

Alzheimer's disease and its nutritional regulation – a review.

La enfermedad de Alzheimer y su regulación nutricional: una revisión.

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ABSTRACT

Purpose: There are very few reported findings on Alzheimer's disease and treatment for the same. Hence this review article was undertaken. Some studies show that Alzheimer's is a degenerative disease. It occurs over a course of time and leads to dementia. Various supplements of prebiotics, virgin coconut oil (VCO), micronutrient supplementations were identified to be helpful in etiology of this disease. Alzheimer's disease is a degenerative brain disease and most common form of dementia. **Methods:** Prevalence of Alzheimer's disease is increasing all around the world, especially in India. With the view of this increased prevalence various medical and nutritional treatments were identified for its cure 1) Role of Virgin coconut oil in Alzheimer's disease, 2) Role of prebiotics and probiotics supplementation in Alzheimer's disease, other dietary supplements like Vitamin E, zinc etc.4) Role of aluminum intake on etiology of Alzheimer's disease. **Results:** It can be concluded that there is beneficial role of VCO, prebiotics, probiotics and other micronutrient supplementation like Vitamin A, Vitamin E, and Vitamin B12 in prevention as well as treatment of Alzheimer's disease. **Conclusion:** This review paper focuses on every aspect of Alzheimer's disease, but still more nutrition-based research should be carried out to validate the data. As this disease is not considered as life threatening disease, moreover it is a silent killer.

Key words: Alzheimer's disease, Virgin Coconut Oil (VCO), prebiotics, probiotics, dementia.

RESUMEN

Propósito: Hay muy pocos hallazgos reportados sobre la enfermedad de Alzheimer y su tratamiento. De ahí que se haya llevado a cabo este artículo de revisión. Algunos estudios demuestran que el Alzheimer es una enfermedad degenerativa. Ocurre con el tiempo y conduce a la demencia. Se identificó que varios suplementos de prebióticos, aceite de coco virgen (VCO) y suplementos de micronutrientes son útiles en la etiología de esta enfermedad. La enfermedad de Alzheimer es una enfermedad cerebral degenerativa y la forma más común de demencia. **Métodos:** La prevalencia de la enfermedad de Alzheimer está aumentando en todo el mundo, especialmente en la India. Con vistas a esta mayor prevalencia, se identificaron varios tratamientos médicos y nutricionales para su cura: 1) Papel del aceite de coco virgen en la enfermedad de Alzheimer, 2) Papel de los suplementos de prebióticos y probióticos en la enfermedad de Alzheimer, otros suplementos dietéticos como vitamina E, zinc, etc. 4) Papel de la ingesta de aluminio en la etiología de la enfermedad de Alzheimer. **Resultados:** Se puede concluir que existe un papel beneficioso del VCO, los prebióticos, los probióticos y otros suplementos de micronutrientes como la vitamina A, la vitamina E y la vitamina B12 en la prevención y el tratamiento de la

enfermedad de Alzheimer. Conclusión: Este artículo de revisión se centra en todos los aspectos de la enfermedad de Alzheimer, pero aún se deben realizar más investigaciones basadas en la nutrición para validar los datos. Como esta enfermedad no se considera una enfermedad que ponga en peligro la vida, además es un asesino silencioso.

Palabras clave: enfermedad de Alzheimer, aceite de coco virgen (VCO), prebióticos, probióticos, demencia.

INTRODUCTION

Alzheimer's disease is a degenerative brain disease and most common form of dementia. Alzheimer's is a type of dementia which causes problems with thinking, memory and behaviour. Symptoms develop slowly and worsen over a time severe enough to interfere with day to day tasks. Oxidative stress is a major contributor to pathogenesis of any neurodegenerative disease. Alzheimer's is not the normal part of aging, age is just a risk factor for AD. In Alzheimer's disease high levels of certain protein inside and outside the brain cells damages the cell and makes it difficult for them to stay healthy and communicate with each other. The area of the damage in case of AD is hippocampus which is for learning and memory causing memory loss to be the first reason for Alzheimer's disease. In case of dementia these are the first regions of cell damage hence Alzheimer's is the earliest stage of dementia. (26) (2) (1)

EARLY SIGNS OF ALZHEIMER'S DISEASE

Forgetting recently learned information a kind of memory loss that disrupts the daily life, difficulties in planning or problem solving abilities, difficulty to complete daily tasks at home, work or leisure, confusion with time and place, trouble in understanding visual images and spatial relationships, they have trouble in finding correct words for speaking or writing, misplacing things and are unable to find them, decreased or poor judgment, withdrawal from social activities and work, changes in mood and personality. Alzheimer's is a neurodegenerative diseases leading to dementia in later life. Many a time's age related changes are confused with Alzheimer's disease. Age related changes include making a bad decision once in a while, missing a monthly payment, losing a track of which day it is and again recollecting, sometimes forgetting which word to use and forgetting things but gets back to it after a while. Signs of Alzheimer's include decrease in ability to make a decision or judgment, inability to manage a budget, completely forgetting about date or season, difficulty in having conversation almost at all the time and misplacing things and cannot retrace them back. (3) (1)

