

Dementias Staving Off the Aging Process

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Objectives

- Brief overview of Dementias epidemiology, etiology, and progression of disease
- Review non-pharmacological interventions utilized for the prevention or reducing the progression of dementia's.
- Discuss pharmacological options available for combating the progression of dementia's.
- Explore usefulness of alternative medicines in the disease processes of dementia.

Dementias Overview

- Classification of Dementias
 - Alzheimer's Disease
 - Vascular Dementia
 - Parkinson's Disease related dementia
 - Lewy Bodies Dementia
 - Frontotemporal Dementia
- Epidemiology
 - 4.5 million Americans afflicted with AD
 - Most prevalent in persons >65 years of age
 - Survival after onset of symptoms is an average of ~8 years; reducing lifespan by ~50% compared to persons without AD

Dementias Overview

- Etiology
 - Genetics
 - Apolipoprotein E
 - Presenilin protein mutations
 - Variation of angiotensin-converting enzyme gene
 - Environmental Factors
 - Age
 - Reduced reserve capacity of brain
 - Head injury
 - Vascular Risk Factors

Dementias Overview

- Progression of Disease
 - Neuroanatomical
 - Development of signature lesions- neuritic plaques and neurofibrillary tangles
 - Neuron degeneration and cholinergic pathway destruction
 - Clinical Presentation
 - Cognitive decline progressively worsening over time
 - Difficulty with finances, food preparation, etc.
 - Behavioral disturbances can occur in more moderate stages
 - Loss of daily functioning
 - Incontinent, unable to speak, mobility issues, etc.

Non-Pharmacological Treatments

- Modifying vascular risk factors such as dyslipidemia, hypertension, atherosclerosis, smoking, obesity, and diabetes through dietary and lifestyle changes
- Physical Activity
 - Supported by observational studies
 - RCT of 6 months of home exercise regimen versus usual care showed improvement on the ADAS-Cog
- Cognitive Training
 - Reality orientation, cognitive retraining, skills training produce short term cognitive improvements

Pharmacological Treatments Acetylcholinesterase Inhibitors

- Available Products
 - Aricept® (donepezil)- tablet, solution, ODT
 - Exelon® (rivastigmine)- capsule, solution, patch
 - Razadyne® (galantamine)- tablet, extended-release capsule, solution
 - Cognex® (tacrine)- capsule
- Indication
 - Mild to Moderate AD; donepezil approved for use in severe AD
- ADRs
 - Gastrointestinal (nausea, vomiting, and diarrhea)

Pharmacological Treatments N-Methyl-D-Aspartate Receptor Antagonist

- Available Products
 - Namenda® (memantine)- tablet, solution
- Indication
 - Moderate to severe AD
 - Used adjunctively with cholinesterase inhibitors
- ADRs
 - Dizziness, headache, and diarrhea/constipation

Alternative Medicine Tocopherol (Vitamin E)

- MOA- Free radical scavenger resulting in antioxidant properties
- Efficacy
 - Maybe beneficial in AD (not mild cognitive impairment) but patients also found to be at higher risk for heart failure
 - Currently not recommended based on a lack of adequate trials
- Dosing
 - 2000 IU per day in divided doses
- ADRs
 - Gastrointestinal cramps, diarrhea, nausea, dizziness, and risk of bleeding

Alternative Medicine NSAIDS

- MOA- Reduction in cytokine-mediated inflammatory processes may reduce risk of neurodegeneration associated with development of dementias
- Efficacy
 - Epidemiological studies have shown a risk reduction between long term use of NSAIDs and cognitive decline
 - Randomized clinical trials do not generate similar findings
- Dosing varies based on agent
- ADRs
 - Gastritis, GI bleeding risk, and abdominal pain

Alternative Medicine Estrogen

- MOA- Neuroprotective effects on neural cells by stimulating axon and dendritic growth, promotion of cholinergic activity, increase cerebral blood flow and modulating expression of apoE gene
- Efficacy
 - WHI studies found incidence of dementia nearly double in treatment groups
- Dosing
 - 0.625mg/day of conjugated estrogen; +/- 2.5mg/day MPA
- ADRs
 - Increased risk of breast cancer, stroke, heart disease, and pulmonary embolism

Alternative Medicine Vitamin B12 and Folic Acid

- MOA- reduces level of homocysteine; thought to reduce cognitive decline or worsening of AD
- Efficacy
 - RCT involving 340 patients found no improvement or slowing of cognitive decline with high dose supplementation
 - May be beneficial in patients with high homocysteine levels
- Dosing
 - High Dose: 5mg folate + 25mg B6 + 1mg B12
 - Folic acid ranged from 750mcg- 15mg/day
- ADRs
 - Well-tolerated; blurred vision, depression

Future Treatment Options

- HMG-CoA Reductase Inhibitors
 - Atorvastatin
 - Simvastatin
- Phase III Clinical Trials
 - Gamma- Secretase Inhibitors
 - Anti-Amyloid Beta peptide agents
 - 5-HT_{1A} antagonist

Assessment Questions

1. True or False. Modifying vascular risk factors such as blood pressure can help to reduce risk of developing dementia?
2. True or False. Vitamin E has been found to be beneficial in patients with mild cognitive impairment.
3. True or False. New therapies are targeting the reduction of amyloid precursor protein, a component responsible for plaque build-up in Alzheimer's Disease.

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