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ALZHEIMER'S DISEASE: A COMPREHENSIVE REVIEW OF PATHOPHYSIOLOGY AND MANAGEMENT APPROACHES

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ABSTRACT

Alzheimer's disease (AD), a progressive neurodegenerative disorder, is the most common cause of dementia among the elderly. Characterized by memory loss, cognitive decline, and personality changes, AD remains incurable, posing significant challenges in geriatric healthcare. This article reviews the pathophysiology, risk factors, diagnostic tools, and current treatment modalities, highlighting the potential of integrating Ayurvedic therapies with modern medical approaches for improved management strategies.

INTRODUCTION

Alzheimer’s disease is an irreversible condition that progressively destroys memory, thinking abilities, and the ability to carry out simple tasks. Affecting millions globally, AD predominantly impacts people aged 65 and older. The prevalence rate in India is approximately 7.4%, with over 3.69 million cases reported. AD was first described by Dr. Alois Alzheimer in 1906, following his observations of a patient named Auguste Deter.

Pathophysiology

The disease is marked by two hallmark pathologies:

Beta-Amyloid Plaques: Dense deposits of proteins and cellular material accumulating outside neurons, leading to synaptic dysfunction.

Neurofibrillary Tangles (NFTs): Twisted fibers of hyperphosphorylated tau protein inside neurons, disrupting neuronal transport systems.

Other contributing factors include oxidative stress, mitochondrial dysfunction, inflammation, and cholinergic deficits, all leading to progressive neuronal death.

Risk factors: Several factors increase susceptibility to AD, including:

Age: Predominantly affects individuals above 65 years.

Genetics: Mutations in genes such as PSEN1, PSEN2, and APP are linked to early-onset AD, while the APOE4 allele increases risk in late-onset cases.

Lifestyle factors: Obesity, diabetes, hypertension, and low education levels are associated with higher risk.

Symptoms and Stages: Symptoms progress through three stages:

1. **Mild stage:** Recent memory loss, mood changes, and language difficulties.
2. **Moderate stage:** Behavioral changes, confusion, and inability to learn new information.
3. **Severe stage:** Complete loss of recognition, verbal skills, and daily functioning, often leading to death within 3–10 years of diagnosis.

Diagnosis

AD diagnosis relies on cognitive testing, imaging techniques like CT or MRI scans, and biomarkers from cerebrospinal fluid. The Mini-Mental State Examination (MMSE) is commonly used, with scores below 24 indicating cognitive impairment.

Treatment approaches

1. Pharmacological treatments

Cholinesterase inhibitors (e.g., donepezil, rivastigmine) enhance cholinergic function but provide only temporary relief.

NMDA receptor antagonists (e.g., memantine) reduce glutamate-induced excitotoxicity.

2. Non-Pharmacological approaches

Regular physical activity and cognitive stimulation through activities like crossword puzzles and reading slow disease progression.

A healthy diet and social interactions improve overall well-being.

3. Ayurvedic perspective on managing alzheimer's disease

Ayurvedic therapies aim to control Alzheimer's disease by addressing the root causes, such as oxidative stress, neuroinflammation, and neurodegeneration, which are pivotal in the disease's progression. While not curative, these interventions focus on slowing the disease's progression, enhancing cognitive functions, and improving the quality of life. Below are key Ayurvedic and herbal interventions with their active constituents and mechanisms:

1. Ginkgo biloba[1]

Active constituents: Flavonoids (Quercetin, Kaempferol), Terpenoids (Ginkgolides).Ginkgo biloba is known to improve blood flow to the brain, reduce oxidative stress, and protect against neuroinflammation by scavenging free radicals. It inhibits beta-amyloid aggregation and supports cognitive functions.

2. Galanthus woronowii

Active constituents: Galantamine.

Galantamine, a natural cholinesterase inhibitor, improves cholinergic neurotransmission, stabilizing memory and cognitive functions. It enhances synaptic plasticity and prevents neuronal damage.

3. Curcuma longa (Turmeric)[2]

Active constituents: Curcumin.

Curcumin has potent anti-inflammatory and antioxidant properties, reducing amyloid-beta plaque deposition. It modulates microglial activity, thereby controlling neuroinflammation and oxidative damage.

4. Centella asiatica (Brahmi)[3]

Active constituents: Triterpenoids, Asiaticoside.

This herb enhances memory and cognitive functions by promoting dendritic growth and reducing beta-amyloid plaques. It also exhibits neuroprotective effects by enhancing antioxidant enzyme activity in the brain.

5. Withania somnifera (Ashwagandha)

Active constituents: Withanolides, Withaferin A.

Ashwagandha reduces oxidative stress and inflammation while promoting the degradation of amyloid-beta plaques. It also protects against neuronal loss and improves synaptic function.

6. Bacopa monnieri (Brahmi)

Active constituents: Bacosides A and B.

Bacopa monnieri enhances synaptic activity, reduces oxidative stress, and prevents beta-amyloid aggregation. It is widely recognized for its ability to improve memory and cognitive performance.

7. Vinca minor (Periwinkle)

Active constituents: Vinpocetine.

Vinpocetine improves cerebral blood flow, protects against neuroinflammation, and reduces excitotoxicity by modulating glutamate pathways. It supports neural integrity and delays cognitive decline.

8. Allium sativum (Garlic)[4]

Active constituents: Allicin, Sulfur compounds.

Garlic exhibits antioxidant and anti-inflammatory properties. It reduces cholesterol levels, improving cerebral circulation and protecting neurons from oxidative stress.

9. Coptis chinensis (Chinese Goldthread)[5]

Active constituents: Berberine.

Berberine enhances neuronal survival by reducing neuroinflammation and oxidative stress. It inhibits tau protein hyperphosphorylation, preventing neurofibrillary tangle formation.

10. Rosmarinus officinalis (Rosemary)

Active constituents: Rosmarinic acid, Carnosic acid.

Rosemary stimulates memory and concentration by modulating neurotransmitter activity. It protects neurons from amyloid-beta toxicity and oxidative stress.

DISCUSSION

Alzheimer's disease remains a challenge due to its progressive nature and the lack of a cure. Current pharmacological treatments target symptoms but fail to address disease progression. Ayurvedic interventions offer a complementary approach by targeting underlying pathophysiological mechanisms, including neuroinflammation and oxidative damage. An integrated approach combining Ayurvedic therapies with modern medicine could pave the way for improved management strategies, though further research and clinical trials are needed to validate these findings.

CONCLUSION

While a definitive cure for Alzheimer's disease is yet to be found, combining Ayurvedic insights with modern medical advancements offers hope in managing the disease more effectively. This integrative approach not only aims to alleviate symptoms but also seeks to address the disease's root causes, improving the quality of life for patients and caregivers alike.

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