**Vitamin E and Brain Health: Are Supplements Advisable for All?**

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**Introduction**

 Although one may not realize it, nutritional intake is capable of acting as one of the body's best methods of preventing disease and other health conditions. Various health conditions are caused by nutritional deficiencies as well as other lifestyle factors but fulfilling a nutritious and well-balanced diet could be one of the best preventative measures. Health conditions such as dementia and Alzheimer’s disease have been associated with various nutrient intakes including vitamin E. Dementia is one of the most prevalent health conditions that affects the quality of life for older adults. The CDC, as well as the Alzheimer’s association, report that Alzheimer’s disease is the 6th leading cause of death in the United States and it currently impacts roughly 5 million Americans (CDC, 2020) (Alzheimer’s Association, 2020). The Alzheimer’s Association also reports that 1 out of every 3 senior citizens will die with Alzheimer’s or dementia (Alzheimer’s Association, 2020). Research indicates that women are more likely to suffer from Alzheimer’s disease or another form of dementia. Those who are of the African American ethnicity are twice as likely to develop dementia than someone who is white, and Hispanic people are 1.5 times as likely to develop dementia than someone who is white (Alzheimer’s Association, 2020). Additionally, those who have Down Syndrome are vulnerable to Alzheimer’s as oxidative stress is a mechanism of both conditions (Sano et al., 2016.) Vitamin E is believed to prevent or delay the onset of Alzheimer’s disease, all-cause dementia (dementia), and cognitive impairment (no dementia) (CIND) (Basambombo, Carmichael, Côté & Laurin, 2017). Vitamin E plays various roles in the body but one of its main roles is using its antioxidative properties to prevent free radicals from causing oxidative damage to cells in the body. Due to these functions in the body, it is believed that vitamin E can be an effective measure in the fight against dementia and we will further explore upon the role of vitamin E in prevention of dementia.

**Research Question**

What is the effect of vitamin E supplementation on brain health and the risk of development and progression of dementia in older adults?

**Literature Search**

**Medical Subject Heading (MeSH)**

Alzheimer’s or Dementia AND Vitamin E AND Clinical Trial - Belitskaya-Levy

Dementia AND Vitamin E - Dysken; Sano

Dementia OR Alzheimer’s OR Cognitive Impairment OR Memory Loss AND Vitamin E AND Cohort Study OR Case Control Study - Basambombo

Vitamin E and Alzheimer’s in Medline - Lloret

Vitamin E supplements AND Dementia - Rondanelli

**Literature Review**

 There are a variety of studies that help us understand how vitamin E impacts the body. These studies and other resources are crucial in understanding and furthering our knowledge about vitamin E. Vitamin E can be commonly used in the development and treatment of Alzheimer’s disease as well as other forms of dementia. Lloret and her colleagues conducted a meta-analysis to better understand if vitamin E can be beneficial in the treatment of Alzheimer’s and other dementias. They reviewed a total of 19 studies with both positive and negative results after assessing the relationship between vitamin E and Alzheimer’s disease. The studies that were reviewed were published anytime between 1992 and 2017. This meta-analysis used this data to assess if vitamin E is an effective treatment of dementia and Alzheimer’s disease (Lloret et al., 2019). Out of all of the studies that were reviewed, there were many studies that had mixed results on the effectiveness of vitamin E but one common thing that was found is that those who had low plasma vitamin E are more likely to experience dementia than those who have higher vitamin E levels (Lloret et al., 2019).  Although the results are mixed and they cannot conclude if vitamin E supplementation is effective, they believe it is possible that the antioxidant properties and other functions of vitamin E can delay the onset of Alzheimer’s and other dementias (Lloret et al., 2019). The authors of this article believe that some of the studies they reviewed may have not seen results due to errors in data extrapolation, as well as various other factors such as bioavailability of vitamin E, the age and lifestyle factors of the subjects, genetics as well as the different forms of vitamin E that were studied (Lloret et al., 2019). This analysis is important to the current nutrition community since it provides us with up-to-date information on the effectiveness of vitamin E and the development of dementia as well as possible theories on why studies may have been unsuccessful. This meta-analysis had reviewed various studies with mixed results and cannot give a distinct answer on the effectiveness of vitamin E on Alzheimer's disease. As a result of this conclusion, the authors believe that more studies must be conducted on this topic.

