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Effectiveness of vitamin D supplements in the patients suffering from Alzheimer disease

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Abstract
Introduction: Vitamin D is a steroid hormone. It crosses the blood brain barrier and binds with receptors present in neurons and glial cells of various parts of central nervous system like hippocampus, cortex, sub-cortex etc. Due to its antioxidant property and regulating intra-neuronal calcium homeostasis, it can be hypothesized that vitamin D has a role to play in preventing age related cognitive decline.
Materials and Methods: Total of 160 patients were included in the study. MMSE is useful for evaluating the subjects having dementia syndrome because these subjects cooperate well only for short duration. Mini Mental state examination score was used for the assessment of dementia. They were included in the study on the basis of serum vitamin D level and MMSE score.
Results: The collected data showed that mean serum vitamin D levels were found to be lower in group A when compared to group B. After 3 months of treatment with supplements, the score of post treatment MMSE was found to be higher in group A as compared to group B. After 6 months of treatment with supplements, the score of post treatment MMSE was found to be higher in group A as compared to group B.
Discussion & Conclusion: Vitamin D acts like a neurosteroid hormone in areas of neurotransmission and neuro-immunomodulation. Patients on medical therapy for dementia has also shown improve results with regulation of vitamin D. It has also exhibited neuro-protective properties against glutamate toxicity through antioxidant effects thus preventing apoptosis. The present study is one of on-going steps in the direction of establishing role of Vitamin D in prevention and treatment of senile dementia.

Keywords: Alzheimer disease, cognitive function, dementia, vitamin D

Introduction
One of the great challenges faced by neuropsychologists over the past 50 years is to understand the cognitive and behavioral manifestations of dementia and their relationship to underlying brain pathology. This challenge has grown substantially over the years with the aging of the population and the age-related nature of many dementia-producing neurodegenerative diseases [1]. AD is a chronic neurodegenerative disorder characterized histopathologically by the presence of amyloid-β (Aβ) peptides in extracellular senile plaques and the formation of intracellular neurofibrillary tangles (NFTs) composed of hyperphosphorylated, microtubule-associated protein tau. Because dementia can also arise from a number of etiologies that masquerade as or coexist with AD, pathological confirmation at autopsy (or rarely, biopsy in living individuals) has traditionally been necessary for definitive diagnosis [2].
In the last years, the World Health Organization (WHO) indicates dementia as a public health priority. About 50 million people worldwide are affected by dementia nowadays; among these patients, about 60% live in low- and middle-income countries. The total number of people with dementia is estimated to increase to 82 million in 2030 and 152 million in 2050. Every year, about 10 million people progress to dementia [3, 4].
Vitamin D is a fat-soluble steroid vitamin with a definitive role in bone health. Beyond its role in the regulation of bone health, it also plays an important role in the functioning of other systems such as cardiovascular, endocrine, and nervous systems. Ultraviolet radiation (UVR) is the major source of vitamin D [5]. Typically, vitamin D deficiency is defined as a 25(OH) D level of less than 50 nmol/L, with severe deficiency defined as less than 25 nmol/L and insufficiency between 50 and 75 nmol/L. Vitamin D can reach the brain by crossing the blood-brain barrier (BBB) through passive diffusion.

The active form, 1,25 (OH)D, binds to the vitamin D receptor (VDR) and influences gene expression [6]. Vitamin D exerts its action via VDR present in neurons, glial cells of the hippocampus, orbitofrontal-cortex, cingulate, amygdala, and thalamus. Its neuroprotective, anti-inflammatory, and antioxidant effect on neurons promotes brain health. Vitamin D promotes the production of neurotrophic factors such as nerve growth factor (NGF).

Many studies have consistently reported the increase in neuronal growth in rat hippocampal cell cultures enriched with vitamin D [7]. The NGF and other neurotrophic factors promote the survival of both hippocampal and cortical neurons. Vitamin D has been implicated to be crucial in maintaining the cognitive function in old age.

Vitamin D receptors are present in the brain regions responsible for memory development and cognitive functions and may also be involved in plaque clearance [6, 7]. Furthermore, the cutoffs for vitamin D deficiency and the optimum value for physical and mental health have not yet reached a global consensus [8].

Vitamin D is a steroid hormone. It crosses the blood brain barrier and binds with receptors present in neurons and glial cells of various parts of central nervous system like hippocampus, cortex, sub-cortex etc [9].

It controls intra-neuronal calcium homeostasis by regulating the voltage gated calcium channels thus prevents neuronal necrosis. Being a steroid hormone it also has antioxidant property. It facilitates cellular functions that reduce oxidative stress induced by glutamate and dopaminergic toxins. Thus it prevents apoptosis of dopaminergic neurons [9]. Due to its antioxidant property and regulating intra-neuronal calcium homeostasis, it can be hypothesized that vitamin D has a role to play in preventing age related cognitive decline.

