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A REVIEW OF NUTRITIONAL EFFECTS ON COGNITIVE DECLINE AND PROGRESSION TO DEMENTIA

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ABSTRACT

Dementia is characterised by progressive loss of memory leading to impairment of daily activities and deficiency in social interaction**.** With increasing life expectancy, the prevalence of dementia will increase in the next few decades, and will have a phenomenal emotional and economic impact. Diet and nutrition is becoming the potential modifiable contributor on age associated cognitive decline. A greater adherence to Mediterranean diet (Me Diet) shown reduced incidence of Alzheimer's disease. In a number of studies the association between Dietary approach to stop hypertension and Mediterranean Diet with age related cognitive changes were examined. In this article we review the various possible nutritional factors and actions of dietary components and patterns on cognitive decline and dementia.

KEYWORDS: Dementia, cognitive decline, nutrition, Alzheimer's disease, aging, diet.

INTRODUCTION

All cause dementia is defined as decline in cognitive function, severe enough to impair a person's ability to conduct instrumental activities of daily living. Dementia is one of the

disabling disorders affecting adult and elderly populations. With increasing life expectancy, the prevalence of dementia will increase in the next few decades, and will have a phenomenal emotional and economic impact. Thus, cognitive impairment and dementia are one of the major public health concerns in the 21st century. There are about 47 million dementia patients worldwide with about 8 million newly diagnosed cases annually. In India 1.8 million people are affected with dementia. Dementia is characterised by progressive loss of memory leading to impairment of daily activities and deficiency in social interaction. The treatment of dementia is basically directed towards management of cognitive and behavioural symptoms of dementia. Particularly effective treatments are available for most common symptoms of dementia.[1-2]

About 60-75% of them have Alzheimer's disease followed by vascular and Lewy bodies dementia.[1,2] With increasing life expectancy the prevalence of dementia will increase in next few decades and will have a phenomenal emotional and economic impact. Hence dementia and cognitive impairment are the major health concerns in the 21st century.to improve the behavioural symptoms and for delaying cognitive decline associated with dementia various drugs are used. Acetyl cholinesterase inhibitors such as Donepezil, Galantamine and Rivastigmine are recommended in mild to moderate case of dementia. Memantine or Memantine in combination with acetyl cholinesterase inhibitors are used for severe cases of dementia. For behavioural symptoms in patients with dementia the atypical antipsychotics such as Olanzapine, Quetiapine, Risperidone and Clozapine are the first line pharmacological treatments.[1-2]

Diet and nutrition is becoming the potential modifiable contributor on age associated cognitive decline [3].Various micro nutrients, minerals, vitamins and dietary essential fatty acids forming neuronal membranes with various actions have been studies [4-6].Various dietary patterns and nutritional factors form synergistic interaction of different components present in a food pattern.[7]

In this article we review the various possible nutritional factors and actions of dietary components and patterns on cognitive decline and dementia.

Possible metabolic and molecular mechanisms contributing to dementia and cognitive decline

Obesity in adulthood

The traditional risk factors for the development of cognitive decline and AD are cardiovascular disease and type 2 diabetes mellitus.[8] Central obesity, hyperglycaemia, hypertension, artherogenic, dyslipidemia, prothrombotic state is responsible for accumulation of visceral adiposity in midlife associated with overeating and sedentarism [9] with deleterious consequences in late life.

Overweight can lead to vascular consequences such as hypertension, dyslipidaemia and type 2 diabetes mellitus which are risk factors for dementia [8].In obese patients, high level of amyloid proteins have been found which lead to cognitive decline or dementia. A longitudinal study reported that being obese in midlife may cause lower blood brain barrier integrity.[10]

Outsize adipose tissue leads to accumulation and activation of macrophages which trigger neuroinflammation and immune cells present in adipose tissue may secrete proinflammatory factors and acute inflammatory cytokines which cause low grade chronic inflammation.[11] Saturated fatty acids induce inflammatory responses in microglia with production of nuclear factors kappa B (NF-KB).this leads to apoptosis of neurons involved in central regulation of energy balance, BP, body weight ,central and glucose homeostasis.[12]

Chronic Metablic Inflammation and Oxidative Stress

Age related degenerative disease is characterised by a pro-oxidant, pro-inflammatory state which result in harmful damage on cellular components. Brain is more susceptible to oxidative damage, since cerebral metabolism needs large amount of energy and is dependent on aerobic conditions as well as it is rich in polysaturated fatty acids which are oxidisable and transition metals which facilitate free radical generation.[13]

Comparing to other body structures the brain has four levels of anti-oxidant systems .This might increase the chances of brain tissue damage due to neurotoxic peptide accumulation such as amyloid Beta[13].Innate immune responses are initiated with the production of inflammatory mediators due to the binding of aggregated and misfolded proteins to microglia toll like receptors. Neuroinflammation is an protective mechanism, it becomes harmful when not controlled and chronic by increased release of free radical, nitric oxide, complementary

factors, cytokines or excitatory amino acids,[14] Beta amyloid accumulation causes neuroinflammation thus leading to injury.[15]

Autophagy and Prothrombotic State

Autophagy involves clearance of misfolded proteins and aggregate such as amyloid whose efficiency declines with aging and altered in dementia.[16]

