCDS-ADRDA) .These criteria include: (1) neuropsychological testing, progressive memory loss, impairment of activities of daily living, and other symptoms such as aphasia (language impairment), apraxia (language impairment); Possible Alzheimer's disease diagnosed with dementia confirmed by motor skills), and agnosia (loss of perception). All of these symptoms can appear by age 40 to 90, even in the absence of systemic or brain damage. They are not the main cause of dementia and (3) definite Alzheimer's disease confirmed by histo pathological confirmation by biopsy or autopsy [11,12]. In 2011, the National Institute on Aging-Alzheimer's Association made several changes and updated the 1984 NINCDS-ADRDA criteria to increase specificity and sensitivity in diagnosing Alzheimer's disease. Newly proposed criteria include possible and possible AD dementia for clinical use andpossible or possible AD dementia with patho physiological evidence for research purposes. Some include AD dementia. There are two categories of biomarkers for Alzheimer's disease. (a) brain amyloid markers such as positron emission tomography (PET) and cerebrospinal fluid (CSF), and (b) nerve damage markers such as cerebrospinal fluid tau and fluoro deoxyglucose (FDG).Magnetic resonance imaging (MRI) for metabolic activity and atrophy measurements [13,14,15].

ALZHEIMER'S DISEASE'S NEUROPATHY

There are two types of neuro pathological changes in AD that provide clues to disease progression and symptoms and include: (1) positive lesions (due to accumulation), accumulation of neuro fibrillary tangles and amyloid plaques; , dystrophic neurite markers, threads and other deposits found in brains of patients with neuropil AD.(2) Negative lesions characterized by massive atrophy (due to loss) plus neuronal, neuropil and synaptic loss. In addition, other factors can cause neuro degeneration, such as neuro inflammation, oxidative stress, and damage tocholinergic neurons [16,17,18].

STAGES OF ALZHEIMER'S DISEASE

The clinical stages of Alzheimer's disease can be divided into

(1) a preclinical or pre symptomatic stage, which can last several years or more; This stage is characterized by mild memory loss and early pathological changes in the cortex and hippocampus, without impairment of daily activities, and without the clinical signs and symptoms of AD.

(2) Patients with mild or early stages of AD who have several symptoms, such as difficulty in daily living with poor concentration and memory, disorientation to place and time, mood changes, and onset of depression.

(3) Intermediate stage AD in which the disease spreads to areas of the cerebral cortex, making it difficult to recognize family and friends, increasing memory loss, loss of impulse control, and difficulty reading, writing, and speaking.

(4) Severe AD or end-stage, including spread of disease across cortical areas with severe accumulation of neuritic plaques and neuro fibrillary tangles, leading to progressive functional and cognitive impairment, in which patients Unrecognizable to family members, may become bedridden with difficulty swallowing and urinating, and ultimately lead to patient death from these complications.

DEFINITION AND CHARACTERIZATION

Dementia is defined as the chronic, acquired loss of two or more cognitive abilities caused by brain disease or injury. This definition has been used in clinical practice for decades, although recent changes in the Diagnostic Statistical Manual, 5th Edition, have moved away from using the term dementia and have recognized that dementia can be present with impairment in a single domain (i.e. by this definition, a patient with a severe expressive aphasia could be classified as having dementia).Memory requires there acording, storage, and retrieval of information. The most common clinical presentation of AD is a slow onset and gradually progressive loss of memory, typically with inability tol earn new information and particularly autobiographical information, such as recent eventsin ones' life. This is because AD preferentially affects the brain networks involved in episodic memory. Examples of episodic amnesia include forgetting appointments, paying bills, and taking medications. People with AD usually repeat questions and conversations. The memory loss is often accompanied by subjective memory complaints. Difficulty recalling names which are recalled later, is common in aging but is not a typicalearly sign of dementia. Mild cognitive impairment (MCI) is defined by performance that islower than normal on objective neuropsychological testing of cognition, but with maintain daily functions (e.g., maintained abilities to function within society such as for daily activities at work, home, and in social settings, and maintained activities of daily living suchas for personal care) and therefore not consistent with dementia MCI can be categorized into "amnestic" MCI, in which reduced performance on memory is the key finding, versus"non-amnestic" MCI, in which reduced cognitive performance is in a non-memory domain such as language. MCI can also be characterized into "single domain" versus "multi-domain" MCI, in which multiple cognitive performance measures are impaired. MCI 6does not necessarily progress to dementia and the patient's cognitive status may become normal or fluctuate between MCI, normal cognition and dementia. Cognitive changes are associated with several neurodegenerative diseases (such as early stages of Lewy body disease), cerebro vascular diseases (e.g., intermittent small strokes), and psychiatric conditions (e.g., depression, anxiety). It also exists in some state. Drugs that affect cognition (eg, opioids) and variability in cognitive test scores.

