International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

The Role of Calcitriol and Folic Acid in Patients with Alzheimer's Disease: A Literature Review

Claraiva Mayung

Trisakti University
Email: *claraclaraiva[at]gmail.com*

Abstract: ***Until now, the role of various micronutrients on the risk of Alzheimer's disease is still widely debated, including the role of calcitriol and folic acid in patients with alzheimer's disease. The study aims to present the results of an analysis related to the significant role of calcitriol and folic acid in alzheimer's disease. The criteria for articles used in this literature review study are 1) focus on the role of calcitriol and folic acid in alzheimer's disease; 2) articles published in national l and international journals; 3) articles published in the last 10 years; 4) contain keywords calcitriol or folic acid and alzheimer. The total number of articles used in this study was 9 articles, mostly from international journals. The results showed that folic acid is one of the micronutrients that affect cognitive function and alzheimer's risk where folic acid administration in alzheimer's patients can improve cognitive processes. Furthermore, the role of calcitriol and vitamin D on the risk of alzheimer is believed to be very important where calcitriol deficiency can increase the risk of alzheimer. Therefore, it is important for people, especially the elderly, to pay attention to the intake of macro and micro nutrients in the body. This literature review is expected to be a reference for the general public to pay attention to nutritional content, especially calcitriol and folic acid to prevent alzheimer's disease.***

Keywords: alzheimer disease, calcitriol, folic acid, neurodengenerative disease, vitamin D

1. Background

Developments and advances in medicine have made human life expectancy longer and reduced the risk of death. The low mortality rate has made the elderly population quite large. The increase in life expectancy and length of human life with the development of medical science is a positive thing because everyone should strive to maintain survival. However, the elderly are very vulnerable to various diseases and some of these diseases cannot be treated. One of the diseases that elderly people are prone to is dementia. Gustri (2019) states that dementia is a human condition that experiences cognitive decline that is severe enough to interfere with activities in daily life both personal and social activities. Old age is an age where it is very risky to suffer from dementia as Hartati and Widayanti (2010) state that increasing age is in line with the increasing risk of suffering from dementia. Therefore, dementia is a frightening specter for the elderly population and society.

Dementia causes a person to lose memory of daily activities, memory of others, memory of time and place, and even lose memory of oneself (Setyowati et al.2019). One of the dementias that is often found in the community is Alzheimer's. Alzheimer's disease is a neurodegenerative disease in which the death of nerve cells in the brain will cause a decline and decrease in cognitive and intellectual power, resulting in disruption of social activities and professional activities of a person (Sari et al., 2022). Nisa and Lisiswanti (2016) explain that among the main factors that cause someone to suffer from alzheimer's are age, genetics and family history as well as social activity factors where aging is the biggest risk factor for this disease. Meanwhile, Sengkey et al. (2017) state that alzheimer's is the fourth leading cause of death for the elderly population in developed countries where women suffer more than men. Alzheimer's dementia is characterized by progressive atrophy and gliosis of the temporal lobe and hippocampus then accompanied by other related cortices and finally in the primary motor and sensory cortex (Nisa and Lisiswanti, 2016). In the management of alzheimer's disease, there is no drug that can cure it to date and the administration of drugs can only reduce the rate of development of alzheimer's suffered by humans (Sianturi, 2021). Therefore, what can be done for the treatment of alzheimer's disease is to prevent the occurrence of this disease to prevent the progressivity of alzheimer's itself.

Being old is not the only cause of someone suffering from alzheimer's, but of course it is related to other risk factors including family history and genetics. As Purnakarya (2009) explains that eating patterns, education level, nutritional status, macronutrient intake, and micronutrient intake also greatly affect the risk of alzheimer's. Krisdyana (2020) adds that there are many factors that cause dementia, including nutritional intake and nutritional status. Gustri (2019) explains that nutrient intake is an important factor that affects the health of the elderly community and reduces the risks associated with aging and deterioration of intellectual function. So, nutrition is an important part of the risk of suffering from alzheimer's. Macronutrient intake in the body is a nutrient that is needed by the body in large quantities including carbohydrates, protein and fat where high intake of fat and saturated fat can increase the risk of senile dementia. In addition to macronutrients, micronutrients are also important to consider which also have a significant effect on body health. As Gustri (2019) states that micronutrients are also needed by the body, including the elderly, which function to regulate the body in launching the oxidation process, maintaining normal nerve and muscle function, for tissue vitality and supporting various other body functions.

