Vitamin B12 supplementation and cognitive scores in geriatric patients with Mild Cognitive Impairment

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ABSTRACT

Background: The Neurodegenerative diseases are increasingly affecting the elderly with a severe impact on their brain health. There is a wide gap in supplementation based studies for increasing the cognition levels of the geriatric population, especially in developing countries like India which are at extreme risk of developing neurological disorders. And recently Vitamin B12 has drawn considerable attention due to its ability to improve the cognitive status. Current literature has linked the possibility of alleviating neurological disorders in the elderly with effective vitamin B12 management. Abundant animal and human models have proved that supplementation of vitamin B12 is beneficial for the restoration of cognitive functions.

Objective: To supplement vitamin B12 deficient mild cognitively impaired geriatric patients with injectable doses of vitamin B12 followed by impact evaluation.

Methods: Screening of the mild cognitively impaired patients was carried out using the Mini-Mental State Examination and Yamaguchi Fox Pigeon Imitation test. Baseline information was elicited from the patients residing in urban Vadodara (a district in the state of Gujarat), India. This included socio-demographic, medical and drug history, anthropometric and physical activity pattern, in addition to biochemical parameters comprising of serum vitamin B12 and glycated haemoglobin profile. A sub-sample of 60 patients with mild cognitive impairment (MCI) demonstrating severe vitamin B12 deficiency were conveniently enrolled for injectable doses of Vitamin B12 in the dosage of 1,000 µg every day for one week, followed by 1,000 µg every week for 4 weeks & finishing with 1,000 µg for the remaining 4 months. An intervention six-month after the experiment with all the parameters were elicited.

Results: Vitamin B12 supplementation resulted in a significant (p<0.001) improvement in the MMSE scores of the patients with a rise of 9.63% in the total patients. Gender-wise division also highlighted a significant increase (p<0.001) in the scores by 6.79% and 12.46% in overall males
and females and a 10.20% and 8.24% rise for young-old (60-69 yrs) and old-old (70-85 yrs) categories, respectively. As a result, 27 patients progressed towards the normal category from the MCI state being assessed by MMSE scores. In the same manner, YGFPIT too demonstrated a 38% increase in normal with 35% males, 42% females, 41% young–old and 31% old-old moving to normal status. Thus, a total number of 28 patients progressed to the normal condition as per YGFPIT.

**Conclusion:** Ultimately, vitamin B12 supplementation was discovered to be significantly effective, as the placing of serum vitamin B12 within MCI patients caused a turn from the deficiency state to sufficient levels and in turn increased their performance in MMSE and YFPIT scores.

**Keywords:** Mild Cognitive Impairment, vitamin B12, geriatrics, cognition

**INTRODUCTION:**
Neurodegenerative diseases may directly affect memory performance, thereby leading to functional impairments [1]. MCI is a syndrome defined as cognitive decline which is greater than expected for an individual's age and education level but does not notably interfere with activities of daily life. Some people with mild cognitive impairment appear to remain stable or return to normal over time, but more than half of individuals progress to dementia within 5 years. MCI can thus be regarded as a risk state for dementia, and its identification could lead to secondary prevention by controlling risk factors such as systolic hypertension. The amnestic subtype of mild cognitive impairment has a high risk of progression to Alzheimer's disease, and it could constitute a prodromal stage of this disorder [6].

Vitamin B12 is vital for the synthesis of myelin, the protective sheath surrounding many nerves in the periphery, spinal cord, and brain. Low levels of vitamin B12 have been associated with neurocognitive disorders [7]. Vitamin B12 deficiency due to malnutrition or malabsorption may lead to pernicious anemia and neurological disorders. It is still a common practice to treat patients with neurological symptoms with intramuscular cyanocobalamin injections [12]. Patients with cognitive deficits demonstrated notable improvement, namely in language and frontal lobe functions, after the vitamin B12 supplementation [4]. In light of these surrounding studies, the study aimed to supplement vitamin B12 deficient MCI geriatric patients with injectable doses of vitamin B12 followed by impact evaluation.

**MATERIALS AND METHODS**
**Study design and MCI diagnosis:** Preliminary screening for the identification of the elderly suffering from MCI (mild cognitive impairment) involved 120 subjects (males and females) aged 60 -85 years who were selected from a private out-patient department (O.P.D.), in addition to the University Health Centre of The Maharaja Sayajirao University of Baroda (govt.) hospitals by purposive sampling. The targeted subjects were studied for the prevalence of MCI by employing a semi-structured questionnaire, based on several cognitive impairment tests but particularly the
Mini Mental State Examination (MMSE); with the MMSE, score points falling within the range of 21-26 indicates a mild category of impairment [5] and Yamaguchi Fox Pigeon Imitation Test (Y.F.P.I.T.[13]). Thereafter, the entire information was elicited through one-to-one interviews, patient medical records and individualized anthropometric measurements, in addition to biophysical determinations. Only those patients fulfilling the inclusion criteria based on the neurological testing and serum vitamin B12 < 300 pg/ml were included in the study.

