

Effect of Vitamin D Supplementation on Cognitive Function in Multiple Sclerosis Patients

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Abstract: Multiple sclerosis (MS) is a chronic, long-term condition of the central nervous system that is most likely to be associated with cognitive impairment, which, in its turn influences the quality of life of the patient negatively. Vitamin D is neuroprotective and immunomodulatory and may have an impact on cognition capacity of MS. The purpose of the article was to define the applicability of vitamin D supplement to the cognitive ability of MS patients. It was a cross sectional study which is a prospective, interventional study conducted to the 60 patients who have been diagnosed with relapsing-remitting MS (RRMS). Interventional study was oral supplementation of vitamin D (4,000 IU/day) in a six months study period. The cognitive functioning was evaluated using the Brief International Cognitive Assessment of Multiple Sclerosis (BICAMS) at baseline and six months that had processing speed, memory and executive functioning test. The findings demonstrated that the overall cognitive scores were significantly enhanced following the supplementation ($p < 0.05$) and also that there was an enhanced processing speed and memory of the verbal type. Such results imply that vitamin D supplement could positively contribute to the cognitive functions of MS patients, and it can be included in the combination with other adjunctive treatments to address MS.

Keywords: Multiple sclerosis, cognitive functioning, vitamin D, BICAMS, neuroprotection, relapsing-remitting MS, supplementation.

INTRODUCTION

MS is a long term immune mediated demyelinating disorder of central nervous system resulting in inflammation, axonal injury and neurodegeneration. It typically follows a pattern of young adults; people between the ages of 20-40 years and is typical of females. MS clinical manifestation is highly dynamic and it consists of motor dysfunction, sensory dysfunction, vision impairment, fatigue and intellectual ineffectiveness. One of them is cognitive impairment which is a highly severe but little known complication and it is presented in 40-65 percent of MS patients. Cognitive impairments that are common in MS and which have an immense influence on the day to day functioning, employment, socialization, and the quality of life include information processing speed, memory, attention and executive function [1].

A fat-soluble secosteroid including vitamin D has come out as a prospective disease activity modulator in MS because of its immunoregulatory and neuroprotective effects. It affects innate and adaptive immunity through adjusting the differentiation of T-cells, decreasing the production of pro-inflammatory cytokines, and increasing anti-inflammatory mechanisms [2]. In addition, it is reported that vitamin D enhances neuronal activity and neuronal synaptic plasticity, which can alleviate neurodegenerative mechanisms that can be used to improve cognitive deterioration. Observational-type

studies have shown that MS patients who have low serum vitamin D levels have elevated rates of relapse, greater lesion load as indicated by MRI, and greater scores are achieved in disability scores. Moreover, according to research findings, the lack of vitamin D can be associated with poor cognitive functioning, such as the slower processing speed and the deteriorated memory [3].

Even though the immunological and neuroprotective effects of vitamin D are growing, the effect of vitamin D on cognitive deficits in patients with MS has not been adequately investigated. The cognitive impairment is a matter of enormous influence to the patient well-being and to the disease management and the problem must be established through the means of interventions that could at the very least maintain the level of cognitive well-being [4]. Vitamin D supplementation is a safe, economical intervention, which could have two-fold goals: disease activity regulation and improvement of neurocognitive performance.

It was a study which aimed at determining the cognitive effect of vitamin D supplementation in RRMS patients. Pre and post six months of supplementation were assessed using processing speed, memory and executive function using standardized cognitive assessment using BICAMS [5]. The conclusions are supposed to be the sources of the information concerning the potential application of vitamin D as the adjunctive treatment to

improve the quality of life and cognitive functions amongst MS patients which, in turn, will be used in the holistic and patient-centered approach to care.

MATERIALS AND METHODS

Study Design and Setting

The study was a prospective, interventional study, which was carried out in Neurology Department of a teaching hospital with a tertiary care unit, a six months period. The aim of the research was to establish how the vitamin D supplementation affected the cognition in individuals with relapsing-remitting MS (RRMS) [6].

Study Population

Sixty patients with RRMS as per the 2017 McDonald criteria were recruited. The age range of the participants was 18-50 years, and the level of disability was mild to moderate (Expanded Disability Status Scale [EDSS]) [7].