STAGES OF ALZHEIMER'S DISEASE

Alzheimer's disease progresses slowly in three stages: mild, moderate and severe. In the mild stage the person may be able to do all the tasks of daily living, function independently but sometimes the person has memory lapses such as forgetting a familiar word or place, forgetting material that is just read, losing or misplacing valuable objects etc. Moderate stage is the longest stage and can typically last for many years. At this stage a person gets confused with words or acts in unexpected ways, forgets about his/her own personal history, feels moody, unable

to recall own telephone number or address, changes in sleep patterns etc. In the severe/ final stage of disease a person loses his ability to respond to environment, communication becomes pain, need extensive help in daily life, changes in physical abilities, has difficulty in communication etc. There is an evidence based on death of neuron cells in mild cognitive impairment as compared to healthy controls. The percentage of cell cycle for immune positive neurons increased in severe cases of Alzheimer's disease. There are a few myths of Alzheimer's disease which include memory loss is a natural part of aging, Alzheimer's disease is not fatal, only older people can get Alzheimer's disease, intake of aspartame causes memory loss and flu shots increase the risk of Alzheimer's disease (2) (1)

RISK FACTORS OF ALZHEIMER'S DISEASE

Three factors which cannot be modified are: Age, family history, genetics

Other modifiable risk factors include: Head injury, heart – head connection [vascular dementia], overall healthy aging, and diet. Pathologically there is formation of senile plaques in brain due to amyloid protein deposition and intracellular neurofibrillary tangles (3) (1)

MEDICAL TESTS OF ALZHEIMER'S DISEASE

Medical tests done to confirm Alzheimer's disease includes: medical history, physical examination and diagnostic test, neurological exam like reflexes, coordination, muscle tone and strength, eye movement, speech, sensation, mental status tests like MMSE, mini – cog, computerized tests cleared by FDA, mood assessment, brain imagining. MMSE and clock drawing are the most effective tests to detect Alzheimer's in subjects with mild cognitive impairment. (4) (1)

TREATMENT OPTIONS OF ALZHEIMER'S DISEASE

There are many treatment options available for patients with Alzheimer's disease they include: medications for memory, treatment for behaviour changes, treatment for sleep changes, alternative treatments like huperzine a, coconut oil, omega-3 fatty acids, phosphatidylserine, ginkgo biloba etc. (4) (1)

RESULT AND DISCUSSION

Prevalence of alzheimer's disease

Global Prevalence:

According to World Alzheimer's Report, 2019, 95% of people from general population all around the world can develop dementia. One in four people think that nothing can be done about dementia prevention or treatment. According to World Alzheimer's Report, 2015, 46.8 million people are living with dementia all around the world in 2015. This number is projected to double every 20 years; 74.7 million by 2030 and 131.5 million by 2050. The report also concluded that there were more than 9.9 million new cases of dementia every year worldwide: one new case every 3.2 seconds. The report showed that in 2015, East Asia was the region with most of the people living with

dementia [9.8 million] followed by Western Europe [7.4 million], South Asia with 5.1 million and North America with 4.8 million (5) (6).

A systematic review of global prevalence of dementia from 1980 to 2009 and meta analysis was carried out to estimate the number of adults of the age of 60 years and above in 21 global burden of disease regions reported that age – standard prevalence for those aged 60 and above varied in a narrow band of 5% - 7% in most of the regions in the world. The prevalence was higher in Latin America (8.5%) and lower in four sub – Saharan African regions (2%-4%). It was estimated that global prevalence of dementia was 35.6 million adults in 2010 and the number was expected to rise to 65.7% in 2030 and 115.4 million in 2050. The study estimated that 58% of the adults with dementia lived in low- or middle-income countries which was expected to rise to 63% in 2010 and 71% in 2050 (7). According to Dementia Report 2012, the number of people living with dementia worldwide were 35.6 million in 2012 and this number will double up by 2030 and triple up by 2050 (8).

National prevalence

According to the World Alzheimer Report 2015, 4.1 million people in India were living with dementia (Martin Prince et al., 2015). A study conducted in India on different types of dementia present undertook first 100 patients seen at a dementia clinic. All the patients were screened clinically with blood tests and brain MRI. The different types of dementia reported were Lewy body dementia [22%], depression [20%], Alzheimer’s disease [13%] and mild cognitive impairment [18%] (9).