**Injectable dosage:** Vitamin B\textsubscript{12} 1000 µg in dosage of 1000 µg every day for one week, followed by 1000 µg every week for 4 weeks and then 1000 µg for the remaining 4 months was selected for intervention.

**Ethical approval:** The study was ethically approved by the Institutional Medical Ethics Committee of the Department of Foods and Nutrition, The Maharaja Sayajirao University of Baroda (No. IEHCR/2012/22). This clinical study trial has also been retrospectively registered in the Clinical Trial Registry of India (CTRI) No. CTRI/2015/03/005602.

**Statistical analysis:** The data was entered in Microsoft Excel 2007 and thereafter analyzed in SPSS 20 (Statistical Package for Social Sciences 20, Chicago, IL, USA). The variables were presented as mean ± standard deviation. Frequencies and percentages were also used to depict the quantification of responses. Statistical significance of the obtained results was derived at a two tailed p-value of <0.05*, p<0.01** and p<0.001***. The interventional impact was assessed by using the paired t-test.

**RESULTS**

**General Profile:**
Socio economic data of MCI subjects revealed that the majority of subjects were married (88%) and practiced Hinduism (94%). Mean age of baseline subjects was approximately 66 years. Percentage of males in the sample were 44% while females were 56%. Majority (76%) of the MCI patients had anemia. More than half (59%) of the patients were obese while 58% were hypertensive. Majority (57%) of the subjects had sedentary a lifestyle pattern with no extra physical activities.

**Supplementation impact on the neuropsychological profile:**
The mean serum vitamin B12 levels were analyzed to be 715.4±243.5 pg/ml and the glycated haemoglobin (HbA1c) values were found to be 6.2±0.7. Vitamin B12 supplementation brought forth a significant (p<0.001) improvement in the MMSE scores of the MCI patients with a rise of 9.63% in the total patients moving towards normality. Gender-wise division also highlighted a significant increase (p<0.001) in the scores by 6.79% and 12.46% in males and females as well as 10.20% and 8.24% rise for young-old (60-69 yrs) and old-old (70-85 yrs) categories, respectively (Table 1).
Table 1: Pre and post MMSE score of MCI patients with vitamin B12 supplementation

<table>
<thead>
<tr>
<th>MMSE Scores (Mean ± SD)</th>
<th>Total (n=60)</th>
<th>Males (n=29)</th>
<th>Females (n=31)</th>
<th>60-69 yrs (n=44)</th>
<th>70-85 yrs (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>24.5±3.28</td>
<td>25.3±2.79</td>
<td>23.7±3.55</td>
<td>24.3±3.29</td>
<td>25.0±3.20</td>
</tr>
<tr>
<td>Post</td>
<td>26.9±3.10</td>
<td>27.0±2.52</td>
<td>26.7±3.59</td>
<td>26.8±3.26</td>
<td>27.0±2.63</td>
</tr>
<tr>
<td>Percentage ↑ / ↓</td>
<td>9.63 ↑</td>
<td>6.79 ↑</td>
<td>12.46 ↑</td>
<td>10.20 ↑</td>
<td>8.24 ↑</td>
</tr>
<tr>
<td>Paired t-test</td>
<td><strong>10.26</strong>*</td>
<td><strong>6.82</strong>*</td>
<td><strong>8.51</strong>*</td>
<td><strong>8.33</strong>*</td>
<td><strong>7.34</strong>*</td>
</tr>
</tbody>
</table>

*** Significant at p<0.001

As observed from the Table 2, about 42% of the total patients improved to the normal category. Similarly, 35% males, 48% females, 32% young-old and 69% old-old progressed to a normal cognitive status. The MMSE scores of patients indicated that 27 MCI patients progressed towards the normal category from the MCI state (Figure 1).

Table 2: Improvement in number of MCI patients to normal cognition levels aided through MMSE detection

<table>
<thead>
<tr>
<th>Number of MCI subjects detected by</th>
<th>Males (n= 53)</th>
<th>Females (n= 67)</th>
<th>60-69 yrs (n= 88)</th>
<th>70-85 yrs (n= 32)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>B12 Doses</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre (n=60)</td>
<td>58 (96.7)</td>
<td>28 (96.5)</td>
<td>30 (96.8)</td>
<td>42 (95.5)</td>
</tr>
<tr>
<td>Post</td>
<td>33 (55.0)</td>
<td>18 (62.0)</td>
<td>15 (48.4)</td>
<td>28 (63.6)</td>
</tr>
<tr>
<td>Shifted from MCI to Normal</td>
<td>25 (41.7)</td>
<td>10 (34.5)</td>
<td>15 (48.38)</td>
<td>14 (31.8)</td>
</tr>
</tbody>
</table>

Numbers in parenthesis indicate percentage, YO=Young Old, OO= Old Old

**Figure 1:** MMSE Scores of MCI patients before and after B12 supplementation
Table 3 characterizes that around 38% increase in normal subjects vitamin B12 supplemented group which included 35% males, 42% females, 41% young–old and 31% old-old. A number of 23 patients progressed to normal condition according to YGPIT (Figure 2).

