Short Communication

Improvement in Peripheral Nerve Conduction with Vitamin B12 Supplementation in Subclinical Vitamin B12 Deficient Young Adults

Sowmya Sharma* and Sambashiviah Sucharita

Department of Physiology,
St. John’s Medical College,
Bangalore

Abstract

Subclinical vitamin B12 deficiency is highly prevalent among the otherwise healthy Indian adults. The present study aimed to evaluate the association between vitamin B12 status and peripheral nerve conduction parameters in healthy young adults. The study also aimed to understand the effect of vitamin B12 supplementation on nerve conduction parameters. 30 healthy adults between the age group of 18-30 years underwent nerve conduction assessment and serum vitamin B12 analysis. There was a significant and positive correlation between vitamin B12 levels and sensory nerve conduction velocity \( r=0.44, p=0.02 \) and sensory nerve amplitude \( r=0.39, p=0.04 \). Out of 30 subjects, 23 subjects had vitamin B12 levels \( \leq \) 200 pmol/L. 10 subjects with subclinical vitamin B12 deficiency were supplemented with cyanocobalamin 100 µg for 4 months. Sensory nerve conduction velocity significantly increased following supplementation \( p<0.05 \). This study demonstrated early functional changes (nerve conduction) even in a subclinical state. The current study also provided evidence on the beneficial effects of vitamin B12 supplementation in the improvement of sensory nerve conduction among young healthy Indians.

Introduction

Long standing vitamin B12 deficiency is clinically associated with neurological complications like peripheral neuropathies, cognitive deficits, dementia and other neuropsychiatric manifestations. Among these complications peripheral neuropathy is known to affect large fibre (type A), resulting in both sensory and motor peripheral neuropathies. Vitamin B12 deficiency is known to cause demyelination and axonal degeneration in peripheral as well as central nervous system (1, 2). Simple non-invasive electro diagnostic nerve conduction tests are commonly used to detect changes in peripheral nervous system. Reduction in wave amplitudes reflect the axonal changes whereas changes due to demyelination is reflected as reduction in conduction velocities (3). Evidence suggests that there was improvement in nerve conduction parameters along with clinical recovery among long standing vitamin B12 deficient individuals after vitamin B12 supplementation (4). However, most of the focus on vitamin B12...
supplementation and its effects on peripheral neural outcome is on the elderly population, where prevalence of vitamin B12 deficiency and peripheral neuropathy is high (5). Vitamin B12 deficiency in young and middle-aged individuals remains least explored and is often under-reported in a clinical setup. For example, in a study from Pune, India, biochemical evidence of vitamin B12 deficiency namely low vitamin B12 levels and hyperhomocystenemia was shown in more than 75% of young and middle aged individuals and most of the participants were apparently healthy without clinical symptoms of vitamin B12 deficiency (6). It is not known if early peripheral neural changes occur in asymptomatic vitamin B12 deficiency. This is important as this age group is not routinely screened for vitamin B12 deficiency in the absence of clinical symptoms. Hence subtle early functional changes if any detected could prevent the occurrence of complications and progression into clinical vitamin B12 deficiency. The objective of the present study was to evaluate the association between vitamin B12 status and peripheral nerve conduction parameters in healthy young adults. Also, the study aimed to understand the effect of vitamin B12 supplementation on the nerve conduction parameters in a subpopulation of subclinical vitamin B12 deficient subjects.

Methods

30 healthy young adults (both males and females) aged between 18 to 35 years were recruited after obtaining written informed consent. The sample size was calculated setting the α at 0.05 and β at 0.2 and using correlation coefficient from a previous study (7). None of the subjects reported any symptoms suggestive of peripheral neuropathy. Subjects who underwent surgery or history of fracture or scars at the sites of stimulation were excluded. Also, subjects with symptoms of malabsorption like increased fatiguability, abdominal distension, flatulence was excluded. The institutional ethical review board approved the research protocol.

