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High Antioxidant Diet and its Effect on Delaying Alzheimer's:

An Integrative Literature Review

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Abstract

Background: Alzheimer's disease (AD) is a neurological disease that is characterized by cognitive deficits and intellectual loss (Oberg & Mischley, 2008). With Alzheimer's so prevalent in society and no effective treatments, it is essential to find preventative strategies when approaching the disease. A diet high in antioxidants may prove as an effective means in delaying, if not preventing, the onset of AD (Polidori & Schulz, 2013). In the absence of adequate antioxidant defense system, oxidative-stress related changes occur in the brain. This leads to cognitive impairment and AD-related alterations and symptoms (Polidori & Schulz, 2013). This very reason is why patient education and the importance of a high antioxidant diet is so critical.

Objectives: The goal of this systematic integrated literature review is to determine whether there is a direct correlation between intake of a high antioxidant diet and delayed symptoms of Alzheimer's disease.

Methods: A systematic integrated literature review search was conducted within the databases CINAHL Complete, Consumer Health Complete-EBSCOhost, Health Source: Nursing/Academic Edition, and PsychINFO. 225 results were yielded through this search.

Results: A synthesis across studies in relation to a high antioxidant diet and prevention of Alzheimer's was analyzed. A consensus points to antioxidant therapy alone not being sufficient enough to prevent, or delay, AD. Statistical outcomes, in all of the studies analyzed, show antioxidants having no effect on cognitive improvement.

Conclusions: A balanced diet, such as the Mediterranean diet, and a healthy lifestyle including physical activity is the best option in preventing the onset of dementia.

Key Words: Alzheimer's, antioxidant, diet

Introduction

Background and Significance

Alzheimer's, a progressive disease, accounting for nearly 60 to 80% of those diagnosed with some form of dementia (Alzheimer's Association, 2017). Visioli and Burgos-Ramos (2016) define Alzheimer's disease (AD) as an irreversible neurodegenerative disorder that results in cognitive decline and progressive memory loss. Intracellular neurofibrillary tangles of hyperphosphorylated tau protein and extracellular senile plaques containing amyloid β peptides ($A\beta$) are both characteristic features of AD. It is estimated that nearly 35.6 million people were living with Alzheimer's in the year 2010 and the number is expected to triple by 2050 (Caldwell, Yao, & Diaz Brinton, 2014). Since presently AD has no defined cure, it is essential to find alternative methods to delay the progression of, and even prevent, the disease from occurring.

Presently the healthcare organizations do not currently offer any feasible pharmacological methods to treat dementia and cognitive decline (Visioli & Burgos-Ramos, 2016). Presently research is being conducted on antioxidant therapies and the relatively low risk they provide in targeting early cognitive and biological changes in the body. Antioxidants fight oxidative damage that is caused by free radicals that build up in the nerve cells (National Institute on Aging, 2016). Free radicals have "taken the role of the main villain in AD pathogenesis and/or progression (Behl 1999; Behl and Moosman 2002 as cited by Souza Ferreirs, Soares de Vasconcelos, Da Costa, Leite da Silva, Da Silva Barbosa, Quadros Gomes...Percario, 2015).

Literature supports that an antioxidant diet would be used as an alternative method to prevent the buildup of free radicals. Antioxidant therapy could be promoted through diet with foods such as cranberries, blackberries, pears, apricots, artichokes, bell peppers, legumes,

walnuts, pomegranate juice, and various others. It is recommended that not just one food group be the sole source of an antioxidant (Mayo Clinic Staff, 2014).

Problem Statement

Alzheimer's is a progressive disease that presently has no cure and is the sixth leading cause of death in the United States with those diagnosed only living an average of eight years after noticeable symptoms (Centers for Disease Control and Prevention [CDC], 2015). When the onset of Alzheimer's occurs memory loss is mild and the individual realizes such and attempts to cover up clues of such happening. As the disease progresses this becomes more difficult since activities of daily life are effected. Early stages of memory loss are mild and as the disease progresses the individual declines and loss of performing daily activities of life become more difficult to where the ability to carry on a conversation and respond to one's environment is totally impaired. (Alzheimer's Association, 2017).

While there are pharmacologic treatments, studies suggest that antioxidants protect the brain from cognitive decline as well (National Institute on Aging, 2016). With Alzheimer's so prevalent in society, it is essential to determine whether a diet high in antioxidants prevents the onset of Alzheimer's. With the baby boomer generation aging, it is projected that by the year 2050, 7.1 million people 65 years of age and older are predicted to have AD. This is a 40% increase from today. (Seegert, 2014). With such a drastic increase in the disease, it's safe to argue that there may be a deficit in the number of medical staff needed to address AD.