DIAGNOSIS AND MANAGEMENT.

Clinical evaluations, differential diagnosis, and management of dementia most commonly occur in the primary care setting, with appropriate specialist input as needed. The 2014 US Preventive Services Task Force indicated that there was in sufficient evidence to evaluate the balance of benefits and harms for universal screening for cognitive impairment using formal screening instruments in community-dwelling adults age65 years and older. While the Task Force concluded that adequate evidence existed for some screening tools that have sufficiently high sensitivity and specificity for identifying dementia, there is no published evidence of the effect of screening For decisions or planning by patients, clinicians, or caregivers. However, report of memory complaints or rapidly-progressive cognitive problems over several months may indicate an underlying medical condition that warrants further evaluation with cognitive, laboratory, and other tests. Evaluation for possible dementia requires a brief medical history, cognitive, and neurological assessment. Medical history remains the most important diagnostic tool and should be obtained from both patients and close family members and friends. 5 Some of her patients complain of forgetfulness, others cannot recall details of their past medical history, and have pathognosi a (i.e., insight into their own illness). One clue that apatient has a memory problem occurs when the

person accompanying them provides the medical history. The history should characterize the nature, magnitude, and course ofcognitive changes. The nature refers to the cognitive domains affected. Is there loss of episodic memory (e.g., what the patient did that morning, yesterday, and last week), or language abilities (e.g., word finding difficulties with circumlocutions)? The magnituderefers to the severity: does the cognitive loss affect daily functions, such as the patient'sability to manage her own affairs (e.g., does she get lost while driving, not pay her bills,forget to take medications)? 12 Is it indolent onset and slow course (for neuro degeneration) or rapid onset and variable and slow course (for cerebrovascular disease)? brain damage (e.g., stroke, Parkinson's disease, head injury), and drugs that may impair cognition (e.g., hypnotics, anxiolytics such as benzodiazepines, analgesics such as codeine-containing drugs, tricyclic antidepressants). and anti cholinergics, such as bladder anti muscarinics). A familyhistory might identify young-onset dementia (onset in persons younger than 65 years) in first-degree relatives, suggesting one of the rare inherited genetic forms of dementia.

CLINICAL EVALUATION OF SUSPECTED DEMENTIA

DEMENTIA IS IDENTIFIED BASED ON:

• Cognitive and functional-focusedincluding family, friend, or caregiver medical history

• Ambulatory or bedside Brief cognitive assessment at Neuropsychological testing if indicated

DEMENTIA ETIOLOGY IS DETERMINED BASED ON:

• Medical history

➢ Neurologic history

➢ General medical history

➢ Family history

• Physical examination

➢ Neurological signs(e.g. cognitive impairment, focal signs, Parkinsonism, etc.)

➢ Associated systemic signs (e.g. vascular and metabolic disease)

• Neuropsychological testing

• Laboratory testing

➢ Thyroid function and vitamin B12 levels

➢ Other tests B. Metabolic, infectious, autoimmune and other etiologies.

