ISSN: 2091-2749 (Print)
2091-2757 (Online)

Acetyl cholinesterase: a potential target for Alzheimer's disease intervention

Sandhya Khadka[1], Rajesh Basnet[2], Sandeep Shrestha[3], Yuchun Wang[4], Radheshyam Gupta[3,5]

[1]Dept. of Pharmacy, Hope International College, Purbanchal University, Lalitpur, Nepal; [2]Dept. of Pharmacy, Maharajgunj Medical Campus, TUTH, IOM, Kathmandu, Nepal; [3]Dept. of Urology , [4]Dept. of Pharmacy, Qiqihar Medical University, Heilongjiang ,China;[5]Dept. of General Surgery, Bariatric and Metabolic Surgery, Nepal Korea Friendship Municipality Hospital, Thimi, Bhaktapur, Nepal.

Abstract

Alzheimer's disease is a neurological disorder in which the death of brain cells causes memory loss and cognitive decline. The role of treatment is not limited to pharmacology, but also involves many factors, such as the psychological, social, and economic aspects of the patient and family. It is important to consider the use of AChe inhibitors in patients with mild to moderate AD, despite cost issues and in the absence of any other immediate progression. Although there are a lots of currently available inhibitor for acetyl cholinesterase but there is no selective potent inhibitor for AD. so, there is an urgent need discover of compounds that are active against Acetyl cholinesterase, along with there is need of molecular modeling for identifying functional groups that may be important for inhibiting Acetyl cholinesterase activity.

Keywords: Alzheimer's disease, dementia, Cholinesterase, neurodegenerative

Correspondence
Dr. Radheshyam Gupta
Nepal Korea Friendship Hospital, Thimi, Bhaktapur, Nepal
Email: radheshyam130@yahoo.com

Peer Reviewers
Prof. Dr. Nabees Man Singh Pradhan
Patan Academy of Health Sciences

Prof. Dr. Jay N Shah
Patan Academy of Health Sciences

Submitted
16 Mar 2020

Accepted
20 May 2020

How to cite this article
Sandhya Khadka, Rajesh Basnet, Sandeep Shrestha, Yuchun Wang, Radheshyam Gupta. Acetyl cholinesterase: a potential target for Alzheimer's disease intervention. Journal of Patan Academy of Health Sciences. 2020Aug;7(2):95-97.

DOI:
https://doi.org/10.3126/jpahs.v7i2.31130

Introduction

Alzheimer's disease (AD) is a progressive degenerative brain disease of unknown origin with atrophy of the cerebral cortex, including plaques and tangles of nerve granules.[1] It develops with age, although there is no evidence that it is caused by the ageing process and is linked to genetics, lifestyle, and environmental factors that affect brain cells over time. In the initial stages of the disease, arise from forgetfulness and mild confusion. As time goes on, recent memories begin to fade. It manifests itself in memory loss, personality change and eventually dementia.[2]

Pathogenesis, Clinical features, Role of acetylcholinesterase inhibitors and Recent developments

Pathogenesis- Alzheimer's disease is associated with a lack of acetylcholine (ACh), a neurotransmitter in the brain. The ACh is regulated by the hydrolytic enzyme acetyl cholinesterase (AChE), which rapidly degrades ACh both in the periphery and the brain.[3] The Ach also inhibits the release of cytokines by the cholinergic anti-inflammatory pathway. The abnormal cholinergic system is associated with mental impairment and a series loss of cholinergic function in the central nervous system and contribute to cognitive symptoms.[4]

Clinical features- The preclinical stage of AD is unclear, without reliable symptoms and signs for early diagnosis before the irreversible manifestation. In the mild dementia stage, difficulties with declarative memory are prominent; depressive symptoms are not infrequent, but the patient manages to live alone.[5] Supervision is needed in the moderate dementia stage as other cognitive domains are affected, together with non-cognitive functions. In late stage with neurological disturbances, a complete dependence is typical of the illness. The life expectancy of patients is reduced, but the period of relative well-being may be prolonged with symptomatic treatment.[6,7]

Role of acetylcholinesterase inhibitors - Understanding the structure of AChE is essential for its high catalytic efficiency and the molecular basis for ACh recognition by other ACh binding proteins (ACh receptors), and the pharmacological and toxicological mechanisms of the drugs. The use of AChE inhibitors (AChEIs) is one aspect of the treatment regimen for AD.An integrated approach that combines drug therapy with multidisciplinary team assessments, community supports are important. Early use of AChe inhibitors helps in the overall assessment and diagnosis of AD, as not all patients are responsive to treatment. Families and caregivers need to be aware of the limitations of treatment.[8]A good discussion at the beginning of treatment can help avoid misunderstandings. Together with pharmacology treatment, the psychological, social, and economic aspects of the patient and caregiver are an important consideration. The use of AChe inhibitors in mild to moderate AD may be considered despite the cost issues.[9]