Purpose of Integrative Literature Review

The purpose of the integrative literature review is to determine whether a high antioxidant diet is effective in delaying the onset of Alzheimer disease. Research that examined the efficacy of macronutrients and how they relate to the prevention of cognitive deficit will be evaluated. In addition, research that take gender into consideration will be analyzed. Women, not only represent two-thirds of the population with Alzheimer's disease, but they are also more likely to be diagnosed (Rubin, 2015). Review of literature will determine whether a diet high in antioxidants is more effective for women compared to men and vice versa. Lastly, this review will determine if there are additional non-pharmaceutical interventional that have proven effective in the preventing the onset of Alzheimer's. Information obtained from this integrative literature review should provide healthcare professionals with the opportunity to provide families with the necessary information that will help delay, if not prevent, Alzheimer's.

Research Questions

1. When is the best time to start antioxidant therapy?
2. Should there be more of a focus on diet as a whole, rather than single components of a diet?
3. What other non-pharmaceutical interventions have proven effective in preventing onset of Alzheimer's?

Conceptual Framework

Prevention, or a delay, in the onset of Alzheimer's could be associated to a high antioxidant diet. The Health-Promoting Self-Care System Model (HPSCSM) is a model used to explain an individual's motivation behind taking part in health-promoting behaviors. According to HPSCSM "individuals are capable of developing the knowledge, attitudes, and skills

necessary for deciding upon and performing health-promoting behaviors..." (Simmons, 1990 as cited by Raingruber, 2014). Due to the high value of self-care when promoting health to individuals, it is the nurse's responsibility to collectively provide education in promoting self-care behaviors. In addition, nursing influences conditioning factors such as social, environmental, perceived health state, and healthcare experiences.

Figure 1: Self Care and Health Promoting Behaviors



Methods

Research Design

The design of the study presented here is an integrative literature review aimed to discover whether there is a direct correlation between a high antioxidant diet and prevention of Alzheimer's. In order to complete the integrative literature review, the researcher will search the literature to find articles that pertain to diets high in antioxidants and rates of delay and prevention. The integrative literature review will be conducted using the framework of the Health-Promoting Self-Care System Model (HPSCSM). The framework will help establish an individual's self-care behaviors, specifically diet, and whether these behaviors have influenced prevention of Alzheimer's.

Literature Search Strategies

The DePaul University library search engine was utilized for the integrative literature review in order to gain access to a variety of databases. A review of the following databases was searched: CINAHL Complete, Consumer Health Complete-EBSCOhost, Health Source: Nursing/Academic Edition, and PsychINFO. The keywords that were used to search the databases were "Alzheimer's", "antioxidant", and "diet" which yielded 225 results.

Literature Search Limitation and Inclusion/Exclusion Criteria

The search for the integrative literature review was limited to articles that only addressed diet and nutritional supplementation. Additionally, articles that were published between the years 2003-2016 were assessed. Studies that were not peer-reviewed were excluded from the review. Studies that did not focus on human populations were eliminated with the exception of animal studies that provided a direct correlation between diet and prevention of AD.

Table 1: Diagram of Review Process

	CINAHL	EBSCOhost	Health Source	PsychINFO
Number of studies found using keywords:	97	19	17	92
Number of studies that met inclusion criteria:	36	16	6	31
Number of studies selected based on total content:	3	1	1	4
Number of studies after duplicates were excluded:	0	2	3	5
Total number of articles used: (9)				

Data Analysis

The studies that will be classified in a table under the following categories: author and year; purpose/problem; sample; framework; design; any additional measures that may play a role in preventing AD; and results. The following table will be used in order to compare and contrast each study and determine if a high antioxidant diet is effective in preventing onset of Alzheimer's. Studies presented in the literature review will explore which interventions were successful and unsuccessful in preventing onset of Alzheimer's.

Results

A synthesis across studies in relation to a high antioxidant diet and prevention of Alzheimer's was analyzed. The following chart matrix will be used to analyze the studies that will be used in the systematic literature review. A consensus points to antioxidant therapy alone

not being sufficient enough to prevent, or delay, AD. Statistical outcomes, in all of the studies analyzed, show antioxidants having no effect on cognitive improvement. While this is true, it is important to determine the best window to implement preventative strategies for AD. The prodromal/preclinical window is the area that should be focused on (Caldwell, Yao, & Diaz Brinton, 2015). This window of opportunity can take place anywhere from 20 to 30 years before an individual develops AD (Kamphuis & Scheltens, 2010).