The vascular disorder such as decreased blood flow cerebrovascular dysfunction and blood brain barrier disruption and prothrombotic state such as clot formation, activated platelets, decreased fibrinolysis may cause other factors which contribute to dementia or cognitive decline. Fibrinogen accumulates within Beta amyloid, which promotes B amyloid fibrillation and generation of fibrin which is resistant to degradation. In recent studies when AD patients were compare with that of controlled subjects higher levels of platelet activating factor, acetyl hydrolase activity and oxidised LDL were found.[17]

Effect of dietary components and supplements on cognitive decline and alzheimer's disease

Omega-3- fatty acids

The polysaturated fatty acids are essential components of neuronal cell membranes, it maintain membrane fluidity for synaptic vesicle fusion and neurotransmitter communication. They might be precursor for lipid messengers for the signalling processes to promote neuroprotection or neuronal damage.[18]

In the hippocampus, cortex and cerebellum there is evidence of PUFAs deficit in the aged brain which get worse in AD.[19] Observational evidence has been focused on association between long chain omega-3- fatty acids and cognitive functioning, cognitive decline or dementia.[19]

Magnesium

Magnesium is essential in synaptic conduction, it has effects on stability and viscosity of cell membrane and effects NMDA receptors respond to excitatory amino acids.[20]

Deficiency of magnesium may cause increase in free radical production in tissues increased oxidative tissue damage, increased superoxide anion production by inflammatory cells as well as decrease in cellular and tissue oxidant levels.[21-22]

Tea, Epigallocatechin 3 Gallate (Egcg) and Caffeine

A traditionally indicated cognitive stimulator is tea in Asian countries. Stimulant effect has been confirmed in some studies and is linked to antioxidants contain in the EGCG, L-theanine and caffeine.[23] Tea may also exert neuroprotective action by regulation of stress hormones and inhibition of acetyl cholinesterase.[24]

In animal models of AD, there is evidence of anti-oxidant and B amyloid suppressive properties of caffeine. In this study reduction in amyloid plagues were seen and was associated with stimulation of protein kinase A activity, increased phosphor-CREB levels and reduced phosphor-ERK expression in the animal models.[25-27]

In a case controlled study of older persons with mild cognitive impairment it is reported that high serum levels of caffeine were associated with lack of progression of dementia.[28]

Flavonoids

Flavonoids are found in variety of fruits vegetables and beverages is capable of influencing different aspects of synaptic plasticity which result in improved memory and learning in animals and humans.[29] there are evidences suggesting dietary flavonoids could delay onset or slow the progression of AD.[30]

Resveratrol

Resveratrol is a polyphenol contained in brains. It has antioxidant and anti-inflammatory properties.[31] Studies in AD animals model have shown decreased hippocampal and increased memory performance but the clinical trials in human on cognition of resveratrol are limited.[31]

Vitamins

In a randomised trial from physicians health study and physicians health study II, there were no significant effect seen in cognitive function with short term beta carotenes treatment but with long term administration beneficial effects were seen [32].In randomised control trial showed no significant effect on cognitive function by the administration of supplementation with folic acid vitamin B6 and B12.[33]

Conversely in another randomised control trial in persons aged 60-74 years reported that folic acid and vitamin B12 were beneficial in improving cognitive test [34].In a age related eye

disease study of 6-9 years reported that combination of antioxidant vitamins such as vitamin C, vitamin E, beta-carotene, zinc and copper has no significant effect on cognitive function[35]

Dietary Patterns

A greater adherence to Mediterranean diet(Me diet) shown reduced incidence of Alzheimer's disease.[36] A systematic review of longitudinal cohort of association of mediterranean diet with MCI and AD have found that higher adherence to Mediterranean diet has lower risk of MCI or AD.[37]

In a prospective study the association between DASH and Mediterranean Diet with age related cognitive changes were examined. Higher adherence to DASH and Me Diet were significantly associated with higher MMSE scores [38].The ketogenic dietary pattern are associated with neuroprotective effects in some form of epilepsy but there is no current evidence on Alzheimer's disease. In two cohort sub-studies of the Adventist health study incidence of dementia in those consuming vegetarian diet and meat eating diet were compared .The first showed that those who ate meat has twice chance of having dementia than vegetarians .Second study reported no significant result in incidence of dementia between vegetarians and meat eating subjects.[39]

CONCLUSION

In a number of studies the association between Diet and age related cognitive changes were examined. Several medical conditions such as Cardiovascular diseases, Diabetes Mellitus, obesity are closely related to decline in cognitive function. The pathological mechanisms associated with normal ageing including oxidative stress, neuroinflammation and vascular dysfunction are the same as those contributing to the development of neurological diseases. However, in these pathological conditions, the mechanisms contributing to ageing are triggered by different genetic or environmental factors. Diet and nutrition is becoming the potential modifiable contributor on age associated cognitive decline .Various micro nutrients, minerals, vitamins and dietary essential fatty acids forming neuronal membranes with various actions have been studies .Various dietary patterns and nutritional factors form synergistic interaction of different components present in a food pattern A greater adherence to Mediterranean diet(Me diet) shown reduced incidence of Alzheimer's disease. Higher adherence to DASH and Me Diet were significantly associated with higher MMSE scores.

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