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Review Article

Anti-Cholinesterase Drugs and Its Effects in Alzheimer Disease, And Its Impacts Mainly Targeting Dementia in The Patients

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ABSTRACT

Alzheimer's disorder [AD] is a social and health care problem. The use of anti-cholinesterase has shown effect on decreasing dementia by increasing the levels of neurotransmitter Acetyl choline. We know that the cholinergic system plays an essential role in learning and memory. Some common anti-cholinesterase is donepezil, galantamine, rivastigmine. These drugs are the alkaloids which are isolated from natural sources such as physostigmine, have been recognized as acetyl and butrylcholinestrase inhibitors. Some other natural alkaloids belonging to steroidal and indole class (Amaryllidaceae, Buxaceae) have shown anti-enzymatic properties. These Anticholinesterase are also given combination, like donepezil and galantamine (DonGal) and berberine and tacrine (BerTac). This review article delves into the use of anticholinergic treatment in AD and also throws light on "Cholinergic Hypothesis". However, there is a need of further studies on this class of drugs and better knowledge of biomarkers will further shed a light on the progression of the disease as well as action of the drug.


INTRODUCTION

Alzheimer's is a neurodegenerative disease which mostly effects the elderly people, mostly individuals over the age of 65 years. Around 50 million people are suffering from dementia. The World Health Organization (WHO) has estimated that around 81.1 million dementia cases will occur in developing countries by 2040 due to aging population. AD patients suffer from memory loss,

confusion, cognitive decline, periods of memory loss. It interferes with their daily activity, problem solving, language and other thinking problems. Some of the warning signs associated with dementia are, change in abstract thinking, poor judgement, misplacing things, remembering and reasoning etc. AD is a progressive disease in which there is reduction of signaling from the neurotransmitter acetylcholine (Ach). The brain is

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responsible for many functions and a neurotransmitter called acetylcholine helps the brain cells to communicate with each other, when these cells can't communicate properly some brainy functions such as thinking, judgement and physical movements are affected. There are many factors which cause dementia such as Parkinson's disease, severe head injury, Huntington's disease

and genes (inherited), but the exact pathogenesis of AD is still unknown. Anti-cholinergic (ChEIs) are either of synthetic or of plant origin. They provide symptomatic rather than curative benefit, but they also show many undesired side effects such as blurred vision, dilated pupils increased heart rate.

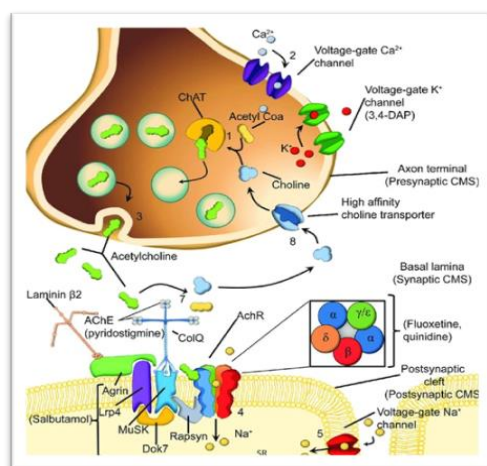
SYMPTOMS OF ALZHEIMER'S



Cholinergic Hypothesis

The cholinergic hypothesis was initially presented over 20 years ago. It suggests that the cognitive impairment seen in people with advanced age and Alzheimer's disease is significantly caused by acetylcholine-containing neurons malfunctioning in the brain. The involvement of additional transmitters in later stages of Alzheimer's disease broadens the search for a long-term treatment option beyond the cholinergic system. However, the cholinergic hypothesis still warrants research in order to learn more precisely how the human

brain cholinergic system affects memory. The vast majority of scientists assume that changes to the cholinergic system did not make a significant contribution to the etiology of AD. This result seems to have been impacted by early clinical finds of cortical cholinergic cell loss in patients with severe AD. An effective approach for investigating the operation of the basal forebrain cholinergic system has recently been created, allowing for the selective removal of basal cholinergic neurons using immunotoxin.

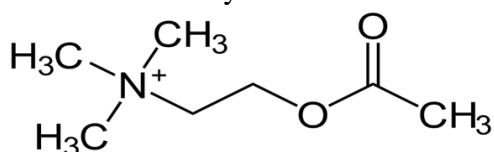


Anti-cholinesterase

Anticholinergics (anticholinergic agents) are chemicals that prevent the neurotransmitter acetylcholine (ACh) from acting at synapses in the central and peripheral nervous systems. These drugs specifically prevent ACh from attaching to its receptor in nerve cells, hence suppressing the parasympathetic nervous system. The smooth muscles in the gastrointestinal tract, urinary tract, lungs, sweat glands, and many other regions of the body move involuntarily due to the parasympathetic nervous system.

Anticholinergics are classified according to the receptors that are affected:

- ❖ The muscarinic acetylcholine receptors are the target of antimuscarinic medications. Antimuscarinics make up the majority of anticholinergic medications.
- ❖ The nicotinic acetylcholine receptors are the target of antinicotinic drugs. The majority of these are structurally linked to curare and are non-depolarizing skeletal muscle relaxants for surgical use. A few are depolarizing substances. As Acetylcholine levels are already low in Alzheimer's patients, Anticholinergic medicines inhibit the activity of acetylcholine, a neurotransmitter involved in memory and learning. ChEIs requires titration to achieve its efficacy typically with an increased drug dose after four weeks. At initial there is a risk of idiosyncratic (ADR). There might be neurobiological adaptation and drug tolerance in chronically dosed patients, which might further need increased level of dosing. So, we doctors opt for lowest level of dosing as it still achieves therapeutic efficacy and reduce the induction of toxicity.



We can also opt for combination therapy. They can provide fixed dose of two or more pharmaceutical agents within a single dosing entity. By opting for combination therapy we can reduce the side effects, delay resistance to the drug, deliver faster results and also provide quality of life. But it should be noted that, it also increases the risk of interactions.

Objective

The sole objective of anticholinergic treatment for dementia revolves around managing symptoms, giving the patient a quality of life. They also include symptomatic management in which the drugs aim to reduce the symptoms of Alzheimer such as hallucination, confusion and behavioral disturbance. Although anticholinergic doesn't cure AD but it can improve the patient's cognitive function to some extent and help prolong independence. The treatment also helps individuals to maintain the ability to perform daily activities without any hindrance. By managing symptoms like aggression and agitation, it can provide a safer environment for the caregivers and patients themselves.

CONCLUSION

The use of anticholinergic in the treatment of AD is a complex topic. They have the potential benefits in managing symptoms like aggression and behavioral disturbances, they come with significant risks, primarily the exacerbation of cognitive decline and confusion. Therefore, the decision to use anticholinergic drugs in AD should be approached with extreme caution. It should involve a thorough risk-benefit analysis and close monitoring by health cares. The major drawback of anticholinergic drugs is regarding their cost-effectiveness. Some combination therapies are costly which can't be affordable for patients with low income, but there are many advantages of combination therapy as many patients struggle with drug regimens, especially when dealing with multiple chronic conditions.

The evolving landscape of AD research and treatment offers promising alternatives to anticholinergic drugs. Advances in disease-modifying therapies, early diagnosis and personalized treatment plans offer for more effective and safer ways to manage AD in the future.

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