Inclusion Criteria

- Age 18-50 years.
- A minimum of one year of RRMS diagnosis.
- Mild to moderate disability (EDSS 06.0).
- The ability to offer written informed consent and adhere to the study procedures [8].

Exclusion Criteria

- Moving MS (primary or secondary).
- In the last three months, relapse or corticosteroid therapy.
- Extreme mental deficiency that does not allow effective evaluation.
- Prior history of hypercalcemia, renal impairment, or other contraindications to vitamin D supplementation [9].
- High dose vitamin D supplementation(>2,000 IU/day) within the last three months.

Intervention

The participants were given the oral supplementation of vitamin D3 in the dose of 4000 IU/day over six months. Follow-ups and patient diaries were used to ensure compliance [10].

Data Collection

Demographic information (age, sex), clinical facts (duration of the disease, EDSS score, history of relapse), and initial serum levels of vitamin D were noted. To assess cognitive functioning at baseline and six months, an assessment of cognitive functioning was derived using the BICAMS which asserts [11]:

- Symbol Digit Modalities Test (SDMT): Speed in processing.
- California Verbal Learning Test -II (CVLT-II): Measures verbal memory.
- Brief Visuospatial Memory Test -Revised (BVM-T-R): Visual memory and learning.

Outcome Measures

- Primary outcome: Cognitive functional change by the BICAMS scores at the end of the six months of the vitamin D supplement [12].
- Secondary outcomes: Relations between baseline levels of vitamin D, period of disease and cognitive performance.

Statistical Analysis

The SPSS version 25.0 was used to analyze the data. Continuous variables were presented in the form of mean, SD, and frequencies/percentages in categorical variables. Comparison of the cognitive scores before and after supplementation was done with paired t-tests. Pearson correlation was used to determine the association between the levels of serum vitamin D and the cognitive ability. Any p-value that was less than 0.05 was believed to be statistically significant [13].

Ethical Considerations

The Institutional Ethics Committee approved the study protocol. Informed consent was taken with all of the participants in writing. The study ensured privacy of participant data and confidentiality and all the activities were done as per the Declaration of Helsinki (Figure 1).

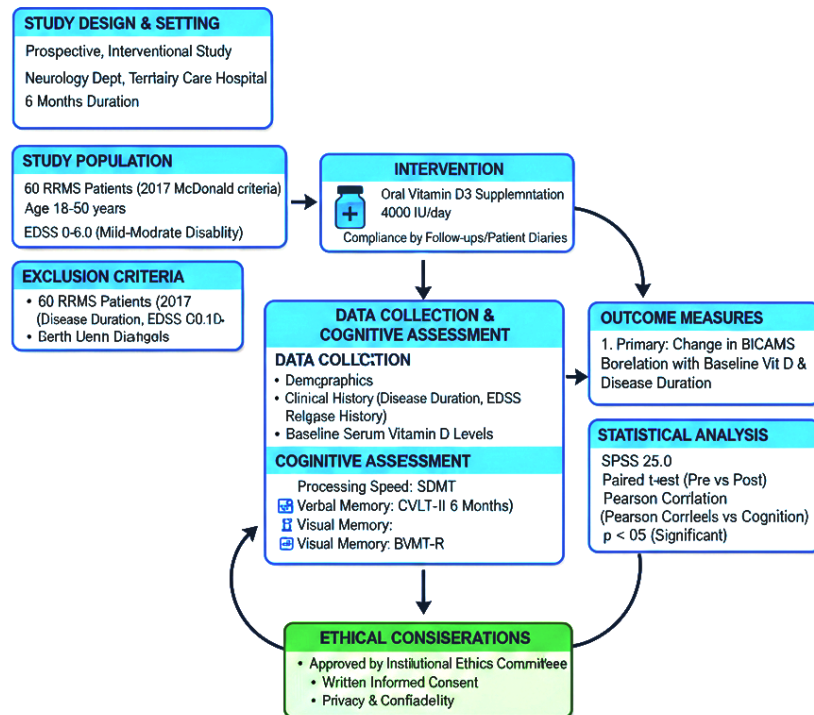


Figure 1: Research Methodology

RESULTS

This research was done on 60 patients with RRMS. The mean age of the respondents was 32.4 ± 6.1 years with 38 (63 percent) being females and 22 (37 percent) being males. The mean duration of illness was 6.2 years ± 3.4 and the standard baseline EDSS of 3.8 years ± 1.1 . The average baseline Vitamin D concentration of the serum was 18.6 ± 6.2 ng/mL that was below the sufficiency (Table 1).