A door-to-door survey was conducted in rural community in Kerala to identify elderly people aged 60 years and above. A total of 2067 elderly people were screened with a vernacular adaptation of MMSE Scale. All those who has a score of 23 and below were evaluated using a detailed neuropsychological evaluation by CAMDEX – Section B and the caregivers of these adults with cognitive impairment were interviewed using CAMDEX – Section H to confirm history of impairment in social and personal functioning. Then the subjects with confirmed cognitive impairment were evaluated if they satisfy the DSM – III – R criteria for dementia. The results concluded that 66 cases of dementia were identified from 2067 adults aged 60 and above. A prevalence rate of 33.9 per thousand was observed. 58% of the dementia cases were diagnosed as vascular dementia and 41% satisfied the criteria for ICD – 10 dementia in Alzheimer’s disease. The study reported that there were more women in disease group also smoking and hypertension were associated with vascular dementia and family history of dementia was more likely in Alzheimer’s disease group (10).

A study conducted in Vadodara, India on 250 elderly (age: 60 – 85 years) subjects using MMSE and Cognitive impairment scale concluded that 40% of subjects were found at borderline score for mild cognitive impairment and 26% of subjects were found towards moderate MMSE score. Lower MMSE scores were positively correlated with advancement in age. When MMSE scores were compared the data indicated that severity of dementia was found higher in females as compared to males. Assessed nutritional status of 250 elderly subjects and the results concluded that the severity of cognitive impairment increases with age and reported that deficiency of nutrients related to

mental health like vitamin B12, folic acid, and vitamin E can be considered as a risk factor for cognitive impairment and dementia (11).

Effect of Alzheimer's in various diseases:

Several mice were fed with a high salt diet and studied for a period of three years. The results showed that high salt diet is linked to an increased risk of cerebrovascular disease and dementia (12).

In research conducted in China on C57BL/6J mice were divided into two groups one with normal – salt diet and another with high – salt diet for a period of 12 weeks. Cognitive ability and oxidative stress were measured. The results concluded that high – salt diet significantly impaired retention of spatial memory (13).

A study was conducted on three hundred and seventeen healthy children with no previously diagnosed neurological or psychiatric disorder. They were assessed using a food frequency questionnaire and neurocognitive tests included symbol digit modalities (SDMT). Verbal memory and SDMT percentile results showed positive correlation with potassium intake (14).

Several researchers conducted a study on volunteered subjects aged 50 and above from tribal and rural areas of Dharampuri district, Tamilnadu India were enrolled, and polymorphism was analyzed using PCR – RFLP. Fasting lipid levels and memory function were assessed using simplified version of Global Clinical Dementia rating. The data predicted that positive correlation was present between cholesterol – associated genes and their influence to altered lipid profile and memory loss symptoms which possibly link to gene – polymorphism and susceptibility for dementia (15)

Research conducted in Japan enrolled 1081 subjects who were above the age of 60 and not suffering from dementia. A food frequency questionnaire was used to assess potassium, calcium and magnesium intake. The results of this 17 year follow up study reported that high self – reported dietary intakes of potassium, calcium and magnesium reduced the risk of dementia (16).

As seen in the review above there are many harmful effects of Alzheimer's disease in various diseases and there are very few nutritional management methods for the disease. A few of the methods which can be helpful in nutritional management of Alzheimer's disease are supplementation with virgin coconut oil, prebiotics, probiotics, Vitamin E, Vitamin B12 etc. as they are elaborated further

Supplementation of virgin coconut oil (VCO) and Alzheimer's disease

Virgin Coconut Oil [VCO] is a coconut oil that is made up of medium chain triglycerides which are metabolized differently [provide quick source for energy and less likely to be stored as fat] and hence beneficial for health (17).

In AD, there appears to be a pathological decrease in the brain's ability to use glucose. Neurobiological evidences suggests that ketone bodies are effective alternate substrate for the brain. Elevation in plasma ketone body through oral supplementation of MCT improves cognitive function in elderly and possibly have therapeutic benefits in patients with AD (19).

A study was carried out to assess the possible effect of VCO on aluminum chloride induced AD rats. In the study Alzheimer's was induced in rats by injecting aluminum chloride for 45 days (40ml/kg/day) followed by oral administration of 5ml/day of VCO for 30 days. The results showed that there was significant decrease in malondialdehyde [MDA] levels in cortex and increase in glutathione [GSH] levels in both hippocampus and cortex in rats treated with VCO concluding that VCO has a potential protection against neurodegeneration in AD in both cortical and hippocampal neurons and also has potential prophylactic effect for memory enhancement, anti-excitotoxicity and antioxidants in rats with AD (19).

