

Vitamin D Deficiency and the Increased Risk of Developing Dementia and Alzheimer's Disease

Morgan Dalcerra, Amanda Garcia* and Hollie-Ann McKiel

Nursing Department, California State University Channel Islands, California, USA

*Corresponding author: Amanda Garcia, Nursing Department, California State University Channel Islands, CA 93012, USA, E-mail: amanda.garcia918@myci.csuci.edu

Received date: July 24, 2017; Accepted date: October 03, 2017; Published date: October 06, 2017

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Citation: Dalcerra M, Garcia A, McKiel H (2017) Vitamin D Deficiency and the Increased Risk of Developing Dementia and Alzheimer's Disease. J Geriatr Med Res. Vol.1 No.1: 03.

Abstract

Vitamin D Deficiency and the Increased Risk of Developing Dementia and Alzheimer's Disease. There is significant evidence supporting the inverse relationship between vitamin D deficiency and risks of dementia-related conditions including Alzheimer's disease (AD). Through an extensive review of current literature and recent studies from 2008-2017, our research explores the connection between vitamin D deficiency and the development of dementia and AD. This is significant for nursing because the patient population that is provided care by nurses is suffering from AD at an increasing rate without a cure. Vitamin D deficiency increases the risk of developing dementia and AD; therefore, the older adult and those at risk for developing AD should increase vitamin D consumption by increasing dietary intake or by taking vitamin D supplementation.

Keywords: Vitamin D; Alzheimer's disease; Dementia cases

Background

Dementia is an umbrella term used to describe mental decline that can affect day-to-day activities ranging from mild to severe cases ("Dementia," 2017). There are several neurological cognitive disorders that fall under the dementia umbrella, including AD which accounts for 60-80% of dementia cases. ("Dementia," 2017). AD is a "progressive irreversible degenerative neurologic disorder" that develops gradually with increasing loss in cognitive function and personality disturbances Hinkle et al. [1].

Vitamin D is a broad term used for two specific terms called ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3). Vitamin D2 is a naturally occurring vitamin that is found in plants; vitamin D3 is created in the body when exposed to sunlight Burchum et al. [2]. Although these are two different compounds, they produce very similar effects in the body and

are therefore commonly clumped into one term, vitamin D. According to the Office of Dietary Supplements (n.d.), vitamin D is found in few naturally occurring foods, therefore, supplementation and sunlight exposure are important components to meet adequate serum blood levels.

Some of the receptors in the brain are specifically for vitamin D, which means that vitamin D is influencing an individual's cognition, resulting in the common signs and symptoms seen in patients with AD. Research has shown that individuals with AD have fewer vitamin D receptors in the hippocampus, also known as the memory center of the brain Oudshoorn et al. [3]. The brain relies on vitamin D receptors for protection against the things that can damage it, including the development of the plaques and tangles that form in AD Soni et al. Vitamin D regulates the release of nerve growth factor (NGF), a very important molecule for neuronal survival of hippocampal neurons as well as cortical neurons Gezen-Ak, Dursun & Yilmazar [4]. NGF prevents the death of and stimulates the function of basal forebrain cholinergic neurons that undergo early and prominent degeneration in AD Tuszynski et al. [5]. If vitamin D can slow the progression of the disease and perhaps even prevent such cognitive impairments, then this would be a remarkable breakthrough for the medical community and the public at large.

Experimental Results

Gezen-Ak et al. [4] identified that NGF is vital to the survival, growth, maintenance, and proliferation of neurons. This study involving rat embryos shown that vitamin D plays an important role in increasing the production of NGF. The results yielded significant evidence that vitamin D applied to hippocampal neurons revealed statistically significant increased amounts of NGF when compared to the control group Gezen-Ak et al. [4]. The experiment was repeated three times yielding the same results and used biophysiologic measures increasing the credibility. The findings appear to be valid and despite not being conducted on human subjects, contribute meaningful evidence to be discussed in clinical nursing practice regarding Vitamin D treatment and AD. In understanding how NGF plays

a vital role in cognition, vitamin D may benefit those at risk for dementia and AD.

A study was conducted to investigate if high dose vitamin D supplementation could enhance cognition among healthy adults Pettersen [5]. A population sample of 82 individuals were either exposed to high dose (4000 IU/d) or low dose (400 IU/d) vitamin D3 for eighteen weeks Pettersen [5]. Results showed that performance improved in the high dose group on nonverbal (visual) memory Pettersen. This concluded that nonverbal (visual) memory seems to benefit from higher doses of vitamin D, especially participants who were deemed vitamin D deficient (less than 75 nmol/L) at baseline Pettersen [5]. This study found that high dose vitamin D supplementation enhanced nonverbal (visual) memory in healthy adults.