In addition to the previous study which discussed the possible role vitamin E’s antioxidant properties had on delaying the onset and progression of Alzheimer’s disease and other dementias, a cohort study, done by Basambombo, Carmichael, Côté and Laurin from the Canadian Study of Health and Aging, studied a similar relationship. This cohort study analyzed a total of 5,269 participants aged 65 years and older to determine if both the combined and separate treatment of vitamin E and C supplements had a significant impact on reducing the risk of cognitive impairment (no dementia) (CIND), Alzheimer's disease, and all-cause-dementia within this population (Basambombo, Carmichael, Côté & Laurin, 2017). The participants of this study were randomly selected between 1991 and 1992 from living institutions, and rural communities in Ontario Canada (Basambombo, Carmichael, Côté & Laurin, 2017). Data was collected on participants at baseline, again at 5 years after baseline, and again at 10 years after baseline (Basambombo, Carmichael, Côté & Laurin, 2017). Vitamin intake was reported according to frequency by participants of the study. The results of this cohort study showed that the regular consumption of vitamin E and C supplements reduced the risk of developing Alzheimer’s disease by 42%, reduced the risk of developing all-cause-dementia by 40%, and reduced the risk of developing CIND by 30% (Basambombo, Carmichael, Côté & Laurin, 2017). In regard to vitamin E’s effect alone on these diseases, the regular supplementation of vitamin E helped reduce Alzheimer’s disease by 46%, reduce all-cause dementia by 47%, and reduce CIND by 32% (Basambombo, Carmichael, Côté & Laurin, 2017). Based on their findings, the authors of this study concluded that the supplementation of both vitamin E and vitamin C, together and separately, help prevent the risk of developing Alzheimer’s disease and all-cause dementia, and to a lesser extent, CIND (Basambombo, Carmichael, Côté & Laurin, 2017). This study is important to include in this review because the strong sample size and design of the study helps to validate the results which were found. However, due to the fact that several other studies have produced mixed results related to the use of vitamins, such as vitamin E and C, for prevention and delay of cognitive decline in Alzheimer’s disease and other dementias, it is essential for further studies to be conducted on this topic to verify the role these vitamins play in regard to CIND, Alzheimer’s and all-cause-dementia.

 Vitamin E has various forms such as the 4 different tocopherols and the various forms of tocotrienols. All of these different forms are believed to have different roles in how our body functions. Another recent meta-analysis was conducted to see how serum tocopherol and tocotrienol levels are associated with various health conditions such as osteoporosis, sarcopenia as well as dementia. Although this study looks more in depth at many of these functions, the part that was most relevant was the research pertaining to cognitive performance. This section analyzed 11 different articles about the effects of tocopherols and tocotrienols on cognitive performances (Rondanelli et al., 2015). After completing their analysis on all of these studies, they found that low serum tocopherols and tocotrienols were associated with a higher risk of developing cognitive disorders such as dementia and Alzheimer’s in older adults (Rondanelli et al., 2015). After completing their assessment on these articles, the authors concluded that vitamin E could be a natural and efficient method in preventing or delaying conditions that affect cognitive functions such as dementia and Alzheimer’s (Rondanelli et al., 2015). This analysis is important because it explains the potential effects on the different forms of vitamin E and the development of dementia. Although many studies provided the authors with significant evidence, a few studies did not produce statistically significant data which means this is a subject in need of further research.

 An important long-term trial regarding vitamin E and Alzheimer’s is the TEAM-AD trial. This study, which was a double-blind, placebo-controlled randomized clinical trial, was conducted by the VA Cooperative Studies Program and evaluated the effect of vitamin E separately or in addition to memantine in veterans with mild to moderate Alzheimer’s that were currently taking acetylcholinesterase. The sample was primarily Caucasian men between the ages of 76 and 79. They were randomized to 4 different groups: one taking 2,000 IU of alpha tocopherol, one taking 20 mg/d of memantine, one taking both 2,000 IU of alpha tocopherol and 20 mg/d of memantine, and one taking placebos. Exactly 613 veterans participated and were in the trial for three years on average. Participants’ functional abilities were measured by the Alzheimer’s Disease Cooperative Study/Activities of Daily Living (ADCS-ADL) Inventory at baseline and after the intervention, in addition to yearly physical exams and blood work. While memantine had no significant effect on the participants, alpha tocopherol resulted in a significant reduction in Alzheimer’s progression. Participants that received the alpha tocopherol were on average 3.15 units higher on the ADCS-ADL Inventory than those on the placebo after the intervention and saw a 19% reduction in their annual rate of decline than those taking the placebo (Dysken, Sano & Asthana, 2014.)  This study showed that between two possible preventatives for Alzheimer’s, vitamin E and memantine, only vitamin E was capable of producing statistically significant results. This study was done for a longer period of time than the average study on Alzheimer’s and had a large sample size, but the sample was limited in numbers regarding women. Additional research is necessary in order to ensure that these effects are generalizable and benefit both men and women.