Both dyslipidemia and Alzheimer's disease (AD) are associated with aging. This study was conducted to examine the effects of VCO on inflammation and oxidative stress in Alzheimer's model (receiving Amyloid – β ($A\beta$)) and high – fat diet model (HFD). 120 male Wistar rats, were divided into 12 groups each of 10 rats namely; healthy control, sham surgery, sham surgery receiving normal saline, HFD, HFD + 8% VCO, HFD + 10% VCO, $A\beta$ receiving rats, $A\beta$ + 8% VCO, $A\beta$ + 10% VCO, $A\beta$ + HFD, $A\beta$ + 8% VCO, HFD + 10% VCO + $A\beta$ following memory and learning tests. The results concluded that $A\beta$ and HFD fed rats had significantly impaired memory and learning by activating NLRP 3 receptors and oxidative stress. The Congo Red, Crystal Violet staining and immunohistochemistry (IHC) test showed that VCO reduced $A\beta$ plaques and phosphorylated Tau protein and showed a potential neuroprotective effect (20). In a 6 week trial using quasi experimental non-randomized pre - post interventional design, 31 subjects (21 females and 10 males) with moderate to severe AD diagnosed as per DSM IV TR criteria were enrolled in the study. Subjects were on normal diet and continued taking prescribed AD medication. Baseline data was collected using ADAS – Cog and CIBIC – Plus. Daily oral administration of 20ml of Extra Virgin Coconut Oil and the active administration continued for 4 weeks from the baseline data. The post data was collected using ADAS – Cog and CIBIC – Plus at 2nd, 4th and 6th week from the baseline respectively. The results suggested that there was no significant improvement in CIBIC – Plus score, LDL levels, Triglyceride levels, Total Cholesterol levels. There was a little improvement in HDL levels. The mean improvement in ADAS – Cog was 2.6 in the second week, 4.1 at fourth week and 6.1 at sixth week. The data concluded that addition of coconut oil is likely to have a beneficial effect in cognitive function of subjects suffering from moderate – severe AD and the effect sustained for at least 2 weeks after the oil administration stopped. No deleterious effect on overall lipid profile can be elicited. (21).

A prospective study conducted in Nutricion Hospital, Spain to evaluate the impact of extra virgin coconut oil (EVCO) in the development of Alzheimer's disease and to determine its impact on variables such as sex and whether suffering from diabetes or not. The study was conducted on 44 subjects aged between 65 years to 85 years and they were divided randomly into two groups: control and intervention. The intervention group received 40ml of EVCO for a period of 21 days and the parameters evaluated were mini test score and LOBO cognitive test pre and post intervention in both the groups. (22).

A prospective, longitudinal, qualitative, analytical, experimental study through a clinical trial was conducted in Nutricion Hospital, Spain, where 44 subjects with Alzheimer's disease living in the region of Ribera [Valencia] were enrolled. They were divided into two equal groups: control and experimental group, the 22 subjects in the

experimental group received supplementation of 40ml of coconut oil daily, divided in two parts: 20ml in breakfast and 20ml in meal. All the 44 subjects before and after intervention period were assessed using MMSE scale specifically to check skills of orientation, language building, fixing, calculation – concentration and memory areas. The result emphasized that there was significant improvement in subjects who received supplementation in the areas of orientation and language construction. The results showed that there was a significant improvement in MEC – LOBO scores of subjects in experimental group (38.42%) as compared to control group (1.22%). Women had a better post test score as compared to men in experimental group and presence of diabetes affected the scores. (23).

A prospective, longitudinal, qualitative, analytical, experimental study was carried out in Spain which enrolled 44 subjects with AD who were randomly allocated in two homogenous group of 22 each: experimental group and control group. The experimental group received a coconut oil enriched Mediterranean diet for 21 days. The cognitive changes were determined using a 7-minute screen test, which analyzed temporal orientation, visuospatial and visuoconstructive abilities and semantic and episodic memory. The results showed that the subjects in experimental group after following the intervention for 21 days had improved episodic, temporal orientation and semantic memory. More positive response was obtained in women with mild - moderate AD, although other improvements in males and severe state were shown. The data concluded that Mediterranean diet improved cognitive function in subjects with AD, but the improvement varies with sex and degree of severity. The result emphasized that there was significant improvement in subjects who received supplementation in the areas of orientation and language construction. It was observed in patients who received coconut oil that cognitive improvement after completion of the intervention, statistically significant improved in the orientation and language-construction areas. (24).