A prospective study was conducted to determine whether low serum vitamin D levels were associated with an increased risk of developing dementia and AD Littlejohns et al. [6]. This study recruited 1,658 participants who had their serum vitamin D level measured initially and at a mean follow-up time of 5.6 years Littlejohns et al. [6]. Results showed that out of the sample population, "171 participants developed all-cause dementia including 102 cases of AD" Littlejohns et al. [6]. This prospective study was needed to further investigate the association between low vitamin D levels and dementia as well as AD.

Littlejohns et al. [6] observed a strong relationship between serum vitamin D levels and risk of both dementia and AD. These findings support our thesis that vitamin D deficiency is associated with an increased risk of dementia and AD. This study is very important to the nursing community because it is a crucial and continual role of nurse to educate patients. Vitamin D is a simple intervention nurses can utilize in teaching patients who suffer from dementia/AD or those at risk, to help slow the disease progression and improve cognition.

An additional study was conducted at Angers University Hospital in Angers, France for seven months on patients who were admitted and diagnosed with dementia Annweiler et al. [7]. Serum vitamin D levels, 25(OH)D, were drawn and defined as severe vitamin D deficiency if levels were below 10 ng/mL Annweiler et al. [7]. A total of 228 voluntary participants were included in the study, with 138 participants placed in the severely vitamin D deficient group Annweiler et al. [7]. This study found that severe 25(OH)D deficiency was the main factor associated with the participants who had moderate to severe dementia Annweiler et al. [7]. Although there may be additional factors influencing the data, this overwhelmingly majority of diagnosed patients who were severely vitamin D deficient is compelling evidence to support our thesis of serum vitamin D deficiency and risk of developing dementia/AD.

Sommer et al. [8] found 1,870 research articles that were related to sunlight exposure or vitamin D deficiency in relation to dementia. Upon analysis, six articles were selected to be included in this systematic review and meta-analysis, with a total of 18,974 adults included in the study Sommer et al. [8]. The meta-analysis concluded there was a considerably higher

risk for developing dementia in those with severe vitamin D deficiency than those with adequate levels of vitamin D Sommer et al. [8]. Although there is no definitive link between vitamin D deficiency and dementia, this systematic review and meta-analysis have shown findings that are substantial in the progressive research investigating the connection between vitamin D deficiency and risk of dementia.

A review was published by Annweiler [9] that discussed the role of vitamin D in dementia prevention. This article identified several nonrandomized controlled studies in which older adults improved cognitively after 1-15 months of vitamin D supplementation Annweiler [9]. Based on the studies this article reviewed, "it appears crucial to maintain vitamin D concentrations at sufficiently high levels to slow, prevent, or improve neurocognitive decline" Annweiler [9].

Vitamin D plays a major role in neurophysiology and neuroprotection. According to this article, "Vitamin D regulates the synthesis of neurotrophic agents, such as nerve growth factor, glial cell line-derived neurotrophic factor, and neurotrophin, thereby controlling neuronal differentiation and maturation" Annweiler [9]. Vitamin D may offer neuroprotection against AD by reversing age-related inflammatory alterations in the hippocampus and weaken the buildup of amyloid plaques Annweiler [9]. It is known that serum vitamin D concentration decline with age, so maintaining high levels throughout the lifespan may prevent age-related neurological disorders Annweiler [9]. This review emphasizes the importance of sufficient levels of vitamin D in the brain to prevent the onset of dementia.

Annweiler et al. [10] observed a higher dietary Vitamin D intake was associated with a lower risk of developing Alzheimer's Disease in 498 women who were 75 years or older. The study's aim was to determine whether the dietary intake of vitamin D was an independent predictor of the onset of dementia within 7 years among women aged 75 years and older Annweiler et al. [10]. Self-administered food questionnaires were used to assess dietary intake based on food types, then sorted into quintiles to evaluate the ability to predict AD Annweiler et al. [10]. This study did have limitations including that it was self-report, so findings could be skewed, but consideration of confounding bias were considered to achieve the most reliable results possible. Ultimately, "The highest consumption of dietary vitamin D was associated with a decreased incidence of AD by 4.35 times," Annweiler et al. [10]. The findings suggest supplementary evidence that low levels of vitamin D will increase risk of developing AD. This study concluded that women consuming the most vitamin D had more than a four-fold decrease in the incidence of AD.