Following recruitment, each subject underwent anthropometry, nerve conduction assessment, vitamin B12 estimation and complete hemogram. Vitamin B12 was determined using a Chemiluminescent immunoassay (UnicelDxI 600, California, USA), with an inter-assay CV of 6.6-8.5% and intra-assay CV of 4.8-6.9%.

Nerve conduction assessment

Nerve conduction assessment was performed on the median nerve and included both motor and sensory assessment (Recorders and Medicare systems, Chandigarh, India). The median nerve was selected due to easy accessibility and since changes, for example, age related, are more evident in the median nerve (8). A normal room temperature (mean: 25°C) and a skin temperature of over 31°C were maintained. For the motor nerve conduction studies, surface electrodes were used. For obtaining the median nerve compound motor action potential (CMAP), the active electrode was placed on the abductor pollicis brevis motor point with the reference electrode placed distally. The stimulation was given 8 cm proximally at wrist. A second stimulus was applied to the median nerve at the antecubital fossa. Using a supramaximal impulse for both stimulation sites, the CMAP was recorded and forearm NCV was obtained. For orthodromic sensory nerve conduction studies, surface ring electrodes were used. The recording electrode was located on the second and third digit just distal to the metacarpophalangeal joint region and the reference electrode was placed 4 cm more distal on the respective digit. The median nerve was excited 7 cm and 14 cm proximal to active electrode at wrist with a supramaximal current intensity. Evaluated variables included the conduction velocities and amplitudes (3).

Vitamin B₁₂ supplementation

Out of the 30 subjects recruited for the study, 23 subjects had serum vitamin B12 levels < 200 pmol/L. 12 subjects were supplemented following sample size estimation and 10 subjects completed 4 months of supplementation (9). Subjects were categorized as being high risk of vitamin B-12 deficiency if they had vitamin B12 concentrations of < 200 pmol/L (10). Cyanocobalamin (100 µg) was given as a single daily dose for 4 months (11). Blood samples were collected at midpoint (2 months) and end of 4 months to
assess the compliance and improvement in serum vitamin B12 status. Nerve conduction assessment was repeated post supplementation.

Statistical analysis:

The normality of the data was examined using Shapiro-Wilk test. The data are expressed as mean (standard deviation). Correlation between vitamin B12 status and nerve conduction parameters were examined using Pearson’s correlation coefficient. Nerve conduction parameters were compared before and after supplementation using paired ‘t’ test. Results were considered significant if P<0.05. All statistical analyses were performed using SPSS (v20, SPSS, Chicago, IL, USA).

Results

The recruited subjects were 21±3 years of age with a BMI of 22.2±3.3 kg/m². Mean vitamin B12 level was 149.4±54 pmol/L. Pearson’s correlation analysis showed significant and positive correlation between vitamin B12 levels and sensory nerve conduction velocity (r=0.44, p=0.02) and sensory nerve amplitude (r=0.39, p=0.04). There was no correlation between vitamin B12 levels and the motor nerve conduction parameters (Fig. 1). Out of 30 subjects, 23 subjects...
had vitamin B12 levels ≤ 200 pmol/L. In a subgroup, following supplementation, there was 114% increment in plasma vitamin B12 (p<0.05). Sensory nerve conduction velocity significantly increased following supplementation (p<0.05). Other nerve conduction parameters were comparable before and after supplementation (Table I).

### TABLE I: Biochemical and nerve conduction parameters pre and post supplementation.

<table>
<thead>
<tr>
<th>Study Parameters</th>
<th>Pre-supplementation</th>
<th>Post-supplementation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biochemical Parameters</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin B12 (pmol/L)</td>
<td>142.9±36.6</td>
<td>302.8±113.2*</td>
</tr>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>15.1±0.7</td>
<td>15.3±0.9</td>
</tr>
<tr>
<td>MCV (fl)</td>
<td>87.6±3.4</td>
<td>85.0±3.1</td>
</tr>
<tr>
<td>MCH (pg)</td>
<td>28.6±1.4</td>
<td>28.9±1.2</td>
</tr>
<tr>
<td>MCHC (%)</td>
<td>32.8±1.0</td>
<td>34.0±1.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Median nerve conduction parameters</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensory nerve velocity (m/sec²)</td>
<td>58.7±5.7</td>
</tr>
<tr>
<td>Motor nerve velocity (m/sec²)</td>
<td>58.7±3.6</td>
</tr>
<tr>
<td>Sensory nerve amplitude (mvolts)</td>
<td>31.0±6.9</td>
</tr>
<tr>
<td>Motor nerve amplitude (mvolts)</td>
<td>18.0±6.4</td>
</tr>
</tbody>
</table>