Role of prebiotics and probiotics supplementation in Alzheimer's disease

A prebiotic is “a selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal micro flora that confers benefits upon host wellbeing and health”, whereas synergistic combinations of pro- and prebiotics are called synbiotics. They are dietary fibers with a well-established positive impact on the intestinal micro flora. Other health effects of prebiotics (prevention of diarrhea or constipation, modulation of the metabolism of the intestinal flora, cancer prevention, positive effects on lipid metabolism, stimulation of mineral adsorption and immunomodulatory properties) are indirect, i.e. mediated by the intestinal micro flora, and therefore less-well proven. (25)

A study conducted on subjects with AD studied therapeutic effect of the traditional medicine, *M. officinalis*, on various neurological diseases such as AD and reported that Oligosaccharides from *Morrinda Officinalis*, are useful Prebiotics and cause substantial memory improvements in animal models of AD via modulating the interaction between gut ecology and brain physiology (26).

In a study mice were administered FOS, GOS or a combination of FOS + GOS for a period of 3 weeks. The results reveal that chronic prebiotic [FOS + GOS] treated mice exhibited both antidepressant and anxiolytic effect.

Prebiotics administration also increased fecal acetate and propionate and reduced isobutyrate concentrations which can be correlated with positive effects seen on behaviour (27).

A study conducted in 42 subjects with mild to moderate Alzheimer's disease of age group between 65 – 80 years, with a score of ≥ 12 on ADAS – cog scale were supplemented with a fixed dose of Melissa Officinalis extract for a period of four months. The results conclude that there was a significant better outcome obtained in subjects who received supplementation of Melissa Officinalis as compared to controls (28).

A study was conducted to observe the neuroprotective effect and antioxidant activity of Passiflora edulis fruit flavonoid fraction, aqueous extract, and juice in aluminum chloride-induced Alzheimer's disease rats. Fruit pulp and peel juice was extracted and fed for one week to 3 months old Wistar rats weighing between 200 and 230 g. the results revealed that the highest total phenolic and flavonoids' contents, the best DPPH scavenging activity and the ability to reduce ferric ion (Fe^{3+}) were obtained with peel aqueous extract. The administration of the peel aqueous extract, juice, and flavonoid fraction resulted in a significant decrease ($P < 0.05$) in plasma and tissue levels of malondialdehyde compared to the positive control (PC). The levels of tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), cyclooxygenase-2 (COX-2), and amyloid β -42 (β -42) were significantly reduced whereas the activities of catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), and glutathione level were significantly higher in the treated than that in the untreated Alzheimer's rats (PC) groups ($P < 0.05$), respectively, in the hippocampus and in plasma, brain, and liver homogenates following the administration of juice, flavonoid fraction, and extracts (both doses). Treatment of AD-rats with PE ameliorated neurobehavioral changes, as evidenced by the improvement in brain function, as well as, modulation of AChE, and confirmed by the histological changes and Morris water maze test. The effect of aqueous extract was slightly greater than that of the flavonoids fraction, thus suggesting that flavonoids account for most of the Passiflora edulis antioxidant activity and neuroprotective effect. (29)

Other dietary supplements in Alzheimer's disease

The few dietary supplements which have shown a beneficial effect in the etiology of Alzheimer's disease. Vitamin B12, Zinc, Vitamin A, Vitamin E etc. are the supplementation which helps to stop progression of Alzheimer's disease to dementia.

A study examined if the use of lithium was able to prevent memory impairment in adult zebra fish. Also the evaluation was done to see the effects of lithium on anxiety – like behaviour and acetylcholinesterase activity. The study demonstrated that lithium prevents memory impairment induced by scopolamine, decreases exploration and increases the activity of acetylcholinesterase. The results concluded that it is possible to use lithium in therapeutic treatments aimed at improving cognition (30).

A study was carried out to investigate the long term effects of marginal vitamin A deficiency [MVAD] on pathogenesis of AD in rats. The male rats were injected amyloid β ($A\beta$ 1 – 42 in CA3 area of the hippocampus. The results found that there was significant aggravation in $A\beta$ 1 – 42 in MVAD induced rats which lead to learning and memory deficits (31).

A randomized, placebo – controlled double blinded trial was carried out on 119 subjects with mild – moderate AD. The subjects were randomly divided to two groups: one which received 50g of resveratrol and another group which received 50g of placebo. The results indicated that CSF A β 40 and plasma A β 40 declined in the subjects who received resveratrol resulting in significant improvement (32).

A study conducted on 232 subjects with AD measured through MMSE and ADAS – cog scale were supplemented with lithium. The results suggests that lithium significantly declined cognitive degeneration as compared to placebo (33).

A study conducted in 119 subjects with mild to moderate Alzheimer’s disease. 1 g of resveratrol was supplemented for 52 weeks and the results concluded that the supplementation decreased CSF MMP9, modulates neuro – inflammation and induces adaptive immunity (34).