 A follow up substudy to Dysken, Sano and Asthana’s 2014 study on veterans was conducted and published in 2018. This substudy followed the same 613 veterans from the first study. Apolipoprotein E (APOE) genotypes are associated with an increased risk of developing Alzheimer’s disease (Belitskaya-Lévy et al., 2018). In the previous study from 2014, 415 of the 613 veterans were found to have this genotype. Results from the 415 participants with APOE genotypes in Dysken, Sano and Asthana’s study were further analyzed in this substudy. The purpose of the substudy was to understand the role that the APOE genotype plays in regard to treatments aimed to delay the progression of functional decline in people with Alzheimer’s disease (Belitskaya-Lévy et al., 2018). Additional results that were acquired from the substudy were that participants with the ε4 alleles of this genotype were found to have a faster functional decline in response to treatments as compared to participants who did not have these alleles (Belitskaya-Lévy et al., 2018). However, the regular supplementation of vitamin E was shown to delay progression of functional decline in patients with the ε4 alleles as compared to the placebo (Belitskaya-Lévy et al., 2018). Although these results were not significant, regardless of the large sample size, this study is important to reference in this review because it deals with treatment options, such as vitamin E supplementation, in delaying the progression of Alzheimer's disease and other dementias. This study indicates that vitamin E supplementation, in those who have the ε4 alleles of the APOE genotype, helps delay the progression of Alzheimer’s diseases and functional decline (Belitskaya-Lévy et al., 2018).

In comparison, a study regarding Alzheimer’s prevention in participants with Down Syndrome showed that vitamin E had no significant effect. As both Down Syndrome and Alzheimer’s are affected by oxidative stress, researchers believed vitamin E supplementation and its antioxidant properties would reduce Alzheimer’s diagnoses in this population. This study was a randomized, double-blinded, controlled clinical trial where participants were over the age of 50, had Down Syndrome, and lived in a community dwelling. The majority of participants were Caucasian males who did not have dementia. A total of 337 participants were randomized to either a group that received 2,000 IU of vitamin E daily or a placebo. For three years, data was collected every 6 months in the form of vital signs, medical examinations, and symptom checklists. Dementia was measured with the DSM-IV and the Brief Praxis Test (BPT) measured clinical and cognitive changes over time. There was an overall rate of 11% for dementia after the intervention and no statistical difference was found between the two groups (Sane et al., 2016.) The researchers found that there were no significant differences regarding cognitive, functional, behavioral, or clinical outcomes (Sano et al., 2016). Vitamin E was not found to be preventative for persons with Down Syndrome in regard to Alzheimer’s. As the study included participants over the age of 50, which is seen as advanced age for those with Down Syndrome, additional research is necessary in the preventative effects of vitamin E in younger participants.

**Conclusion and Community Applications**

Based on the results and conclusions of the studies which were analyzed in this review, it was evident that vitamin E supplementation does have an impact on preventing Alzheimer’s disease, and dementia, and delaying the progression of cognitive and functional decline in people with Alzheimer’s dementia, CIND, and other dementias. However, from the collective results of this review we cannot say that the role of vitamin E on memory function and brain health is significant in older adults suffering from these diseases. There are still many other articles with mixed results in regard to this relationship, therefore, it is clear that several other studies need to be conducted in order for the medical community to develop a definitive and concrete answer in regard to vitamin E’s effect on delaying cognitive decline in these diseases.  Although more research must be done on this subject, there are a few ways we can apply these studies to our communities. Nutrition education is the best way of sharing nutrition knowledge. It would be beneficial to the elderly, and to those who are at risk for developing these diseases, to provide them with nutrition education highlighting the importance of consuming healthy amounts of vitamin E due to its potential relationship with dementia. Although much more research needs to be done on the subject of vitamin E and various forms of dementia, there does seem to be an association between this vitamin and these cognitive diseases. It is essential that we incorporate the knowledge and information regarding vitamin E and brain health into education programs for older adults and at-risk populations.

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