Utami (2013) states that among the micronutrients that are often deficient are folic acid, vitamin B6 and vitamin B12. In addition, vitamin D deficiency is also often found in humans (Wicitania, 2016). Everyone of all ages basically

needs micronutrient intake in the body, it's just different in terms of the quantity needed. The elderly community needs to pay attention to micronutrient intake in the body in order to improve cognitive function and to reduce disturbances in cognitive function (Harna et al., 2020). Kristy and Mahmudiono (2022) explained that optimal acquisition of nutrients from food, such as folic acid, omega - 3 fatty acids, amino acids, vitamins B12, A, C, D and E, zinc, selenium, and probiotics, are among the alternatives that can be applied by the community as a preventive effort in reducing mental health - related problems. According to Aisyah (2009), adequate intake of vitamins A, E, C, Fe and Zn is believed to reduce the risk of senile dementia in the elderly. Likewise, research conducted by Triantari (2011) found that the intake of vitamin B12 in the body has a significant influence on cognitive function in the elderly community.

In general, it can be ascertained that adequate micronutrient intake in the body can maintain cognitive function in the elderly community. As Rahmawati et al. (2012) also explained that through the fulfillment of micronutrient intake, vitamins C and E have a significant relationship the cognitive function of the elderly community. One of the concerns in the discussion of micronutrients is folic acid, which is one of the micronutrients needed by the body. According to Kristy and Mahmudiono (2022), folic acid functions to maintain and maintain nerve cells which also includes maintaining nerve cells in the brain so that it can reduce the risk of suffering from mental illness, such as depression. Apart from folic acid, the role of vitamin D is also very important and is minimally discussed in various studies, especially discussions related to carcitriol. Earlia et al. (2020) state that calcitriol [1, 25 (OH) 2D] is the active form of vitamin D and binds to vitamin D receptors (RVD) in the nucleus of target tissues. Glade (2013) states that vitamin D affects many human diseases including cognitive impairment and alzheimer's disease. Not enough research has detailed the function and significant role of calcitriol and folic acid on alzheimer's disease. To find out the significant role of calcitriol and folic acid on alzheimer's disease, a discussion of articles that examine the role of calcitriol and folic acid on alzheimer's disease is needed. Therefore, this research is a literature review on the topic of the role of calcitriol and folic acid on alzheimer's disease. This literature review is expected to be a reference for the general public to pay attention to nutritional content, especially calcitriol and folic acid to prevent alzheimer's disease.

Research Methods

The writing of this article uses a literature review technique which is carried out based on various relevant previous studies. In general, writing a literature review article or literature review consists of 4 stages, namely 1) selection of themes and topics that are the focus of the review; 2) search and collection of articles relevant to the topic or theme that has been determined previously; 3) the process of analyzing and synthesizing the literature obtained; 4) organization of writing. The main topics discussed in this article are related to the role of carcitriol on alzheimer's disease and the role of folic acid on alzheimer's disease. Journal selection techniques are carried out by considering keywords and years of publication. The keywords used as a reference for the selection of articles used are carcitriol, Folic Acid and alzheimer's disease. Therefore, the criteria for articles used in this literature review study are 1) focus on the role of carcitriol and folic acid in alzheimer's disease; 2) articles published in national and international journals; 3) articles published in the last 10 years; 4) contain keywords calcitriol or folic acid and alzheimer. Articles that did not meet the above criteria were not included in the literature review. The total number of articles used in this study was 9 articles, mostly from international journals.