A study was conducted on 251 AD subjects and 308 controls to study the serum concentration of retinol, two forms of Vitamin E (α - and γ - tocopherols) and six carotenoids using HPLC method and were assessed for regression analyses. The results demonstrated that the serum levels of α tocopherols and all six carotenoids was significantly lower in subjects with AD as compared to healthy controls (35).

Aluminum intake and Alzheimer’s disease

A study exposed rats to soluble salts of aluminum (AlCl₃) for long durations and checked its influence on mitochondrial respiration activity in the liver, brain and heart. The results showed that long term exposure to aluminum resulted in 100% increase in aluminum content in brain and liver mitochondria but in heart there was 11 folds increase, indicating the effect of aluminum were indirect rather than direct due to accumulation of aluminum (36).

A paper article reviewed the epidemiological evidence that linked aluminum to AD. The data suggested that 9 out of 13 published epidemiological studies showed that aluminum in drinking water was positively correlated with presence of AD. It also showed that aluminum in drinking water may be particularly bioavailable (37).

An 8 year follow up study conducted in France investigated effect of silica and aluminum in drinking water on the risk of Alzheimer's disease and dementia. The sample size was 3,777 subjects aged 65 years and above. The results concluded that relative risk for dementia after adjusting age, gender, educational level, area of residence and wine consumption was 1.99 for subjects who were exposed to aluminum (concentration of 0.1 mg/L) (38).

A study was conducted to evaluate the concentrations of aluminum, magnesium and phosphorus concentration in 5 different brain regions in 3 Alzheimer disease and 3 control subjects. The results showed that significantly high amount of aluminum and low amounts of magnesium and phosphorus was present in some regions of brains of AD subjects as compared to controls (39).

CONCLUSION

In the view of literature sited above, several studies have shown the increasing prevalence of Alzheimer’s disease at an alarming rate. Alzheimer’s is still unknown as life threatening disease to many population and is a

disease with silent progression until it reaches to dementia (severe) state. The currently available medical treatments focus on the dementia state rather than the progression of Alzheimer's disease. There are very few researches available on impact of Alzheimer's disease especially nutritional management on progression of disease. It is important to recognize Alzheimer's disease at an early state (mild – moderate) to slow its progression towards dementia. Hence more studies are required on the disease and its nutritional management.

ABBREVIATIONS

1. AD: Alzheimer's disease
2. VCO: Virgin Coconut Oil
3. MMSE: Mini-Mental State Examination
4. FDA: Food and Drug Administration
5. MRI: Magnetic resonance imaging
6. CAMDEX: Cambridge Mental Disorders of the Elderly Examination
7. SDMT: Symbol digit modalities
8. HFD: High fat diet
9. CIBIC – Plus: Clinician's Interview-Based Impression of Change Plus Caregiver Input
10. LDL: Low Density Lipoprotein
11. EVCO: Extra virgin coconut oil
12. DPPH: 2,2-diphenyl-1-picrylhydra

REFERANCES

Alzheimer's Association, www.alz.org

Yan Yang, Elliott J. Mufson and Karl Herrup, (2003). Neuronal Cell Death Is Preceded by Cell Cycle Events at All Stages of Alzheimer's Disease, Journal of Neuroscience, Volume 23(7), DOI: <https://doi.org/10.1523/JNEUROSCI.23-07-02557.2003>

Anil Kumar and Arti Singh Ekavali, (2015). A review on Alzheimer's disease pathophysiology and its management: an update. Pharmacological reports, 195 -203. <https://doi.org/10.1016/j.pharep.2014.09.004>

Sebastian Palmqvist , Joakim Hertzze, Lennart Minthon, Carina Wattmo, Henrik Zetterberg, Kaj Blennow, Elisabet Londos and Oskar Hansson, (2012). Comparison of brief cognitive tests and CSF biomarkers in predicting Alzheimer's disease in mild cognitive impairment: Six – year follow up study. Plos.org. <https://doi.org/10.1371/journal.pone.0038639>

World Alzheimer's Report 2019: The global impact of Dementia

Martin Prince, Anders Wimo, Dr. Maelenn Gurechet, Gemma - Claire Ali, Dr. Yu – Tzu – Wu, & Dr. Mathew Prina. World Alzheimer's Report 2015: The global impact of Dementia.

