Management of Alzheimer's Disease Through Nutrition

Ashok Chakraborty[1*], Smita Guha[2]

[1]*Sacred Heart University, Department of Chemistry, Fairfield, CT, USA*

[2]*St. John's University, Queens, NY, USA*

*Corresponding Author: *Ashok Chakraborty, Sacred Heart University, Department of Chemistry, Fairfield, CT, USA*

Abstract

Alzheimer's disease and its related health issues are still incurable. It starts generally at age 50 or above and without having any sex bar. Alzheimer's symptoms mainly start from forgetfulness and ultimately end up with dementia, an irreversible complete loss of memory. There is no therapy available though scientists are trying to get some clue for gene and cell therapy, but effective solutions are yet to be obtained. In this scenario, management of the disease through diets, and the pros and cons of the right food choice for the benefit of AD patients have been discussed here. The Mediterranean diet along with DASH diet, in short, known as a MIND diet, are effective for maintaining the better cognition effect and quality of life among AD individuals.

1. INTRODUCTION

Alzheimer's disease (AD) is described as an irreversible decline in cognitive and functional abilities, loss of memory and ultimately results dementia, and premature death [1]. This disease generally starts at ages around 50 or above, but early onset of the ailments has also been noted in familial cases indicating some genes are involved along with other sporadic causes [2]. The number of AD cases is gradually growing by number every year, and therefore becomes a major socioeconomic issue [3]. Although the cause of AD is not well-understood, but the deposition of accumulated amyloid-beta peptide (Aβ) and the formation of neurofibrillary *tau* protein tangles in the brain have been documented **[4].** As a cause of AD while nothing is clear at this time, epsilon 4 allele of the apolipoprotein E gene (APOE *ε*4), diabetes, and smoking are found to be associated with the onset of AD. However, cognitive engagement and physical activities can decrease the risk of AD, as noted [5]. Currently, there is no effective cure of the AD symptoms, however, there is a good correlation between nutrition and the biochemistry of AD as observed during studies with animal models [6-15]. These indicate that may be the appropriate nutritional intervention, a good approach for reducing the risk of AD onset and its progression.

2. AD IS ASSOCIATED WITH BOTH OBESITY AND MALNUTRITION

Both, obesity and malnutrition are associated with AD [16-18]. Obesity (BMI > 30) in midlife while found to increase the risk of AD, the late-life obesity is associated with the reduced risk of AD [16]. Therefore, manipulation of adiposity could be a guideline to prevent AD [19-23].

3. THE EFFECTS OF MACRO-NUTRIENTS ON THE RISK OF AD

3.1. Fats and Fatty acids

Monounsaturated Fatty Acids (MUFAs) and its derivatives have anti-inflammatory effects *in*

vivo [24]. Higher monounsaturated fatty acid, but not the higher saturated fatty acid, can improve the cognitive function [25]. Total fat, polyunsaturated fatty acid, trans-fat intakes are not found to be associated with cognition changes [26].

Derivatives of MUFA, like phenols, have antioxidant effects, therefore intake of which have suggested to be associated with less cognitive decline [27, 28].

3.1.1. Polyunsaturated Fatty Acids (Omega-3 Polyunsaturated Fatty Acids

These fatty acids have been demonstrated to reduce the Aβ production and reverse the pathological symptoms in AD animal models [28-32]. This omega-3 fatty acids can also delay the cognitive aging and memory decline but only in the mild cases of the disease [33-35].

3.1.2. Saturated Fatty Acids

Moderate intake of saturated fatty acids while exert an increased risk of AD and dementia, especially to APOE epslion4 carriers, a higher intake do not show any such risk. This could be an indication of threshold association of saturated fatty acids with AD [36, 37].

3.1.3. Trans-Fatty Acid (TFA)

TFA might potentially increase the AD risk by producing more Aβ by disturbing the balance of amyloidogenic and non-amyloidogenic processing of amyloid precursor protein [38]. However, in other clinical study no relation was found between greater intake of trans-fat with cognitive decline [38].

3.2. Effects of Carbohydrates

Type 2 diabetes mellitus (T2DM) is a vital risk of getting AD [5]. In the brain of AD patient the reduced level of insulin and its receptor expression have been reported [39-42]. Therefore, a diet high in carbohydrates may cause glycation of multiple neural proteins and develops an AD symptoms [43-45]. However, reliable data from clinical trials with such a diet and AD developments are yet to obtain.

3.3. Effects of Proteins

Meat: Processed meat, especially the red meat is considered as a vital risk factor for developing dementia.

Fish contains long chain omega-3 fatty acids, EPA, and DHA and can reduce the risk of having AD and dementia, especially among them who are the non-carriers of the APOE epslion4 **[46-**

50]. In a study with more than 800 participants aged from 65 to 94 years, it was found that number AD occurrence is less (~60%) in people who consume fish quite often in a week compared with those who rarely or never ate fish [49].

Eggs: In one study it was found that eggs showed a positive effect on neurocognitive function [51].

4. EFFECTS MICRONUTRIENTS (VITAMINS, AND TRACE METALS) ON AD

- *Vitamin A and β-carotene* reduces the deposition of accumulated amyloid β-peptide (Aβ) and fibrils [52-54].