Discussion

Relevant Findings

Ancelin, Christen and Ritchie (2007) found that that the consumption of antioxidants is more likely to be preventative rather than curative when it comes to mild cognitive impairment. This finding points to antioxidants having more of an impact on mild cognitive impairment (MCI) rather than dementia. Additionally, a combination of substances could potentially provide a benefit towards targeting dementia and Alzheimer's. "Combination of vitamins, minerals and herbal antioxidants could offer greater potential benefit than any single antioxidant, especially if the agents work in different cellular compartments or have complementary mechanisms of action" (Ancelin, Christen, & Ritchie, 2007, p. 13). While this may be true, it is unclear as to which proportion and doses should be used for each substance to be beneficial. This is an area that would require further research.

Polidori and Schulz expressed similar findings in their review. Antioxidants alone are not sufficient enough to delay the onset of Alzheimer's. Rather, a combination of a healthy lifestyle and balanced diet, including antioxidants, is the method that should be used to target and delay the onset of AD. The Mediterranean diet is a prime example of a balanced diet that has scientific

evidenced for being protective against the onset of dementia. “The Mediterranean diet is a diet characterized by high intake of fish, vegetables, legumes, fruits, cereals, unsaturated fatty acids mostly in the form of olive oil, low intake of dairy products, meat and saturated fatty acids as well as regular but moderate intake of alcohol” (Polidori and Schulz, 2014, p. 382). Specifically, the fruits and vegetables are a high source of antioxidants micronutrients and synergism of these food groups’ contents. It would be safe to assume then that this diet, paired with a healthy lifestyle, would be a suitable choice for those that have risk factors for AD.

Kamphuis and Scheltens (2010) concluded that a single nutrient is insufficient in providing protection against the onset of dementia. Instead, a multi-nutritional intervention is needed in order to target multiple disease aspects such as inflammation, oxidative stress, A β , synaptic loss, and the vascular system (Kamphuis and Scheltens, 2010). Additionally, timing the nutritional intervention is key to increase potential benefits. “Pathological changes in the brains of persons at risk for developing AD can develop as early as 20 to 30 years prior to clinical dementia symptoms (Kamphuis and Scheltens, 2010, p. 772). With this in mind, the earlier the supplementation is started, the better.

Otaegui-Arrazola et al. (2014) determined through review that “epidemiological cross-sectional and longitudinal studies in humans shows a protective role of dietary and supplemented intake of n-3 PUFAs and fish against AD and cognitive aging. On the other hand, no such effect has been consistently observed for antioxidants and B vitamin intake either from diet or supplements” (pg. 17). This review also concluded that timing for treatment and supplementation for AD as there is evidence that the disease can begin anywhere from 10-15 years before clinical symptoms appear (Otaegui-Arrazola et al., 2014). Otaegui-Arrazola et al. (2014) explain that future studies should focus on younger populations to target this time frame.

Souza Ferreira et al. (2015) didn't come up with any conclusive evidence in regards to antioxidants having an effect on the onset of AD symptoms. More studies are needed in order to determine whether using antioxidants can either reduce the risk or slow the progression of AD. For the meantime, antioxidant therapy is still considered a low-risk therapeutic strategy if using multiple antioxidants. Souza Ferreira et al. (2015) state "the use of a single antioxidant for long periods can be harmful because the molecule may be oxidized and become a pro-oxidative substance" (p.606). When using multiple antioxidants, the potential for toxicity is decreased.

Source/Year	Purpose/ Problem	Sample	Framework	Design	Additional Measures	Results
Ancelin, M. L., Christen, Y., & Ritchie, K., (2007)	“Therapeutic interventions for the prodromal stages of dementia are currently being sought with a view to delaying if not preventing disease onset” (pg. 1).	769 patients with MCI; 1,059 elderly; 117 elderly; 3,385 men; 14, 968 women; 894 ≥ 65 years...	None	Review article looking at clinical trials; several epidemiological reviews	Smoking is associated with a poor diet and increase in the load of free radicals. Smoking cessation is highly recommended.	It is suggested that the consumption of antioxidants is more likely to be preventative rather than curative when it comes to mild cognitive impairment. Table 2b in this review article shows the association between vitamin intake in the diet and positive effect on cognition. In regards to vitamin C consumption, 4 studies showed a positive effect on cognition, 4 studies showed a negative effect and 2 studies showed no difference. In regards to β-carotene consumption, 2 studies showed a positive effect on cognition, 3 studies