- Renata Bryce, Wanger Ribeiro, Martin Prince, Emiliano Albanese, Anders Wimo & Cleusa P. Ferri (2013). The global prevalence of dementia: A systematic review and metaanalysis. *Alzheimer's and Dementia* Volume 9, 63-75. DOI: 10.1016/j.jalz.2012.11.007
- Dementia Report 2012. *Dementia: a public health priority*. Mental Health Publications, World Health Organization 2012.
- Chandra V, & Mehta VS. (2017). Distribution of types of dementia in the first 100 patients seen at dementia clinic in India. *Journal of Alzheimer's Distribution*, 59(3), 797-801. DOI: 10.3233/jad-170251
- Shaji S, Tony Abraham et al. (2018). An epidemiological study of dementia in a rural community in Kerala, India. *The British Journal of Psychiatry*; Volume 168, Issue 6. DOI: <https://doi.org/10.1192/bjp.168.6.745>
- K Chauhan, Aditika Agrawal, & Riddhi Thakkar (2013). Assessment of Nutritional Status of elderly with mild dementia in urban Vadodara. *Asian Resonance/ Volume II*, 194-200.
- David Brea et al. (2018). Dietary salt promotes neurovascular and cognitive dysfunction through a gut - initiated TH17 response. *Journal of nature neuroscience*, Volume 21, 240-249. DOI: 10.1038/s41593-017-0059-z
- Yun - Zi Li et al. (2014). High - salt diet enhances hippocampal oxidative stress and cognitive impairment in mice. *Journal of Neurobiology of Learning and Memory*. Volume 114, 10-15. DOI: 10.1016/j.nlm.2014.04.010
- Jin Young Kim and Seung Wan Kang (2017). Relationships between Dietary intake and Cognitive function in healthy Korean Children and adolescents. *Journal of Lifestyle Medicine*, Volume 1, 10-17.
DOI: 10.15280/jlm.2017.7.1.10
- Periyasamy, Sabapathy et al. (2017). Association studies of specific cholesterol related genes [APOE, LPL and CETP] with lipid profile and memory function: A correlative study among the rural and tribal population of Dharampuri district, India. *Journal of Alzheimer's disease*, Volume 60, 195-207. DOI: 10.3233/JAD-170272
- Mio Ozawa et al. (2012). Self-reported dietary intake of potassium, calcium, and magnesium and risk of dementia in the Japanese: The Hisayama Study. *Journal of the American Geriatrics Society*, Volume 60, Issue 8. DOI: 10.1111/j.1532-5415.2012.04061.x
- Julie Murray (2017) Benefits of Organic coconut oil. xpnworld.com
- Reger MA, Henderson ST, Hale C, Cholerton B, Baker LD, Watson GS, Hyde K, Chapman D, & Craft S (2004). Effect of beta - hydroxybutyrate on cognition in memory - impaired adults. *Journal of Neurobiological Aging*, 25(3), 311- 314.
- Alghamdi BSA (2018). Possible prophylactic anti - excitotoxic and antioxidant effects of virgin coconut oil on aluminum chloride induced Alzheimer's in rat models. *Journal of Integrated Neuroscience*, 17(3-4), 593-607. DOI: 10.3233/JIN-180089
- Mirzaei F, Komaki A et al. (2018). Virgin Coconut Oil [VCO] by normalizing NLRP3 inflammasome showed potential neuroprotective effect in Amyloid - β induced toxicity and high - fat diet fed rat. *Journal of Food Chemistry and Toxicology*, Volume 118, 68-83. DOI: 10.1016/j.fct.2018.04.064