• Structural brain imaging with CT or MRI

➢ AD: generalized or focal cortical atrophy, often asymmetric (hippocampal atrophy)

➢Vascular Contribution to Cognitive Impairment and Dementia: Stroke or White Matter Lesions

➢ Fronto temporal dementia: frontal lobe or anterior temporal lobe atrophy

➢ Other abnormalities such as brain mass (e.g., tumor) and hydrocephalus

• Referral to a specialist, for additional neurologic and medical testing, if specific etiologies suspected

➢ Brain tests: electroencephalogram [EEG]

➢ Vascular tests: head and neck magnetic resonance angiogram (MRA) or computed tomography angiogram (CTA)

➢ Cardiac tests: electrocardiogram [ECG], echocardiography, ambulatory cardiac rhythm monitoring

*Depending on the clinical presentation, consider blood tests for a CBC, ESR, chem 7 which includes a glucose level, renal and liver function tests, folic acid, and a RPR.

CONCLUSION

Alzheimer's disease is now recognized as a global health problem. Consequently, theNational Institute on Aging-Alzheimer's Association reclassified and updated hisNINCDS-ADRDA criteria of 1984 to provide specificity, sensitivity, and early detection of herpatients at risk of developing AD. improved. Several criteria have been proposed for a more accurate diagnosis ofAD, including clinical biomarkers, body fluids, and imaging studies. Nonetheless, treatment of AD remains symptomatic without altering disease prognosis. Inhibitors of the cholinesterase enzyme, such as galantamine, donepezil, and rivastigmine, and NMDA antagonists, such as memantine, improve memory and attention but do not impede progression. Several studies have shown that lifestyle changes such as diet and exercise can improve brain health and alleviate AD without medical intervention, and are considered first-line interventions for all AD patients. I'm here. Recently, studies have focused on targeting pathological hallmarks

of AD such as Aβ and p-tau.Future therapies such as disease-modifying therapies may alter AD progression by targeting the Aβ pathway. AN-1792, Solanezumab, bapineuzumab, semagacestat, avagacestat, and tarenflurbil are many agents in clinical trials, withshowing late-stage efficacy. Other DMTs are still under investigation, including aducanumab, gantenerumab, crenezumab, tideglusib, lithium and others targeting his Aβ and tau pathology. other. Other promising compounds, calledchaperones, such as heat shock protein and vacuolar sorting protein 35 (VPS35), help's other proteins function normally and reach their destination safely within th ecell. It can be used to treat neurodegenerative diseases because it works by Additionally, natural extracts used in Chinese folk medicine show great potential in treating AD by acting on multiple mechanisms. In conclusion, successful AD treatment depends on its early administration and monitoring of patients' disease progression using biomarker diagnostics. The use of future therapies and combination therapies that target tau pathology may have the potential to slow the progression of AD pathology.There is an urgent need to develop effective, selective and effective drugs to treat AD patients and those at risk of developing AD.