2. Results and Discussion

This section discusses the results and discussions related to the results of the literature review on the role of calcitriol and folic acid in preventing alzheimer's disease. The discussion consists of two main parts, namely the first part of the role of folic acid on alzheimer's disease and the role of calcitriol on alzheimer's disease.

1) Role of Folic Acid in Alzheimer's Disease

Based on the results of the literature review on a total of 9 articles that have been determined with criteria that have met the criteria to be used as a source of literature review for the study of the role of carcitriol and folic acid on alzheimer's disease, the significance of the role of calcitriol and folic acid on alzheimer's disease and the effectiveness of the combination of the role of carcitriol and folic acid with other micronutrients against alzheimer's disease both in preventing and reducing the progressivity of alzheimer's in the elderly. A total of 9 articles were reviewed based on reference source, year, method, intervention, and review results. Among the 10 articles, there are 5 articles that examine the role of folic acid in alzheimer's disease. Table 1 shows the results of the review that has been done on 5 articles.

Table 1: Review Results: Role of Folic Acid in Alzheimer's

NO	Reference Source	Sample	Design	Review Results
1	Chen et al.	121 elderly who are over 60 years old	Treatment with donepezil and treatment with or without folic acid	1) Folic acid treatment benefits Alzheimer's disease patients 2) Treatment with a combination of folic acid and donepizel provides benefits for cognition and memory problems
2	Ma et al.	168 people who met the criteria	Treatment with daily folic acid administration (400 µg)	1) Folic acid contains substances to improve memory 2) Folic acid administration for 12 months was shown to significantly improve cognitive processes
3	Setyowati et al.	64 respondents	Analytical Survey Research Methods	1) Most of the elderly suffer from impaired cognitive function caused by low intake of B12 and folic acid
4	Ma et al.	240 people aged 65 years or older	Treatment with folic acid only, Treatment with vitamin B12 only,	1) The combination of folic acid and vitamin B12 significantly affects the cognitive processes of the elderly

			Treatment with folic acid + vitamin B12, control without any treatment1	2) The performance provided by the combination treatment of folic acid and vitamin B12 is better than the treatment with folic acid alone or the treatment with vitamin B12.
5	Hama et al.	45 people with cognitive impairment	Treatment with folic acid intake (5 mg/day) for 28 to 63 days	1) Through consideration of various other factors, folic acid may ameliorate the cognitive impairment of a person with folic acid deficiency, at least for a short period of time.

Folic acid is one of the micronutrients needed by the body to maintain health. As one of the body's micronutrients, folic acid intake in the body is important to be maintained in a balanced condition both at a young age and especially in old age. Based on Table 1, it can be concluded that folic acid has an important influence on human cognitive health, especially in old age. Some studies show that with only folic acid treatment, especially in old age, it is proven to significantly improve cognitive processes (Ma et al., 2016). The results of this study are in line with a survey conducted by Setyowati et al. (2019) that most of the elderly suffer from impaired cognitive function caused by low intake of B12 and folic acid. From some of the above studies it can be concluded that folic acid is one of the micronutrients that affect cognitive function and the risk of alzheimer.

In addition to folic acid, there are many other important micronutrients that are essential for the body that are also important in maintaining normal human cognitive function in old age. As Aisyah (2009) states, adequate intake of vitamins A, E, C, Fe and Zn is believed to reduce the risk of senile dementia in the elderly. Triantari (2011) found that the intake of vitamin B12 in the body has a significant influence on cognitive function in the elderly. Therefore, the combination of folic acid and other nutrients should be able to prevent and improve the cognitive function of people with alzheimer's disease. This is evidenced by research by Ma et al. (2019) that the performance given through a combination treatment of folic acid and vitamin B12 is better in affecting cognitive function than treatment only with folic acid or treatment with vitamin B12. Chen (2016) also explained that treatment with a combination of folic acid and donepezil provides benefits to cognition and memory problems. Likewise, Hama et al. (2020) state that through consideration of various other factors, folic acid can improve cognitive damage in someone who experiences folic acid deficiency. Folic acid contains components that can improve memory. Treatment by giving a combination of folic acid with other important nutrients to people with alzheimer's is believed to provide better cognitive function.