- Kour J, Gandotra S & Van der Waag A. (June 2014). Efficacy of adjunctive extra virgin coconut oil use in moderate to severe Alzheimer's disease. *International Journal of School*, Volume 1, Issue 2. DOI: 10.4172/2469-9837.1000108
- Ivan Hu Yang, Palbo Selvi Sabater, De la Rubia, Sancho Castillo, Rochina MJ, & Manresa Ramon (2015). Coconut oil: Non - alternating drug treatment against Alzheimer's disease. *Nutricion Hospitalaria*, Spain, 32(6), 2822-2827. DOI: 10.3305/nh.2015.32.6.9707
- Alma Maria Bueno Cayo, De la Rubia Orti, Sanchez Alvarez C, Selvi Sabater P, Sancho Castillo, Rochina MJ, & Hu Yang I (2017). How does coconut oil affect cognitive performance in Alzheimer patient? *Nutricoin Hospitalaria*, Spain, 30(2), 352-356. DOI: 10.20960/nh.780
- Drehmer E, Aguilar MA, de la Rubia Orti, Garcia Pardo MP, Sancho Cantus D, Julian Rochina M, & Hu Yang (2018). Improvement of main cognitive functions in patients with Alzheimer's disease after treatment with coconut oil enriched Mediterranean diet: A pilot study. *Journal of Alzheimer's disease*, 65(2), 577-587. DOI: 10.3233/JAD-180184
- Michael de Vrese Email & J. Schrezenmeir (2008). Probiotics, Prebiotics, and Synbiotics. *Journal of Food Biotechnology*. DOI: 10.1007/10_2008_097
- Chen D, Yang Xin, Yang Jian, Liu Ting, Hu Guoyan, Liang Hualun, Tang Xiaocui, Lai Guoxiao, Shui Ou, Zheng Chaoqun & Xie Yizhen (2017). Effects of Oligosaccharides from *Morinda officinalis* on gut microbiota and metabolism of APP/PS1 transgenic mice. *Frontiers in Neurology*, Volume 9, Article 412. DOI: 10.3389/fneur.2018.00412
- Burokas A, Arboleya S, Moloney RD, Peterson VL, Murphy K, Clarke G, Staton C, Dianan TG, & Cryan JF (2017). Targeting the Microbiota-Gut-Brain Axis: Prebiotics Have Anxiolytic and Antidepressant-like Effects and Reverse the Impact of Chronic Stress in Mice. *Journal of Biological Psychiatry*, 87(7), 472-487. DOI: 10.1016/j.biopsych.2016.12.031
- M. Khani, S Akhondzadeh, M Noroozian, M Mohammadi, S Ohadinia, & A H Jamshidi (2018). Melissa officinalis extract in the treatment of patients with mild to moderate Alzheimer's disease: a double blind, randomized, placebo controlled trial. *Journal of Neurology, Neurosurgery and Psychiatry*, Volume 74 (7). DOI: 10.1136/jnnp.74.7.863
- Hermine Tsasfack, Anne Pascal and Diedonne Kuate Neuroprotective effect and antioxidant activity of *Passiflora edulis* fruit flavonoid fraction, aqueous extract, and juice in aluminum chloride-induced Alzheimer's disease rats. *Journal of Nutrire*. 43(23) <https://doi.org/10.1186/s41110-018-0082-1>
- Rodrigo Zanandrea et al. (2017). Lithium prevents scopolamine - induced memory impairment in zebra fish. *Journal of Neuroscience letters*, Volume 664, 34-37. DOI: 10.1016/j.neulet.2017.11.010
- Zeng J, Gong M et al. (2017). Marginal Vitamin A deficiency exacerbates memory deficits following A β 1 – 42 injection in rats. *Current Alzheimer Research*, Volume 14(5), 562-570. doi: 10.2174/1567205013666161223162110
- Ronald G Thomas, Suzanne Craft et al. (2015). A randomized, double - blinded, placebo - controlled trial of resveratrol for Alzheimer's disease. *Journal of Neurology*, Volume 85(16). doi: 10.1212/WNL.0000000000002035

- Kishi T, Annas P, Matsunaga S, Basun H, Hampel H, & Iwata N. (2015). Lithium as a Treatment for Alzheimer's disease: A Systematic Review and Meta-Analysis. *Journal of Alzheimer's disease*, 48(2), 403-410. DOI: 10.3233/JAD-150437
- Charbel Moussa, Michaeline Hebron, Xu Huang, Jaeil Ahn, Robert A., Paul S, R. Scott (2017). Resveratrol regulates neuro-inflammation and induces adaptive immunity in Alzheimer's disease. *Journal of Neuroinflammation*, 14(1). doi: 10.1186/s12974-016-0779-0
- Mullan K, Cardwell CR et al. (2017). Serum concentrations of vitamin E and carotenoids are altered in Alzheimer's disease: A case - control study. *Journal of Alzheimer's Dementia. Journal of Alzheimer's and dementia (NY)*, Volume 3(3), 432 – 439. doi: 10.1016/j.trci.2017.06.006
- Cyril V Swegert, Kunjan R dave, & Surendra S Katyare (1999). Effect of aluminum induced Alzheimer's like condition on oxidative energy metabolism in rat liver, brain and heart mitochondria. *Journal of mechanism of ageing and development/* Volume 112, 27-42. doi: 10.1016/s0047-6374(99)00051-2.
- Trond Peder Flaten (2001). Aluminum as a risk factor in Alzheimer's disease, with emphasis on drinking water. *Journal of Brain Research Bulletin*, Volume 55, Issue 2, 187-196. DOI: 10.1016/s0361-9230(01)00459-2
- Virginie Rondeau, Daniel Commenges et al. (2001). Relation between aluminum concentrations in drinking water and Alzheimer's disease: An 8 year follow - up study. *American Journal of Epidemiology*, Volume 152, Issue 1, 59-66. doi: 10.1093/aje/152.1.59.
- Pali, Noemi et al. (2005). Brain aluminum, magnesium and phosphorus contents of controls and Alzheimer's disease patients. *Journal of Alzheimer's disease*, Volume 7, 273 - 285. DOI: 10.3233/jad-2005-7402

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