- *Vitamins B: (Especially the Folic Acid, Vitamin B6, and Vitamin B12):* These vitamins inhibit the oxidative stress and lower the concentrations of homocysteine, and thus helps AD [55-58].

- *Vitamin C*, as noted both in vitro and in vivo studies, can reduce the Aβ oligomer formation and oxidative stress, and thus expected to help AD symptoms [59, 60].

- *Vitamin D:* Vitamin D deficiency (<10 ng/ml) is significantly associated with the development of AD and dementia with time. Consumption of which for at least 12 months can significantly improve the Aβ peptide-related biomarkers and cognitive function [61].

- *Vitamin E:* It is a lipid-soluble antioxidant, and can scavenge Aβ-associated free radicals [62-65], and results a slower rate of cognitive decline [66]. The mechanism is due to the activation of Sirt-1 and concomitant inhibition of COX-2, 5-lipoxygenase and NFkβ mediated proinflammatory pathways [67].

- **Metals and Metalloids:** Transition metals are believed to play a role in the pathogenesis of AD by forming reactive species through metal amyloid complexes [68, 69].

Copper: Copper is an essential trace metal needed to maintain our body toxic free. However, high dietary intake of copper in conjunction with saturated and trans-fats can cause a cognitive decline [70, 71]. A meta-analysis of 17 studies with 1425 subjects showed higher levels of serum copper in AD patients than controls [72, 73]. However, a randomized, placebo-controlled trial showed no such progression of AD after oral copper supplementation to 68 subjects [74].

Iron: Iron can cause an oxidative stress, and an imbalance in iron homeostasis is thought to be a

precursor of AD [75, 76]. Diets excessive in Fe together with a high intake of saturated fat acids are not recommended to elderly subjects [70]. However, iron supplementation has been reported to improve attention and concentration among children and adults, as well [77].

Zinc: Zinc deficiency was reported to be associated with cognition loss in AD patients. Supplementation of Zinc was found to reduce both the Aβ and *tau* pathologies in AD Ok model [78, 79].

Selenium is a metalloid and play an important role in the antioxidative defense [80, 81]. AD patients showed a significant lower Selenium level in plasma, erythrocytes, and nails when compared to controls [82]. Supplementations of selenium-containing mixtures can improve cognition [83-85]. However, the relationship between selenium supplementation and AD recovery needs further randomized trials.

5. THE EFFECTS OF OTHER KINDS OF FOODS ON AD

Fruits and Vegetables: Fruits and vegetables contain a substantial amount of antioxidants and bioactive compounds like, vitamin E, vitamin C, carotenoids, and flavonoids, and also low in saturated fats, which can decrease the risk of AD and dementia **[86-88].**

Vegetable (only): Vegetables, especially green leafy vegetables, contain more vitamin E than fruits. Therefore, higher vegetable, but not fruit, consumption can slower the rate of cognitive decline as found in a cohort study with 3,718 participants aged 65 years and older [88]. The similar effect was also found with the intake of nuts, cabbage, and root vegetables to diminish age-related cognitive decline in middle-aged individuals [89].

Dairy products: Dairy products are rich in vitamin D, phosphorus, and magnesium, therefore they may reduce the vascular alterations and structural changes in the brain and ultimately reduces the possibilities of having the cognitive decline [90, 91]. However, saturated fat intake from milk products was found to be associated with an increased risk of AD [37, 92]. Unfortunately, no evidences are available yet on the effects of dairy products on AD from a randomized controlled trials.

Drinks:

Caffein: Drinking coffee has been reported to have some protective effect from AD ailments. Coffee being the best source of caffeine it can selectively enhance plasma cytokines and can decrease the risk of AD by 95% as reported **[93, 94]**. However, further prospective studies with proper methodologies are needed to evaluate the benefit of coffee consumption from AD-risk are strongly needed.

Tea: Some observational studies suggest that drinking tea was associated with lower risks of cognitive decline [95, 96]. While black tea was shown to significantly enhance auditory and visual attention compared [97], green tea polyphenols inhibit oxidative stress and protects the individual from having cognitive impairment [98-100]. Further, green tea contains epigallocatechin-3-gallate (EGCG), which has been shown to reduce the β-amyloid deposition and *tau* plaque formation in AD mouse models [101, 102]. The neuro-protective effects of tea consumption could be due to the presence of catechins, L-theanine, polyphenols, and other compounds in tea leaves [103].

Alcohol: Epidemiological studies suggest that light-to-moderate alcohol drinking can reduce the risk of having AD, particularly to them who are the non-carriers of APOE epslion4 **[104-106]**. However, heavy drinking (>2 drinks) along with heavy smoking can cause an early onset of AD especially to those individuals who carry APOE epsilon4 gene **[107]**. However, the mechanisms of the above observations are still unclear. Further, different types of alcohol (wine, beer, and mixed alcohol beverages) may have different effects on AD. Resveratrol and other polyphenols in red wine have been reported to diminish Aβ plaque formation, while beer consumption afford a biofactor, silicon, which can provide benefits to AD **[108-110]**.