						showed a negative effect and 5 studies showed no difference. Lastly, vitamin E consumption was assessed. 4 studies showed a positive effect on cognition, 4 studies showed a negative effect and 2 studies showed no difference.
Kamphuis, P. J. G. H., Scheltens, P., (2010)	“Specific nutrient deficiencies in the elderly, including omega- 3 fatty acids, B-vitamins, and antioxidants among others, may exacerbate pathological processes in the brain” (pg, 765).	220 healthy, free-living women; 6377 women; 818 healthy men and women; 910 healthy men and women ...	None	Review article looking at several epidemiological reviews	Diet as a whole, instead of looking at a single component, is gaining more recognition (i.e. Mediterranean-style diet).	“Current understanding suggests that multi-nutritional (rather than single nutrient) intervention, targeting multiple disease aspects... may have the greatest therapeutic potential” (pg. 772). Of the 9 completed studies that examined the prevention of cognitive decline, only 3 showed signs of positive effects on cognition.

<p>Otaegui-Arrazola, A., Amiano, P., Elbusto, A., Urdaneta, E. & Martínez-Lage, P., (2014)</p>	<p>The effect of diet and nutritional factors on the risk of AD and cognitive aging.</p>	<p>1416 ≥65 years; 815 (65-94) years; 2233 ≥65 years; 8085 ≥65 years; 5395 ≥55 years ...</p>	<p>None</p>	<p>Review article looking at longitudinal observational studies and clinical trials</p>	<p>PUFAs (polyunsaturated fatty acids) have been found to reduce the risk of AD and MCI.</p>	<p>“The available evidence from epidemiological cross-sectional and longitudinal studies in humans shows a protective role of dietary and supplemented intake of n-3 PUFAs and fish against AD and cognitive aging. On the other hand, no such effect has been consistently observed for antioxidants and B vitamin intake either from diet or supplements” (pg. 17).</p>
<p>Polidori, M. C., & Schulz, R. J., (2014)</p>	<p>“This review summarizes knowledge about the impact of nutrition as part of a healthy lifestyle and of micronutrients in particular on delaying and avoiding dementia onset” (pg. 381).</p>	<p>341 patients with AD; 769 patients with MCI; 20 patients with AD; 100 patients with AD</p>	<p>None</p>	<p>Review article looking at clinical trials</p>	<p>A balanced diet, such as the Mediterranean, has gained the highest scientific evidence for the protection against dementia onset. A balanced diet, together with social activities, physical exercise, and</p>	<p>A balanced diet and healthy lifestyle, rather than antioxidants alone, are more effective in delaying the onset of AD.</p>

					cognitive engagement has proven most effective.	
Souza Ferreira, M. E., Soares de Vasconcelos, A., Da Costa Vilhena, T., Leite da Silva, T., Da Silva Barbosa, A., Quadros Gomes, A. R., Fani Dolabela, M. & Percario, S., (2015)	The risk of AD is growing. It's important to understand the underlying process as well as the grounds for antioxidant therapy.	Wasn't specifically stated in the review	None	Review article looking at experimental studies	No other additional measures were mentioned other than the need to further research antioxidant therapy.	More studies are needed in order to determine whether using antioxidants can either reduce the risk or slow the progression of AD.

Conclusion

A consensus points to antioxidant therapy alone not being sufficient enough to prevent, or delay, AD. Instead, research suggests that diet as a whole, in conjunction with exercise, is something that should be addressed. A balanced diet, such as the Mediterranean diet, and a healthy lifestyle including physical activity is the best option in preventing the onset of dementia. According to Kamphuis and Scheltens (2010) importance for diet as a whole is reaching light in the AD community. "Adherence to a Mediterranean-style diet has been associated with a reduced risk for developing AD. Based on studies comparing single versus multiple nutrient supplementation, there is a need for multi-nutrient and, multi-target interventional AD management approached" (p. 770).

Nursing Implications and Future Directions

With the prevalence of AD being so high in the community, it is critical to find ways to hinder and, ideally, prevent the disease. As stated in the conclusion, antioxidant therapy alone is not sufficient enough to prevent or delay AD. Nurses should, instead, promote a healthy lifestyle including diet and exercise, provide patient and family education and be made available to answer any questions. It was noted among numerous articles used in the systematic literature review that more research should be conducted into the efficacy of antioxidant therapy. While it's benefits have been proven in animal models, it has yet to be demonstrated in human models.

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