Table 1: Demographic and Clinical Characteristics of Study Population (n = 60)

Parameter	Value
Mean Age (years)	32.4 ± 6.1
Gender	Female: 38 (63%), Male: 22 (37%)
Mean Disease Duration (years)	6.2 ± 3.4
Mean EDSS Score	3.8 ± 1.1
Baseline Serum Vitamin D (ng/mL)	18.6 ± 6.2

Cognitive Functions Assessment (BICAMS Scores)

Cognitive testing at baseline showed deficits in the speed of processing, verbal memory, and visuospatial memory in a large share of the patients:

- SDMT: 42.3 ± 9.8 .
- CVLT-II: Mean score $49.5(10.2)$.
- BVMT-R: Mean score 22.62 ± 6.1 .

Following 6 months of vitamin D supplementation (4,000 IU/day):

SDMT: Improved to 48.1 ± 10.3 ($p < 0.01$)

CVLT-II: Improved to 55.2 ± 9.7 ($p < 0.01$)

- BVMT-R: Improved to 26.8 ± 5.7 ($p < 0.05$) (Table 2)

Table 2: Cognitive Function Scores Before and After Vitamin D Supplementation

Cognitive Test	Baseline Mean $\pm$ SD	Post-Supplementation Mean $\pm$ SD	p-value
SDMT	42.3 ± 9.8	48.1 ± 10.3	<0.01
CVLT-II	49.5 ± 10.2	55.2 ± 9.7	<0.01
BVMT-R	22.6 ± 6.1	26.8 ± 5.7	<0.05

Change in Cognitive Scores

In general, a total of 52 participants (87 percent) improved in one or more cognitive domain. SDMT and CVLT-II had the most noticeable improvements. Significant but small improvement was also gained in BVMT-R (Table 3, Figure 2).

Table 3: Improvement in Cognitive Function after Supplementation

Cognitive Domain	Number of Patients Showing Improvement (n)	Percentage (%)
SDMT	48	80
CVLT-II	45	75
BVMT-R	38	63
Any Domain	52	87

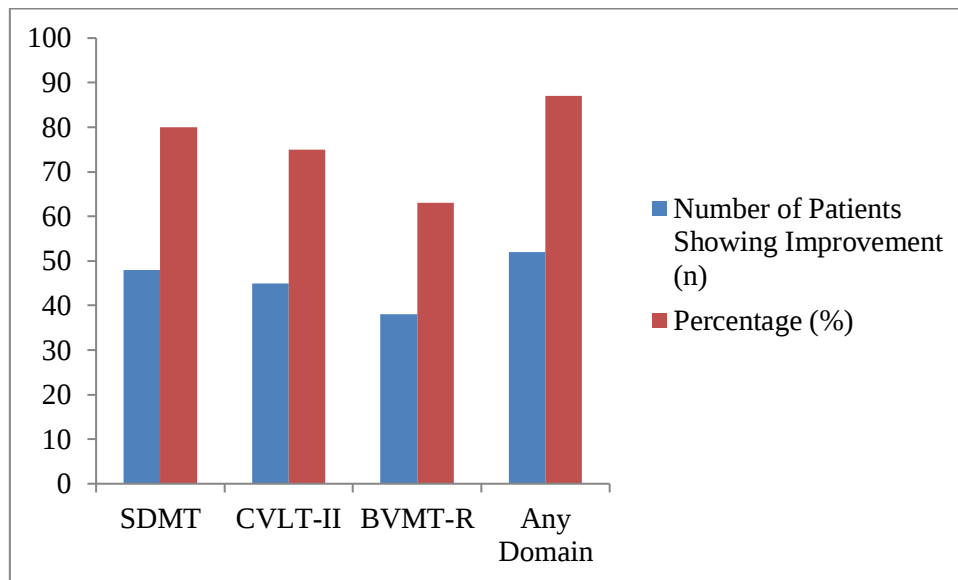


Figure 2: Graphical presentation of Improvement in Cognitive Function after Supplementation