Materials and Methods

The present study was done in the department of neuromedicine associated with the medical college & hospital. The outdoor patients in the patients were included in the study. The ethical committee were informed about the study and the ethical clearance certificate was obtained prior to the start of study. The included patients were informed about the study and the written informed consent was obtained prior to inclusions.

The present study included the patients from urban and rural areas. As per the previous studies, the survey diagnosis and clinical diagnosis shows the prevalence of dementia was found to be in the range of 0.8% to 4.0%. Hence for the present study, the average of the 2.9% was taken for the calculation of the sample size of the study. The following formula was used to calculate the sample size: $n = Z^2PQ / e^2$. Here P = prevalence of the disease, Q = 1 – P, e = estimated error, n = number of samples, Z = differential coefficient.

Total of 160 patients were included in the study. MMSE is useful for evaluating the subjects having dementia syndrome because these subjects cooperate well only for short duration. Mini Mental state examination score was used for the assessment of dementia.

They were included in the study on the basis of serum vitamin D level and MMSE score. The patients with MMSE score less than 24 considered as having cognitive impairment, patients with serum D level less than 30 ng/ml were considered as vitamin D deficiency. Once the patients had satisfied the inclusion criteria they were divided into two groups: Group A consist of study group and Group B patients considered as controls.

The patient with age less than 60 years, the MSME score less than 24, Serum Vitamin D level less than 30 were included in the study were followed as the inclusions criteria. Whereas the patients with age more than 60 years, some of the uncooperative subjects, patients with uncontrolled diabetes, patients with habit of smoking and drug addiction, those who did not signed the informed consent; all were excluded from the study.

Fasting venous blood sample was drawn from the patients for the estimation of serum vitamin D and was stored in -80^0C. Approximately around 4 ml fasting blood was collected by trained nurse. Estimation was done by direct enzyme linked immune sorbent assay (ELISA) kit.

Both Group A and Group B were on same line of medical treatment. Only Group A subjects were supplemented with vitamin D apart from the routine medical treatment. It was given in the form of calcirol granules orally. 100 IU of vitamin D raises serum vitamin D concentration by 0.7 ng/ml. Daily dose of 4000 IU was expected to raise the serum vitamin D concentration by at least 28 ng/ml, with a concentration ultimately reached > 30 ng/ml. Chosen dose did not reach to the toxic level and raised serum concentration within nontoxic limit, so serial serum vitamin D monitoring was not necessary.

For statistical analysis, the independent t test was used for the comparison between the groups. If the value of $p < 0.05$, than it was considered as statistically significant. All the analysis was considered as significant. For statistical analysis the SPSS version 17.0 was used.

Results

The present study was done with the aim to evaluate the effect of vitamin D supplement on the performance in the patients with Alzheimer disease. The present study data were summarized as Mean±SD. The subjects were divided into two different groups as case and control group. The basic parameters of the patients in both the groups were collected and compared. The difference was not found to be statistically significant.

The mean serum level was measured in both the groups. The collected data showed that mean serum vitamin D levels were found to be lower in group A when compared to group B. However when the difference was compared statically it was found to be non-significant.

The pre-treatment MMSE score in group A was found to be high when compared with that of group B, however the difference was not statistically significant. After 3 months of treatment with supplements, the score of post treatment MMSE was found to be higher in group A as compared to group B; however the difference was not found to be statically significant.

After 6 months of treatment with supplements, the score of post treatment MMSE was found to be higher in group A as compared to group B; however the difference was found to be statically significant.

Table 1: Pre-treatment Serum vitamin D levels of both the groups.

Parameters	Group A (n= 80)	Group B (n = 80)	T value	P value
Serum Vit. D	9.34 ± 5.45	10.45±9.45	0.74	0.304

Table 2: Post treatment Serum vitamin D levels of both the groups.

Timeline	Group A (n= 80)	Group B (n = 80)	P value
Baseline	16.23 ± 3.67	17.56 ± 3.25	0.43
3 months	22.12 ± 4.20	20.25 ± 4.92	0.07
6 months	24.78 ± 3.10	22.87 ± 2.17	0.0002

Discussion

Dementia is a clinical syndrome characterized by impairment in several cognitive domains that prevents an individual from living a fully functional and autonomous life. The most common cause of dementia is Alzheimer's disease (AD), accounting for nearly 60 to 80% of all cases [10]. AD is the sixth leading cause of death, with an estimated prevalence of nearly 30 million people worldwide. Dementia has become one of the leading public health problems facing our society. Since burden of dementia inflict on individual, families and societies, so more emphasis has been placed on the study of these diseases [11].