2) Role of Calcitriol in Alzheimer's Disease

Next is a discussion related to the role of calcitriol in alzheimer's disease. A total of 9 articles were reviewed based on reference source, year, method, intervention, and review results. Among the 9 articles, there are 4 articles that examine the role of calcitriol on alzheimer's disease. Table 2 shows the results of reviews that have been carried out on 4 articles.

Table 2: Review Results: Role of Calcitriol (Vitamin D) on Alzheimer's

NO	Reference Source	Sample	Design	Review Results
1	Moon et al.	412 participants	Prospective Study	1) Severe vitamin D deficiency is associated with the risk of cognitive impairment and dementia, especially in the elderly.
2	Feart et al.	916 participants	Prospective Cohort	1) Maintaining adequate vitamin D levels in the body for the elderly can contribute to reducing cognitive decline and preventing dementia
3	Licher et al.	6220 participants aged 55 years or older	Prospective Cohort	1) Low vitamin D concentrations are associated with a higher risk of dementia in humans 2) Vitamin D levels were measured through serum 25 - hydroxyvitamin D levels.
4	Zhao et al.	1759 non - dementia participants aged 65 years or older	Prospective Cohort	1) Vitamin D concentration in the body is associated with dementia risk 2) Higher vitamin D intake has the effect of reducing the risk of dementia in multiethnic groups.

Calcitriol is the best vitamin D supplement for alzheimer's disease because calcitriol is the active form of vitamin D3 metabolites (Lu'o'ng and Nguyễn, 2013). Vitamin D is one of the important nutrients in our body. Based on table 1, it can be concluded that there is a relationship between vitamin D levels in the body and the risk of disruption of cognitive function and dementia in the elderly community. As Moon et al. (2015) explained that severe vitamin D deficiency is associated with the risk of cognitive impairment and dementia, especially in the elderly. Therefore, maintaining adequate vitamin D levels in the body for the elderly can contribute to reducing cognitive decline and preventing dementia (Feart et al., 2017; Zhao et al., (2020). Furthermore, Licher et al. (2017) stated that low vitamin D concentrations are associated with a higher risk of dementia in humans where vitamin D levels are measured through serum levels of 25 - hydroxyvitamin D. In general, it is found that vitamin D levels in the body are believed to have an important role in improving human cognitive function.

So far, not many specific studies have been found that discuss the role of calcitriol on alzheimer's where most vitamin D levels are measured through serum levels of 25 - hydroxyvitamin D. However, calcitriol is a conversion of 25 - hydroxyvitamin D (Salim, 2014) so that the analysis related to 25 - hydroxyvitamin D can also be generalized to calcitriol. Several other relevant studies have also revealed that calcitriol has an important role in the risk of alzheimer's disease. Lu'o'ng and Nguyễn (2011) stated that calcitriol is very well used for alzheimer's disease because it is the active form of vitamin D. Vitamin D with its active form calcitriol is considered a neuroprotective agent (Ali, 2022). So far, the role of calcitriol and vitamin D on alzheimer's risk is believed to be very important where calcitriol deficiency can increase the risk of alzheimer. However, further research is still needed to find a more definitive result through

treatments with calcitriol in alzheimer's patients. Finally, this literature review is expected to be a reference for the general public to pay attention to nutritional content, especially calcitriol and folic acid to prevent alzheimer's disease.

3. Conclusion

Alzheimer's is a neurodegenerative disease in which the death of nerve cells in the brain leads to cognitive and intellectual decline. There are many factors that cause dementia, including nutritional intake and nutritional status. Among the important nutrients in the body are folic acid and calcitriol (vitamin D). Folic acid is one of the micronutrients that affect cognitive function and the risk of alzheimer's where folic acid administration in alzheimer's patients can improve cognitive processes. Treatment by giving a combination of folic acid with other important nutrients to people with alzheimer's is believed to provide better cognitive function. Furthermore, the role of calcitriol and vitamin D on the risk of alzheimer's is believed to be very important where calcitriol deficiency can increase the risk of alzheimer. However, further research is still needed to find a more definitive result through treatments with calcitriol in alzheimer's patients. Therefore, it is important for people, especially the elderly, to pay attention to the intake of macro and micro nutrients in the body. This literature review is expected to be a reference for the general public to pay attention to nutritional content, especially calcitriol and folic acid to prevent alzheimer's disease.