*p<0.05, MCV- Mean Corpuscular Volume, MCH- Mean Corpuscular Haemoglobin, MCHC- Mean Corpuscular Haemoglobin Concentration.

### Discussion

The data from the present study demonstrated an association between vitamin B12 levels and sensory peripheral nerve function. Also, in a subgroup of subclinical vitamin B12 deficient young adults, there was an increase in median sensory nerve velocity following vitamin B12 supplementation which is a reflection of improvement in conduction in myelinated peripheral nerves.

Out of the total recruited 30 subjects, 77% of the study participants had vitamin B12 deficiency based on plasma vitamin B12 cut-off of 200 pmol/l. Studies worldwide have reported varied prevalence rates of vitamin B12 deficiency especially among the young adults. Hence continuum of vitamin B12 status was used to assess association with peripheral nerve function parameters rather than compare the differences between the deficient and replete group.

In the present study, there was no association between the vitamin B12 status and the motor nerve conduction parameters. Evidence from previous studies show direct association between the duration of vitamin B12 deficiency and changes in peripheral nerves with sensory nerve changes appearing much before motor changes (2). The data obtained through this study is consistent with these findings. As the present study involved healthy young adults without any symptoms of neural deficit (peripheral neural and cognitive function), the findings suggest assessment of peripheral neural function especially sensory even in asymptomatic vitamin B12 deficiency may be beneficial in detecting early changes.

Electro diagnostic studies in vitamin B12 deficiency have revealed conflicting results ranging from demyelination as shown by slowing of conduction velocity, to axonal changes as shown by reduced compound action potential to mixed variety (1, 2, 3). Sural nerve biopsy studies in subjects with peripheral neuropathy due to vitamin B12 deficiency have shown variable demyelinating and axonal changes depending on the duration of disease. In patients with shorter duration of illness, studies have revealed acute axonal degeneration with formation of myelin ovoids, whereas with longer duration, there were chronic axonal changes resulting in myelinated fibre depletion, axonal regeneration, and secondary demyelination. Sequential follow-up of such patients showed significant improvement in conduction velocity and amplitude (12).

In the present study, there was improvement in conduction velocity following supplementation. One of the possible mechanism explained is vitamin B12 acts as an essential cofactor for L-methylmalonyl-CoA mutase enzyme, which converts methylmalonyl-CoA to succinyl-CoA. Impairment of this enzyme during vitamin B12 deficiency will result in formation of abnormal fatty acids. Thus excessive odd-chain and branched chain fatty acids would accumulate in membrane lipids of nervous tissue resulting in the altered myelin sheath formation and demyelination (13). The findings following supplementation of small daily doses of vitamin B12 for 4 months suggests early reversal of changes in myelination status. The fact that there was a significant change in the vitamin
B12 following supplementation not only indicate adherence of subjects to the study protocol but can also help in further understanding of the mechanisms. However, one of the limitation of this study was small sample size of the subjects who underwent intervention. Further population-based studies to understand long-term effects of vitamin B12 following supplementation for short duration are required. In conclusion, for the first time this study provides evidence on the beneficial effects of vitamin B12 supplementation in young healthy subjects in the absence of anaemia and any neurological symptoms, underlying the relevance of screening for moderate vitamin B12 deficiency among healthy population.

**Acknowledgements**

Authors would like to thank Mr. Ravikanth for helping with data collection and analysis.

**Conflict of interest:**

The authors declare that there are no conflicts of interest.

**References**