Table 3: Improvement in number of MCI patients to normal status by YFPIT

<table>
<thead>
<tr>
<th>Number of MCI subjects detected by YFPIT tool</th>
<th>Males (n= 53)</th>
<th>Females (n= 67)</th>
<th>60-69 yrs YO (n= 88)</th>
<th>70-85 yrs OO (n= 32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B12 Doses (n=60) Pre</td>
<td>55 (91.7)</td>
<td>28 (96.5)</td>
<td>27 (87.1)</td>
<td>42 (95.5)</td>
</tr>
<tr>
<td></td>
<td>32 (53.3)</td>
<td>18 (62.0)</td>
<td>14 (45.2)</td>
<td>24 (54.5)</td>
</tr>
<tr>
<td>MCI Shifted to Normal</td>
<td>23 (38.3)</td>
<td>10 (34.5)</td>
<td>13 (41.9)</td>
<td>18 (40.9)</td>
</tr>
<tr>
<td></td>
<td>5 (31.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Numbers in parenthesis indicate percentage, YO=Young Old, OO= Old Old

DISCUSSION

Several animal studies have confirmed the effective role of vitamin B12 supplementation in the treatment of memory disorders. However, very few human studies have been carried out to assess the impact of vitamin B12 in relation to cognitive impairment. With this in mind, the present study aimed to assess the impact of vitamin B12 supplementation in MCI patients (N=60) for a period of six months on an injectable dosage, as prescribed by the Association of Physicians of India (API).

In the present study, the mean serum vitamin B12 levels rose to higher levels of 715.4±243.5 pg/ml, indicating the positive effect of vitamin B12 supplementation in the
intervened MCI patients. The HbA1c values of the MCI patients improved very slightly in their borderline control of diabetes after vitamin B12 supplementation.

Similarly, randomized clinical trials (RCTs) have demonstrated that vitamin B12 (cobalamin) treatment was effective and was also better tolerated in elderly patients aged above 60 years were treated for serum vitamin B12 deficiency [1]. Other studies have demonstrated that long-term supplementation of daily oral 400 μg folic acid plus 100 μg vitamin B12 promoted improvement in cognitive functioning after 24 months, particularly in the cases of immediate and delayed memory performance [11].

In an overview, [2] has evaluated that vitamin B12 delays the onset of signs of dementia (and blood abnormalities), provided that the vitamin is administered in a precise clinical timing window before the onset of the first symptoms. Supplementation with cobalamin improves cerebral and cognitive functions in the elderly—it frequently improves the functioning of factors related to the frontal lobe, as well as the language function of those with cognitive disorders.

In the present study, results have depicted a significant improvement in the MMSE scores of MCI patients, with 42% of subjects shifting towards the normal range from their previous MCI condition. The YFPIT also revealed that 38% have shifted to the normal range from the MCI. These are in line with the study by Cunha et al (1995), who reported that all the patients who showed some improvement (MMSE returned to normal values) had mild dementia. Therefore, screening for B12 deficiency should be considered in patients with a recent onset of mild mental status changes. Only a small number of human studies have been carried out in relation to determining vitamin B12’s relation to MCI. We may state that our study is the very first one where the MCI diagnosis, as well as the interventional impact of vitamin B12, has been taken into consideration for improving the cognition levels of MCI patients.

Being on a prescribed regime of 1000 mcg vitamin B12 injectable dosage for six months has efficiently resulted in significant memory improvement of the MCI patients. Moreover, no adverse effects or complaints have been observed on the intervened MCI patients. Thus, this study can serve as a background for further initiation of clinical trials on humans for adding to the database by assessing the impact of vitamin B12 supplementation in the management of cognitive disorders.

**Abbreviations:** MCI, Mild Cognitive Impairment; MMSE, Mini-Mental State Examination; YFPIT, Yamaguchi Fox Pigeon Imitation Test; HbA1c, glycated haemoglobin; API, Association of Physicians of India.

**Author contributions:** KC conceptualized, designed and supervised the study, reviewed and finalized the manuscript; AA did the literature search, data acquisition and analysis, drafted the manuscript.

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**Conflict of interest:** None.
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