REFERENCES

1. De-Paula V.J., Radanovic M., Diniz B.S., Forlenza O.V. Alzheimer's disease. subcell.2 Biochemicals. 2012; 65:329-352. ドイ: 10.1007/978-94-007-5416-4_14. [PubMed][Cross Reference] [Google Scholar]
2. Cipriani G, Dolciotti C, Picchi L, Bonuccelli U. Alzheimer's disease and its disorders: a brief history of Nerve cell. Chemistry. outside. J. neurology. social ital. social clinical
3. Blass J. P. Alzheimer's disease. Dis. A month Dm. 1985;31:1-69.doi: 10.1016/0011-5029(85)90025-2. [PubMed] [Cross-Reference] [Google Scholar]
4. Terry R.D., Davies P. Alzheimer's dementia. Annual Revisio Neuroscience. 1980;3:77–95。10.1146/annurev.ne.03.030180.000453. [PubMed][Crossref] [Google Scholar]
5. Rathmann K.L., Conner C.S. Alzheimer's disease: clinical features, etiology, andtreatment. Drugsmart Clin. Pharm. 1984;18:684-691: 10.1177/106002808401800902. [PubMed] [Cross-Reference] [Google Scholar]
6. Yiannopoulou K.G., Papageorgiou S.G. Alzheimer's diseaseCurrent and future treatments of the disease: an update. J st. Nerve. system Dis. 2020:12.
7. Livingston G, Huntley J, Sommerlad A, Ames D, Ballard C, Banerjee S, Brayne C,Burns A, Cohen-Mansfield J, Cooper C, et al. Dementia Prevention, Intervention, andCare: The Lancet Commission 2020 report from. lancet. 2020;396:413-446 Doi: 1 Doi10.1177/1179573520907397. [PMC free article] [PubMed] [CrossRef] [Google Scholar
8. Schacter AS, Davis KL Alzheimer's disease. Dialogue Klin.Neuroscience. 2000;2:91-100. Doi: 10.1007/s11940-000-0023-0. [PMC free article] [PubMed][CrossRef] [Google Scholar]
9. Jatoi S, Hafeez A, Riaz SU, Ali A, Ghauri MI, Zehra M. Low vitamin B12 levels:minimal cognitive impairment andunderestimated causes of dementia. Cruz. 2020;12:e6976. Doi: 10.7759/cureus.6976. [PMC free article] [PubMed][CrossRef] [Google Scholar]
10. Cho HS, Huang LK, Lee YT, Chan L, Hong CT Suboptimal baseline vitamin B12 is associated with cognitive decline I patients with Alzheimer's disease receiving cholinesterase inhibitor therapy . front. Nerve cell. 2018; 9:325. doi: 10.3389/fneur
11. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM ClinicalDiagnosis of Alzheimer's Disease: Report of the NINCDS-ADRDA Working Group Sponsored by the Department of Health and Human Services Task Force on

Alzheimer's Disease Neurology. 1984;34:939-944. Doi: 10.1212/WNL.34.7.939

12. Neugroschl J., Wang S. Alzheimer's disease: diagnosis and treatment in the spectrum of disease severity. Mount Sinai J. Med. N. J. 2011;78:596–612.doi: 10.1002/msj.20279. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
13. McKhann G.M.、Knopman D.S.、Chertkow H.、Hyman BT、Jack C.R.、Jr.、Kawas C.H.、Klunk W.E.、Koroshetz WJ., Manly J.J., Mayeux R., et al.Diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Agin Association working group for diagnostic guidelines for Alzheimer's disease. Alzheimer's disease dementia. J. Alzheimer's Association. 2011;7:263–269.Doi: 10.1016/j.jalz.2011.03
14. Mayeux R., Stern Y. Epidemiology of Alzheimer's disease. Cold spring herb. perspective.Medical2012;2:a006239.ドイ: 10.1101/cshperspect.a006239. [PMC-freier Artikel] [PubMed][CrossRef] [Google Scholar]
15. Yaari R, Fleisher A.S., Tariot P.N. Updated diagnostic guidelines for Alzheimer's disease. 2011;13:11f01262.doi: 10.4088/PCC.11f01262. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
16. Serrano-Pozo A, Frog M.P., Masliah E., Hyman B.T. Neuropathological changes in Alzheimer's disease. Cold spring herb. perspective. Medicine 2011;1:a006189 doi:10.1101/cshperspect.a006189. [PMC free paper] [PubMed] [CrossRef] [Google Scholar]
17. Spiers-Jones T.L., Hyman B.T.Crossover of amyloid-beta and tau at synapses in Alzheimer's disease. neuron. 2014;82:756-771. Doi: 10.1016/j.neuron.2014.05.004. [PMC Free Article] [PubMed] [CrossRef] [Google Scholar]
18. Singh S.K., Srivastav S., Yadav AK., Srikrishna S., Perry G. An overview of Alzheimer's diseasedisease and several therapeutic approaches targeting Abeta using several synthetic and herbalcompounds. oxidized med cells. Longev. 2016; 2016:7361613.doi: 10.1155/2016/7361613. 10 [PMC free article] [PubMed] [CrossRef] [Google Scholar