References

[1] Aisyah B. (2009). The relationship between micronutrient intake, physical activity, and intelligence training with the incidence of dementia in the elderly in Depok Jaya urban village in 2009. Depok: Faculty of Public Health, Bachelor of Public Health Program, University of Indonesia.

[2] Ali, S. S. M. (2022). Mechanism of vitamin D for protection of alzheimer disease, parkinsonism and multiple sclerosis. International Journal of Pharmacy and Pharmaceutical Studies, 6 (3).

[3] Chen, H., Liu, S., Ji, L., Wu, T., Ji, Y., Zhou, Y.,. . . & Huang, G. (2016). Folic acid supplementation mitigates Alzheimer's disease by reducing inflammation: a randomized controlled trial. Mediators of inflammation, 2016.

[4] Earlia, N., Maulida, M., Hidayati, A., & Pratama, R. (2020). The effect of vitamin D administration on the improvement of clinical symptoms in patients with atopic dermatitis at the genital skin polyclinic of Dr. Zainoel Abidin Banda Aceh Hospital in 2018: A double - blind clinical trial. Journal of Medical Science, 1 (1), 33 - 42.

[5] Feart, C., Helmer, C., Merle, B., Herrmann, F. R., Annweiler, C., Dartigues, J. F.,. . . & Samieri,

[6] C. (2017). Associations of lower vitamin D concentrations with cognitive decline and long - term risk of dementia and Alzheimer's disease in older adults. Alzheimer's & Dementia, 13 (11), 1207 - 1216.

[7] Glade, M. J. (2013). Vitamin D: health panacea or false prophet? Nutrition, 29 (1), 37 - 41.

[8] Gustri, L. (2019). The relationship between nutrient intake and the incidence of dementia. Journal of Nutrition and Health), 7 (2).

[9] Hama, Y., Hamano, T., Shirafuji, N., Hayashi, K., Ueno, A., Enomoto, S.,. . . & Nakamoto, Y. (2020). Influences of folate supplementation on homocysteine and cognition in patients with folate deficiency and cognitive impairment. Nutrients, 12 (10), 3138.

[10] Harna, H., Arianti, J., & Nuzrina, R. (2020). The relationship between micronutrient intake and physical activity with cognitive function of the elderly at Kebon Jeruk health center, West Jakarta. Indonesian Micronutrient Media, 11 (2), 117 - 126.

[11] Hartati, S., & Widayanti, C. G. (2010). Clock drawing: an assessment for dementia (Descriptive study on elderly people in Semarang city). Undip Journal of Psychology, 7 (1).

[12] Krisdyana, B. (2020). The relationship between nutrient intake, nutritional status and blood pressure with dementia in the elderly. Doctoral dissertation: Sebelas Maret University.

[13] Kristy, N. C., & Mahmudiono, T. (2022). Optimizing nutrient intake as a preventive effort in overcoming mental health problems: a literature review: A Literature Review.

[14] Licher, S., de Bruijn, R. F., Wolters, F. J., Zillikens, M. C., Ikram, M. A., & Ikram, M. K. (2017). Vitamin D and the risk of dementia: the Rotterdam study. Journal of Alzheimer's Disease, 60 (3), 989 - 997.

[15] Lu'o'ng, K. V. Q., & Nguyễn, L. T. H. (2011). The beneficial role of vitamin D in Alzheimer's disease. American Journal of Alzheimer's Disease & Other Dementias®, 26 (7), 511 - 520.

[16] Lương, K. V. Q., & Nguyễn, L. T. H. (2013). The role of vitamin D in Alzheimer's disease: possible genetic and cell signaling mechanisms. American Journal of Alzheimer's Disease & Other Dementias®, 28 (2), 126 - 136.