6. THE EFFECTS OF DIFFERENT DIETARY PATTERNS ON AD (EITHER TO FOLLOW OR TO RESTRICT)

Dietary pattern, a combination of food components that summarizes an overall diet for a study population, can have various effects on cognitive function and AD (Table 1)

Table 1. *Bring the table in one page*

Dietary Patterns	Good or Bad for AD
Western diet	• A Western diet is characterized by higher intake of red and processed meats, refined grains, sweets, and desserts **[111, 112]** • A high-fat Western diet may contribute to the development of AD by impacting Aβ deposition and oxidative stress **[113, 114]**

Japanese Diet.	• Japanese diet mainly contains fish, plant foods (soybean products, seaweeds, vegetables, and fruits), decreased intake of refined carbohydrates and animal fats **[115]** • In a population-based study with a total of >1000 Japanese subjects followed by 15 years, those dietary composition was found to be associated with a reduced risk of AD **[116]**
Healthy Diets	• A healthy diet means consumption of fruits, whole grains, fresh dairy products, vegetables, breakfast cereal, tea, vegetable fat, nuts, and fish but less or none of the followings like, meat, poultry, refined grains, animal fat, and processed meat **[117]** • Participants who follow the healthy diet had a better cognitive performance and a decreased risk of AD **[118, 119]**,
DASH-Style Diets	• The DASH diet (Dietary Approaches to Stop Hypertension) contains plant foods, whole grains, nuts, fruits, vegetables, fish, poultry, and low-fat dairy products **[120]**. • Hypertension is often associated with increased risk for AD **[121]**. A randomized clinical trial with 124 participants who have elevated blood pressure and AD issues became the subjects of the DASH diet and exhibited greater neurocognitive improvements compared to normal subjects along with the controlled blood pressure level **[122]**
Mediterranean Diets (MD)	• The Mediterranean diet is composed of fruits, vegetables, cereals, bread, potatoes, poultry, beans, nuts, olive oil, and fish; a moderate consumption of alcohol; and a lower consumption of red meat and dairy products **[123]** • A meta-analysis with 2,190,627 subjects showed that adherence to the Mediterranean diet can reduce the risk of having AD and also the mortality in AD **[124-126]**
MIND Diet	• The MIND Diet *(Mediterranean-DASH Intervention for Neurodegenerative Delay Diet)* takes the good elements of *Mediterranean Diets (MD)* and DASH diet while minimizing the intake of red meats, butter, margarine, cheese, fast foods, and sweets **[127]** • This diet has been shown to slow down in cognitive decline, and offers a better protection against Alzheimer's disease compared to DASH or MD diets when used separately **[128]**

7. DISCUSSION

Extensive literature studies relating to Alzheimer's diseases and its possible cure when finds no hope, its management through nutrition and choice of correct diet can offer a quality life with better cognition effect. Consumption of refined carbohydrates or a diet with a high glycemic index is associated with increased accumulation of Aβ peptides in the brain. This effect is even worse in APOE-+4 carriers, which is a genetic risk factor associated with AD and dementia, as well as insulin resistance. However, the exact mechanisms underlying this relationship are still unknown [129, 130].

In various randomized trials with standardized diagnostic criteria for AD and also epidemiological studies suggest that antioxidants, vitamins, polyphenols, polyunsaturated fatty acids, fish, fruits, vegetables, tea, and light-to-moderate consumption of alcohol are beneficial for AD. On the other hand, carbohydrates, fats and whole-fat dairy products are detrimental to AD. However, the effect of all the food items individually is hard to assess as they are correlated with each other. Further, randomized trials are not always feasible, but when undertaken it showed that the dietary supplementation of vitamin E, B, and polyunsaturated fatty acids does not reduce cognitive decline and the risk of AD. This could be due to the fact that those nutrients may protect the disease but once started cannot cure them. Further, inadequate time of the study and complexes from several social and behavioral factors across the life course do not show the expected benefits [131].

A Western diet pattern can increase the inflammation levels hence the risk of getting AD [132], whereas the Mediterranean diet has been shown to improve cognitive outcomes, and decrease memory decline [133-135]. A ketogenic diet can reduce the oxidative stress, inflammation and also reduce the negative effects from glucose metabolism in the brain. Therefore such a diet may also be useful in the management of AD [13]. Since in AD patients a high level of oxidative stress has been noticed, adequate intake

of fruits, vegetables, fish, nuts, legumes, cereal and lower intake of meats, high fat diary, sodium, sweets, and refined grains are recommended. Further, vitamin supplements, like Vitamin D, Vitamin B12, Vitamin E, and Vitamin C can help to combat cognitive and memory decline [136-144]. However, further research is needed to improve the quality of evidence relating to the association of many nutrients, foods, and dietary patterns with AD.

8. CONCLUSION

From the above study it appears that some foods are good for brain health and some are not. Especially, red meat, butter, margarine, cheese, fast foods, sweets, and high-sodium foods are better to avoid, and instead it is good to consume: whole grains, fresh fruits, vegetables, fish, beans, nuts and olive oil for better cognition effect and to avoid any risk of having AD in the life course.

9. ACKNOWLEDGMENT

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