

Assessment of effectiveness of vitamin D supplements in the patients suffering from Alzheimer disease

Arghadip Das¹, Himani Jitendrakumar Suthar², Levis Abin Joy³, Vinodh Boopalraj⁴

¹Final year MBBS student, NRS Medical College, Kolkata, West Bengal, India;

²M.B.B.S., G.M.E.R.S Medical College and Hospital, Gandhinagar, Gujarat, India;

³M.B.B.S., Govt Medical College Trivandrum Kerala, India;

⁴M.D. Physician in general medicine/ pediatric medicine, Yerevan State Medical University, Armenia

Corresponding author

Arghadip Das

Final year MBBS student, NRS Medical College, Kolkata, West Bengal, India;

ABSTRACT

Background: Patients with Alzheimer disease (AD), the most common form of dementia. The present study was conducted to assess effectiveness of vitamin D supplements in the patients suffering from Alzheimer disease.

Materials & Methods: 60 patients of Alzheimer disease of both genders were divided into 3 groups of 20 each. Group I were prescribed memantine alone, group II were prescribed vitamin D alone and group III were prescribed memantine plus vitamin D for 6 months. Cognitive change with the mini-mental state examination (MMSE) was assessed.

Results: Group I had 20 males and 10 females, group II had 12 males and 18 females and group III had 16 males and 14 females. The mean MMSE score before treatment in group I was 16.8 and after treatment was 16.4, in group II before treatment was 18.3 and after treatment was 17.5, in group III before treatment was 13.4 and after treatment was 17.2. The difference was significant ($P < 0.05$).

Conclusion: Patients who took memantine plus vitamin D had a statistically and clinically relevant gain in cognition as compared to memantine and vitamin D alone.

Key words: Alzheimer disease, Memantine, Vitamin D

INTRODUCTION

Patients with Alzheimer disease (AD), the most common form of dementia. There is decrease in brain cholinergic activity and glutamatergic excitotoxicity that leads to loss of synaptic plasticity and neuronal death and patients manifest as loss of ability to learn and remember.¹

There is evidence of aberrations in the vitamin D-endocrine system in patients with AD. Both AD and osteoporosis occur more frequently in women.² However, little is known about bone changes and vitamin D status in this particular population.³ A growing interest in Vitamin D role in both brain development and function in adulthood led several authors to investigate the 25(OH)D circulating levels in AD patients. The brain displays the capability to produce and receive Vitamin D's active form, which is deemed to support neurotransmission, synaptic plasticity, and neuroprotection.⁴ From a pathophysiologic point of view, the relation between Vitamin D and AD onset and progression has been explained by impressive in vitro and in vivo studies.⁵ Given that amyloid plaques, along with neurofibrillary tangles, represent features of AD, it has been shown that 1,25(OH)₂D can help the amyloid plaques phagocytosis and clearance by the innate immune cells. Treating AD with

acetylcholinesterase inhibitors compensates for the decrease in brain cholinergic activity by keeping higher levels of acetylcholine in synapses, but these drugs do not alter the pathogenesis.⁶The present study was conducted to assess effectiveness of vitamin D supplements in the patients suffering from Alzheimer disease.

MATERIALS & METHODS

The present study consisted of 60 patients of Alzheimer disease of both genders. They were enrolled with their written consent.

Data such as name, age, gender etc. was recorded. Patients were divided into 3 groups of 20 each. Group I were prescribed memantine alone, group II were prescribed vitamin D alone and group III were prescribed memantine plus vitamin D for 6 months. In all patients, cognitive change with the mini-mental state examination (MMSE) was assessed. Results of the study was assessed statistically using Mann Whitney U test. P value less than 0.05 was considered significant.