[17] Ma, F., Wu, T., Zhao, J., Song, A., Liu, H., Xu, W., & Huang, G. (2016). Folic acid supplementation improves cognitive function by reducing the levels of peripheral inflammatory cytokines in elderly Chinese subjects with MCI. Scientific reports, 6 (1), 1 - 11.

[18] Ma, F., Zhou, X., Li, Q., Zhao, J., Song, A., An, P.,. . . & Huang, G. (2019). Effects of folic acid and vitamin B12, alone and in combination on cognitive function and inflammatory factors in the elderly with mild cognitive impairment: A single - blind experimental design. Current Alzheimer Research, 16 (7), 622 - 632.

[19] Moon, J. H., Lim, S., Han, J. W., Kim, K. M., Choi, S. H., Kim, K. W., & Jang, H. C. (2015).

[20] Serum 25 - hydroxyvitamin D level and the risk of mild cognitive impairment and dementia: the Korean Longitudinal Study on Health and Aging (KL o SHA). Clinical Endocrinology, 83 (1), 36 - 42.

[21] Nisa, K. M., & Lisiswanti, R. (2016). Risk factors for alzheimer's dementia. Majority Journal, 5 (4), 86 - 90.

[22] Olsson, E., Byberg, L., Karlström, B., Cederholm, T., Melhus, H., Sjögren, P., & Kilander, L. (2017). Vitamin D is not associated with incident dementia or cognitive impairment: an 18 - y follow - up study in community - living older men. The American journal of clinical nutrition, 105 (4), 936 - 943.

[23] Purnakarya, I. (2009). The role of macronutrients on

the incidence of dementia in the elderly.
[24] Journal of Andalas Public Health, 3 (2), 89 - 92.
[25] Rahmawati, A., Pramantara, I. D. P., & Purba, M. (2012). Micronutrient intake with cognitive function in the elderly. Indonesian Journal of Clinical Nutrition, 8 (4), 195 - 201.
[26] Salim, M. N. (2014). Renal microscopic structure with vitamin d3 administration in ovarectomized rats. Scientific Journal of Animal Husbandry, 2 (1), 23 - 28.
[27] Sari, L. K., Salman, S., & Hilmi, I. L. (2023). Increased dementia through smoking: Literature Review. Journal of Pharmaceutics, 11 (3), 194 - 200.
[28] Sengkey, A. H., Mulyadi, N., & Bawotong, J. (2017). The relationship between depression and social interaction of the elderly in tombasian atas village, west kawangkoan sub - district. Journal of Nursing, 5 (1).
[29] Setyowati, E., Santosa, N. I., & Kridawati, A. (2019). The relationship of vitamin B12 and folic acid intake with cognitive function of the elderly. Endurance Journal: Scientific Review of Health Problems, 4 (1), 184 - 191.
[30] Sianturi, A. G. M. (2021). Staging, diagnosis, and management of alzheimer's disease. Indonesian Health Magazine, 2 (2), 39 - 44.
[31] Triantari R. (2011). The relationship between intake of vitamin B6, vitamin B12, folic acid, physical activity and homocysteine levels with cognitive status of the elderly. Semarang: Department of Nutrition Science, Faculty of Medicine, Diponegoro University.
[32] Wicitania, N. (2016). Nutritional risk factors for the incidence of dementia in the elderly at Panti Werda Elim Semarang. Thesis.
[33] Utami C. P., Sri Anna M., and Melly Latifah.2013. Food consumption patterns, physical activity, disease history, family history of dementia, and the incidence of dementia in the elderly at Panti Werdha Tresna Bogor. Faculty of Human Ecology (FEMA), Bogor Agricultural University.
[34] Zhao, C., Tsapanou, A., Manly, J., Schupf, N., Brickman, A. M., & Gu, Y. (2020). Vitamin D intake is associated with dementia risk in the Washington Heights - Inwood Columbia Aging Project (WHICAP). Alzheimer's & Dementia, 16 (10), 1393 - 1401.