Recent developments- To date, none of the pharmacological agents has shown a clear benefit to AD patients. The AChEIs can directly inhibit the production of cytokines by microglia and monocytes. Hence, it's efficacy in part is because of the anti-inflammatory effects. The effect of AChEIs can be achieved by enhancing the transmission of AChE drug form neurons to neurons. The imbalance between the generation and removal of amyloid-β (Aβ) is an early and emerging factor in Alzheimer's disease.[10]

In AD, female morbidity is twice as high as male and terminal symptoms may vary from person to person. Medication can temporarily relieve some symptoms or slow the progression of the disease in some people. Despite various advancements, AD remains a problem world-wide and requires further development in therapies and treatments.[11]

Conclusion

There are a lot of acetyl cholinesterase inhibitors in use, but lacks selective potent inhibitor for the management of Alzheimer's disease. Further characterization of available compounds for selectivity and key protein-ligand interactions is needed.

Acknowledgements

I would like to thank everybody important to the successful completion of this review article.

Conflict of Interest

None

Funding

None

Author Contribution

We declare that all the listed authors have participated actively in the review study.SK and RB designed the review, conducted a literature search, wrote and revised the manuscript, read and approved the final manuscript by SS, YW and RG. At the end of the study, all authors have read and approved the manuscript.

Reference

1. Mayeux R. Epidemiology of neurodegeneration. Annu Rev Neurosci. 2003;26:81-104. DOI | PubMed | GoogleScholar | PDF |Weblink
2. Masters CL, Bateman R, Blennow K, Rowe CC, Sperling RA, Cummings JL. Alzheimes disease. Nat Rev Dis Primers. 2015;1:15056. DOI | PubMed | GoogleScholar | Weblink
3. Candeias E, Duarte AI, Carvalho C, Correia SC, Cardoso S, Santos RX, Plácido AI, Perry G, Moreira PI. The impairment of insulin signaling in Alzheimer's disease. IUBMB life. 2012;64(12):951-7. DOI | PubMed | GoogleScholar | Weblink
4. Wenk GL. Neuropathologic changes in Alzheimer's disease. J Clin Psychiatry. 2003;64(Suppl 9):7-10.PubMed | GoogleScholar |Weblink
5. Perry EK, Tomlinson BE, Blessed G, Bergmann K, Gibson PH, Perry RH. Correlation of cholinergic abnormalities with senile plaques and mental test scores in senile dementia. Br Med J. 1978;2(6150):1457-9.DOI | PubMed | GoogleScholar | PDF |Weblink
6. Forstl H, Kurz A. Clinical features of Alzheimer's disease. Eur Arch Psychiatry Clin Neurosci .1999;249:288-90. DOI | PubMed | GoogleScholar |Weblink
7. McDaniel KD, Kazee AM, Eskin TA, Hamill RW. Tardive dyskinesia in Alzheimer's disease: clinical features and neuropathologic correlates. J Geriatr Psychiatry Neurol. 1991;4(2):79-85.DOI | PubMed | GoogleScholar | PDF
8. Momeni P, Pittman A, Lashley T, Vandrovcova J, Malzer E, Luk C, et al. Clinical and pathological features of an Alzheimer's disease patient with the MAPT Delta K280 mutation. NeurobiolAging. 2009;30(3):388-93.DOI | PubMed | GoogleScholar | PDF |Weblink
9. Szeto JY, Lewis SJ. Current treatment options for Alzheimer's disease and Parkinson's disease dementia. CurrNeuropharmacol . 2016;14(4):326-38. DOI | PubMed | GoogleScholar | PDF | Weblink
10. Colović MB, Krstić DZ, Lazarević-Pašti TD, Bondžić AM, Vasić VM. Acetylcholinesterase inhibitors: pharmacology and toxicology. CurrNeuropharmacol. 2013;11(3):315-35.DOI | PubMed | GoogleScholar | PDF | Weblink
11. Abbasowa L, Heegaard NH. A systematic review of amyloid-β peptides as putative mediators of the association between affective disorders and Alzheimers disease. J Affect Disord .2014;168:167-83. DOI | PubMed | GoogleScholar | Weblink