Recommendations/Suggestions for Patients

In, "Clinical Roundup: Selected Treatment Options for Alzheimer's Disease," (2015), it was shown that after a seven year follow up, the risk of developing AD was decreased fivefold if taking more than 800 IU of vitamin D a day. This compilation of selected treatments for AD discussed CAM

therapies and cited recently published studies from peer reviewed journals. Considering these results with additional study findings, it should be recommended to patients at risk for AD to begin a regimen including at least 800 IU of vitamin D supplementation daily ("Clinical Roundup," 2015). It is crucial that healthcare providers make sure that patients are receiving adequate amounts of vitamin D through their diet or by taking supplementation of vitamin D.

A previously cited study, Gezen-Ak et al. [11] supported the supplementation of vitamin D for patients at risk for developing AD as a preventative action. The study found that the understanding of vitamin D as a molecular mechanism and the role it plays in cognition could promote the use in treatment and prevention of AD Gezen-Ak et al. [11]. This study used biophysiologic measures to determine the influence of vitamin D on NGF, a critical molecule in the survival of neurons. Biophysiologic measures are highly reliable and these results should be greatly considered when determining vitamin D recommendations for the older adult.

Additional evidence to defend the vitamin D recommendation for patients is from Annweiler et al. [11,12] which advocates for older adults being screened for hypovitaminosis D and receiving appropriate supplementation to decrease the risk of developing AD. This was a consensus finding of international experts in this field based on Yu et al. [12,13] which found fewer amyloid plaques in vitamin D3 enriched diets of transgenic mice. Although this study does not include human subjects, it demonstrates a key factor in the commonly thought etiology of AD, the amyloid plaques. In addition to this finding, an increase in NGF was also found in these mice, which has been replicated in other studies. If vitamin D could increase NGF while decreasing the number of amyloid plaques, then increasing vitamin D intake is a compelling suggestion for the patient at risk of developing AD to supplement with vitamin D.

Fields et al. [14,15] examined activity and sunlight exposure to analyze a correlation to serum vitamin D levels in 100 men over the age of 60. This article found that exposure to light can account for as much as 90 percent of an individual's vitamin D requirement Fields et al. [15]. This study further found that participants with inadequate vitamin D levels had dramatically less average daily exposure to light when compared to participants with normal vitamin D levels Fields et al. [15]. Although there may have been other factors influencing these results, this article supports increasing daily sunlight exposure in patients who are vitamin D deficient.

While many of the studies evaluating Vitamin D demonstrate the benefits, few are not without controversy. Sanders et al. revealed in a randomized control trial of over 2,200 women aged 70 or over, that high dose Vitamin D had an increased risk of falls and fractures. Kotlarczyk et al. supplemented female residents over 65 years of age with osteoporosis in long-term care by following the Institute of Medicine guidelines of 800 IU of Vitamin D a day for the older adult, every day for two years. Even though the 25(OH) D levels were adequate, more falls were seen after supplementation than at baseline and all groups declined in

cognitive functioning. Malihi et al. [16-21] identified multiple studies totaling 19,833 participants on the long-term effects of Vitamin D supplementation. They concluded that long term supplementation of Vitamin D did result in an increased risk of hypercalcemia and hypercalciuria, but not kidney stones. These studies should be considered when discussing Vitamin D supplementation.

Conclusion

The role of vitamin D is not yet entirely understood in patients with dementia and AD because there may be additional factors contributing to the disease progression such as environment, genetics, and lifestyle. However, there is significant statistical evidence demonstrating the influence vitamin D has on cognition and factors demonstrating the commonly seen symptoms of AD. As shown, vitamin D deficiency increases the risk of developing AD and to help prevent or slow the development of AD, the older adult and those at risk should be educated on the critical role of vitamin D in this disease and discuss supplementation to prevent deficiency. Healthcare providers should ensure patients are receiving adequate amounts of vitamin D by increasing dietary intake, increased sunlight exposure, or with supplementation to further reduce the risk of developing AD and to slow the increasing rate of occurrence of AD in our communities.

Future Research

The results provided have shown a compelling connection between vitamin D deficiency and risk of dementia/AD, however, there is still a need for further research. One critical component that has yet to be evaluated is at what age patients should start supplementing vitamin D to maximize their benefits. Another component that has not been studied is whether vitamin D definitively improves cognition in patient with already progressing dementia/AD. Also, future research should focus on if taking vitamin D supplementation prevents a person from getting Alzheimer's Disease? These recommendations on further research will strengthen the results of the current data.

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