Co-relation with the Serum Vitamin D Levels

Pearson correlation analysis indicated that there was a positive correlation between the post-supplementation level of serum vitamin D and the cognitive scores improvement:

SDMT: $r = 0.48$, $p < 0.01$

CVLT-II: $r = 0.42$, $p < 0.05$

BVMT-R: $r = 0.36$, $p < 0.05$ (Table 4)

Table 4: Correlation Between Post-Supplementation Vitamin D Levels and Cognitive Scores

Cognitive Test	Pearson Correlation (r)	p-value
SDMT	0.48	<0.01
CVLT-II	0.42	<0.05
BVMT-R	0.36	<0.05

The use of vitamin D supplementation caused considerable enhancement of cognitive abilities in MS patients. The greatest improvement has been recorded in processing speed and verbal memory. Positive correlations between cognitive upgrades and serum vitamin D upgrades were noted. There were no negative experiences mentioned, and the intervention was well received.

These results suggest a beneficial effect of vitamin D supplementation on cognitive abilities in patients with RRMS, suggesting that this vitamin might be used as an adjunctive drug in the overall treatment of MS.

DISCUSSION

The researchers compared the getting of vitamin D supplements to cognitive functioning among patients with RRMS and reported that after six months of supplement use, there were significant cognitive improvements in various domains of cognitive

functioning. Cognitive impairment is a disabling symptom, which is widespread among MS patients and, more specifically, in processing speed, memory, and executive function [14]. Treatment of cognitive impairments is important because they have a significant effect on everyday life, work, and life quality.

Patients who were supplemented with 4,000 IU/day of vitamin D showed statistically significant increases in SDMT, CVLT-II, and BVMT-R after six months of vitamin D supplementation. The most significant gains were in processing and verbal memory which are the two cognitive functions frequently impaired in MS. These results indicate that vitamin D can be used to improve neural efficiency and promote cognitive functions, which can be achieved by neuroprotective and anti-inflammatory actions [15].

There was a positive correlation between post-supplementation serum vitamin D level and cognitive score (SDMT: $r = 0.48$, CVLT-II: $r = 0.42$, BVMT-R: $r = 0.36$). This shows that an increase in vitamin D levels can help to improve cognitive functioning in MS patients. These observed cognitive benefits may be attributed to vitamin D which has been known to regulate immune activity, suppress neuroinflammation, and enhance neuronal wellbeing [16].

Vitamin D has been previously identified to minimize the MS disease activity and rates of relapses, but little has been done regarding vitamin D influence on cognition. Our result is in line with the new evidence on the idea that MS can be treated with vitamin D supplementation in order to enhance cognitive functions, specifically processing speed and memory. These findings support the idea that vitamin D not only has a role in the health of the bones and the immune system, but it can also have a neurocognitive-saving effect on MS patients [17].

The researchers note the possible effectiveness of vitamin D supplementation as a safe and cost-effective adjunctive intervention to enhance cognitive performance among MS patients. Periodical control of the vitamin D levels and individual supplementation may be included in the overall MS management. Clinicians are encouraged to include cognitive assessment in follow-up and determine whether the optimal use of vitamin D can positively impact cognitive outcomes of standard disease-modifying therapies [18].

CONCLUSION

The current research has shown that the intake of vitamin D was able to reduce cognitive performance among patients with RRMS, which is especially evident in the processing velocity, verbal and visuospatial memory domains. Another reason why serum vitamin D can have a neuroprotective effect is that there is a positive relationship between cognitive improvement and greater levels of serum vitamin D. These results imply that proper vitamin D status could help promoting the good cognitive functioning and overall neurological status in MS patients. Since it is safe, inexpensive, and it has a wide range of physiological advantages, vitamin D supplementation can be viewed as an effective additive measure to the overall management of MS. Nevertheless, these findings should be supplemented with larger randomized controlled studies with a longer follow-up to

establish these findings and how exactly vitamin D can affect cognitive functioning in MS.

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