RESULTS

Table I Distribution of patients

Groups	Group I	Group II	Group III
Drug	Memantine	Vitamin D	Memantine plus vitamin D
M:F	20:10	12:18	16:14

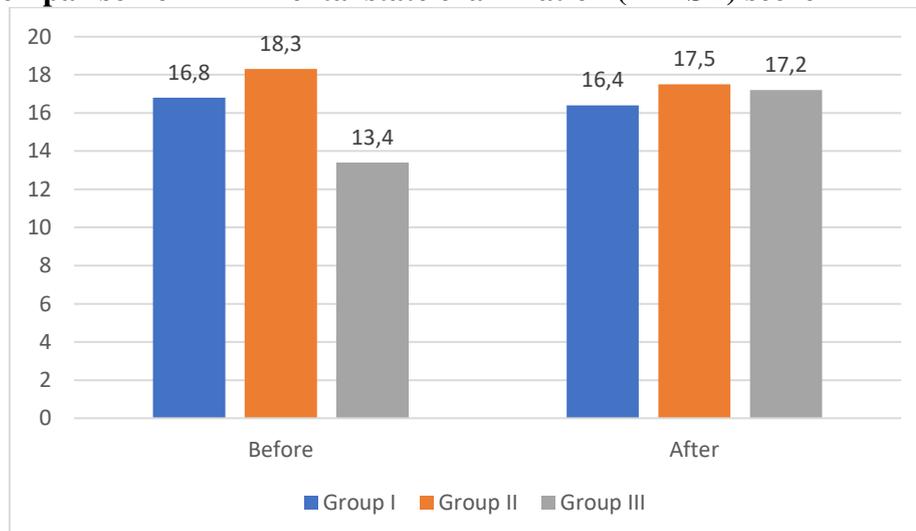
Table I shows that group I had 20 males and 10 females, group II had 12 males and 18 females and group III had 16 males and 14 females.

Table II Comparison of mini-mental state examination (MMSE) score

Groups	Group I	Group II	Group III	P value
Before	16.8	18.3	13.4	0.05
After	16.4	17.5	17.2	0.09
P value	0.90	0.71	0.04	

Table II, graph I shows that mean MMSE score before treatment in group I was 16.8 and after treatment was 16.4, in group II before treatment was 18.3 and after treatment was 17.5, in group III before treatment was 13.4 and after treatment was 17.2. The difference was significant ($P < 0.05$).

Graph I Comparison of mini-mental state examination (MMSE) score



DISCUSSION

Alzheimer's disease (AD) is the most common form of dementia in the elderly. With the accelerating population aging process, the prevalence of AD and dementia is estimated to rise steadily. Despite considerable effort has been devoted to the drug discovery for AD, there is no effective agent to combat it at present.⁷ Thus, it is urgent to identify specific modifiable risk factors for these disorders. In recent years, the associations between vitamin D and AD or dementia have attracted growing interests.⁸ First, accumulating studies indicate that vitamin D deficiency is prevalent in AD and dementia patients and a meta-analysis study supported that AD patients possess lower level of 25-hydroxyvitamin D [25(OH)D] compared with age-matched healthy controls. Second, low 25(OH)D level may be a potential risk factor of developing AD and dementia as supported by recent studies.⁹ The present study was conducted to assess effectiveness of vitamin D supplements in the patients suffering from Alzheimer disease.

In present study we found that group I had 20 males and 10 females, group II had 12 males and 18 females and group III had 16 males and 14 females. Shenet al¹⁰ estimated the association between vitamin D deficiency and risk of developing AD and dementia. Results of meta-analysis showed that subjects with deficient vitamin D status (25(OH)D level < 50 nmol/L) were at increased risk of developing AD by 21 % compared with those possessing 25(OH)D level > 50 nmol/L. Similar analysis also found a significantly increased dementia risk in vitamin D deficient subjects. There is no evidence for significant heterogeneity among the included studies.

We found that mean MMSE score before treatment in group I was 16.8 and after treatment was 16.4, in group II before treatment was 18.3 and after treatment was 17.5, in group III before treatment was 13.4 and after treatment was 17.2. Sato et al¹¹ studied bone mineral density(BMD) and its relation to the biochemical indices of patients with AD. They reported that the BMD of patients with AD was significantly less than that of age-matched controls; in 26% of patients with AD, serum 25-hydroxyvitamin D₃ (25OHD) was at a deficient level (5-10 ng/mL); and in 54%, it was at an osteomalacic level (<5 ng/mL). Concentrations of ionized calcium were significantly lower than in patients, and their concentrations of serum bone Gla-protein and urinary hydroxyproline were significantly higher than those of controls. In another study, there was no significant difference in bone density between participants with mild dementia and normal cognitively women; however, there were significant differences in parathyroid hormone (PTH) and vitamin D levels between group.