Some authors define vitamin D as the "forgotten neurosteroid", indicating the term vitamin as wrong. Vitamin D deficiency could be implicated in different chronic pathologies. For example, it has been hypothesized that Vitamin D could have a role in age-related macular degeneration (AMD), a chronic, late-onset degeneration of the macula, that represents the first cause of vision loss in adults in developed countries [12].

Subjects with MMSE score < 24 are considered as having cognitive impairment (23). All subjects enrolled for study had MMSE score < 24 that is all the subjects had cognitive impairment. MMSE score had been used for cognitive assessment because it is easy to administer and takes minimal training [13].

Vitamin D acts like a neurosteroid hormone in areas of neurotransmission and neuro-immunomodulation. Hypovitaminosis D has been associated with neuromuscular disorders, dementia and Parkinson's disease. Thus, prophylactic vitamin D supplementation may be protective against these neurological disorders. Serum vitamin D level > 30 ng/ml is considered as sufficiency, 20-30 ng/ml insufficiency and if its serum level is less than 20 ng/ml than this condition is called vitamin D deficiency [9].

In the present research work, after completion of the 3 months of supplements, there was increase in MMSE score in group A as compared to group B. However the difference of score between the groups was found to be statistically non-significant. After the completion of 6 months of supplements, there was significant rise in the MMSE score in group A as compared to group B. In the timeline from 3 months to 6 months, the mean change was higher in group A as compared to group B. Vitamin D modulates age related increase in pro-inflammation and amyloid burden. Inadequate weekly vitamin D dietary intake was also associated with cognitive impairment. All the above studies corroborate with the findings of present study.

Conclusion

The result concludes that supplementation of vitamin D has improvement in the cognitive functions of individuals. Patients on medical therapy for dementia has also shown improve results with regulation of vitamin D. It has also exhibited neuro-protective properties against glutamate toxicity through antioxidant effects thus preventing apoptosis. The present study is one of on-going steps in the direction of establishing role of Vitamin D in prevention and treatment of senile dementia.

References

1. Krinsky-McHale SJ, Silverman W. Dementia and mild cognitive impairment in adults with intellectual disability: issues of diagnosis. Developmental disabilities research reviews 2013;18:31-42.
2. Li F, Hearn M, Bennett LE. The role of microbial infection in the pathogenesis of Alzheimer's disease and the opportunity for protection by anti-microbial peptides. Critical Reviews in Microbiology 2021;47:240-53.
3. Braun J. Dementia: A woman's global health issue. Washington: Alzheimer's Disease International 2012.
4. [4] Custodio N, Wheelock A, Thumala D, Slachevsky A: Dementia in Latin America: epidemiological evidence and implications for public policy. Frontiers in aging neuroscience 2017;9:221.
5. Al-Suhaimi EA, Al-Jafary MA. Endocrine roles of vitamin K-dependent-osteocalcin in the relation between bone metabolism and metabolic disorders. Reviews in Endocrine and Metabolic Disorders 2020;21:117-25.
6. Close GL, Leckey J, Patterson M, Bradley W, Owens DJ, Fraser WD, *et al*. The effects of vitamin D3 supplementation on serum total 25 [OH] D concentration and physical performance: a randomised dose–response study. British journal of sports medicine 2013;47:692-6.
7. Farghali M, Ruga S, Morsanuto V, Uberti F. Can Brain Health Be Supported by Vitamin D-Based Supplements? A Critical Review. Brain Sciences 2020;10:660.
8. Olsson E, Byberg L, Karlström B, Cederholm T, Melhus H, Sjögren P, *et al*. Vitamin D is not associated with incident dementia or cognitive impairment: an 18-y follow-up study in community-living old men. The American journal of clinical nutrition 2017;105:936-43.
9. Gangwar AK, Rawat A, Tiwari S, Tiwari S, Narayan J, Tiwari S. Role of vitamin-D in the prevention and treatment of Alzheimer's disease. Indian J Physiol Pharmacol 2015;59:94-9.
10. Zvěřová M. Clinical aspects of Alzheimer's disease. Clinical biochemistry 2019;72:3-6.
11. Association As: Alzheimer's disease facts and figures. Alzheimer's & dementia 2010;6:158-94.
12. Pizza V, Montella S, Luigi Iorio E, Silvestro A, Agresta A, Somma Sd, *et al*. Vitamin D Serum Level in Elderly Patients with Alzheimer's Disease: Preliminary Analysis from Cilento Region. The Open Neurology Journal 2020, 14.
13. Sinclair AJ, Girling AJ, Bayer AJ. Cognitive dysfunction in older subjects with diabetes mellitus: impact on diabetes self-management and use of care services. Diabetes research and clinical practice 2000;50:203-12.