Annweiler et al¹² determined whether treatment with memantine plus vitamin D is more effective than memantine or vitamin D alone in improving cognition among patients with Alzheimer disease (AD). They studied 43 white outpatients (mean 84.7 ± 6.3 years; 65.1% women) with a new diagnosis of AD, who had not taken anti-dementia drugs or vitamin D supplements. They prescribed memantine alone (n = 18), vitamin D alone (n = 17), or memantine plus vitamin D (n = 8) for an average of 6 months. They assessed cognitive change with the Mini-Mental State Examination (MMSE). Before treatment, the 3 groups had comparable MMSE scores. At 6 months, participants taking memantine plus vitamin D increased their MMSE score by 4.0 ± 3.7 points (P = 0.034), while participants taking memantine alone remained stable (change of 0.0 ± 1.8 points; P = 0.891), as did those taking vitamin D alone (0.6 ± 3.1 points; P = 0.504). Treatment with memantine plus vitamin D was associated with improvement in the MMSE score compared to memantine or vitamin D alone after adjustment for covariables (P < 0.01). Mixed regression analysis showed that the visit by combined treatments (memantine plus vitamin D) interaction was significant (P = 0.001), while memantine or vitamin D alone showed no effect.

CONCLUSION

Authors found that patients who took memantine plus vitamin D had a statistically and clinically relevant gain in cognition as compared to memantine and vitamin D alone.

REFERENCES

1. Ballard C, Gauthier S, Corbett A, et al. Alzheimer's disease. *Lancet*. 2011;377:1019–1031.
2. Querfurth HW, LaFerla FM. Alzheimer's disease. *N Engl J Med*. 2010;362:329–344.
3. Rigaux N. Autonomy and dementia. *GeriatrPsycholNeuropsychiatrVieil*. 2011;9:107–115.
4. Herrmann N, Li A, Lanctot K. Memantine in dementia: a review of the current evidence. *Expert OpinPharmacother*. 2011;12:787–800.
5. McShane R, AreosaSastre A, Minakaran N. Memantine for dementia. *Cochrane Database Syst Rev*. 2006;CD003154.
6. Robinson DM, Keating GM. Memantine: a review of its use in Alzheimer's disease. *Drugs*. 2006;66:1515–1534.
7. Orgogozo JM, Rigaud AS, Stoffler A, et al. Efficacy and safety of memantine in patients with mild to moderate vascular dementia: a randomized, placebo-controlled trial (MMM 300). *Stroke*. 2002;33:1834–1839.
8. Schrag A, Schott JM, Alzheimer's Disease Neuroimaging Initiative. What is the clinically relevant change in ADAS-cog score? *J NeurolNeurosurg Psychiatry*. 2012;83:171–173.
9. Cavalli A, Bolognesi ML, Minarini A, et al. Multi-target-directed ligands to combat neurodegenerative diseases. *J Med Chem*. 2008;51:347–372.
10. Shen L, Ji HF. Vitamin D deficiency is associated with increased risk of Alzheimer's disease and dementia: evidence from meta-analysis. *Nutrition journal*. 2015 Dec;14(1):1–5.
11. Sato Y, Asoh T, Oizumi K. High prevalence of vitamin D deficiency and reduced bone mass in elderly women with Alzheimer's disease. *Bone*. 1998; 555-57.
12. Annweiler C, Herrmann FR, Fantino B, Brugg B, Beauchet O. Effectiveness of the combination of memantine plus vitamin D on cognition in patients with Alzheimer disease: a pre-post pilot study. *Cognitive and behavioral neurology*. 2012 Sep 1;25(3):121-7.