ABSTRACT

Neurodegenerative disorders have rung the alarming bell with their burgeoning prevalence and global burden. Mild Cognitive Impairment (MCI) is turning out as a global epidemic of severe concern for developing and low-income economies like ours. India ranked third in the world for having a huge number of people with dementia. MCI is the transitional phase between normal aging process and Alzheimer's disease. Being insidious in nature, its early detection through neuropsychological testing procedure is of utmost importance and if undiagnosed it may lead to irreversible diseases such as Alzheimer's. Hence, to tackle the menace being imposed by MCI, the scientific groups have devised novel therapeutic approaches to counteract the ever increasing epidemic of MCI and complications associated with.

In the current scenario, role of vitamin B12 in improving cognition levels in the geriatric population is gaining wide impetus. Scientific reports have proposed that vitamin B12 supplementation has shown protective effect in treatment of neurological disorders. With these findings providing strong basis, the vitamin B12 might enhance cognitive functions and maintain the overall brain health.

Secondly, flaxseeds amongst the prime functional food are the need-of-the-hour. Flaxseeds are a potent source of omega-3 fatty acids, most significantly alpha-linolenic acid (ALA). It has shown to provide risk modulation against neurological disorders notably Alzheimer's disease, dementia, etc, cardiovascular benefits, beneficial changes in blood lipid profile, protection against some types of cancer and many more.

These valuable properties of vitamin B12 and flaxseeds pave a way forward to further study the content analysis, acceptability of flaxseeds and the efficacy of both on cognitive impairment. Hence, the present study was taken with the three major objectives: 1) Baseline assessment of diet, nutrition and health status of cognitively impaired elderly with MCI. 2) Food product development using omega-3 fatty acid

rich flaxseeds and sensory trials. 3) Intervention and impact evaluation of the MCI elderly group with Omega -3 fatty acids and Vitamin B12 supplementation.

The gas chromatography technique was applied for proximate and fatty acid estimation of raw versus roasted flaxseeds. Then the method of substitution was employed for roasted flaxseeds incorporation in widely popular Indian food items. The products included were *khichdi*, *porridge*, *laddoo* and *mukhwaas* and evaluated for organoleptic assessment using the 9-point Hedonic scale and the Composite scoring test.

In the final phase III of the study trial, 120 willingly consenting elderly were conveniently enrolled under two subgroups namely, Group 1 with methylcobalamin injectable doses for the B12 intervention (n=60) and the Group 2 with methylcobalamin (B12) injectable doses B_{12} plus roasted flaxseeds (omega-3 fatty acid) (n=60) respectively for 6 months period on a dose dependent basis as per prescribed regime of Association of Physicians of India in the sequence of 1000 µg injectable doses everyday for one week, followed by 1000 µg every week for 4 weeks and then 1000 µg monthly dose for a period of four months. Second group was supplemented daily with 20 g roasted flaxseeds (rich omega-3 fatty acid source) having consumed 10 g of roasted flaxseeds at post lunch and post dinner respectively. A pilot study was prior conducted on the patients to be supplemented with 20 g flaxseeds to rule any toxic impact and no deleterious effects were assessed from their kidney and liver function profiles.

In the phase I, 120 subjects (60 -85 yrs) were enrolled by the convenient sampling design from the government and private hospitals of urban Vadodara. Pertinent data was obtained through the patient medical records, neuropsychological test battery screening, one-to–one interviews, and direct measurements. Bio-physical measurement included monitoring of blood pressure, biochemical parameters like serum vitamin B12, haematological profile, glycemic, lipemic and only in the case of patients for flaxseeds administration –the kidney plus liver function tests were performed from the blood samples of the patients.

The results of this phase elicited that almost half (49%) of the baseline subjects were diagnosed with MCI. 57% of the subjects had a sedentary lifestyle pattern. 69% of MCI subjects were obese, 15.8% overweight, 58% hypertensive, 37% pre-hypertensive. The mean serum vitamin B12 was 186 pg/ml and mean total cholesterol was 195 mg/dl. Mean fasting blood glucose and glycated hemoglobin were 98 mg/dl and 6.1% respectively. 82% had poor control of serum B12 level and 20% had borderline control. Diet consumed by patients was deficient by approximately 70% for Vitamin B12 intake and around 87% less than RDA levels for ALA (omega-3) consumption. Pearson's correlation revealed a significant association of BMI ($p<0.001$), RBC ($p<0.05$), HDL ($p<0.001$), triglycerides ($p<0.05$), VLDL ($p<0.05$) and diastolic blood pressure ($p<0.05$) with serum vitamin B12 levels whereas significance was observed between ALA intake with haemoglobin ($p<0.05$), total cholesterol ($p<0.05$) and diastolic blood pressure ($p<0.05$).

The phase II results depicted that roasting profoundly enhanced the ALA content to 56% in roasted form of the flaxseeds as compared to 37% of the raw form from the analysis by the gas chromatography technique. The *porridge*, *globs* and *mukhwaas* were well accepted at the higher (20g) substitution levels in these formulations while *khichdi* was most acceptable at the 10 g substitution level.

Post supplementation of the MCI patients in the phase III, the increased shift towards normal cognition levels by ACE score confirmed 45% in Group 2 and likewise 23% in Group1. MMSE scores adjudged 65% to be cognitively healthy in Group 2 and 41% in Group1. The MNA scores determined that 53% subjects in Group 2 regained normal nutritional status and 45% in Group 1. Significantly higher intakes were depicted than the baseline with 14.8% for dietary intake of vitamin B12 ($p<0.05$) in Group 1 and 1087.5% for dietary omega-3 intake ($p<0.001$) in the Group 2.

The serum vitamin B12 significantly ($p<0.001$) increased by 370% and 276% in case of Group 2 and Group 1. Amongst the lipemic parameters, the significant ($p<0.001$) drop in TC (19%), TG (23.4%), LDL (20.2%) and VLDL (34%) was observed for Group 2 whereas the HDL levels significantly ($p<0.001$) escalated in Group 2 (19.3%) and Group 1(6.8%). Significant ($p<0.001$) decline was detected for TC/HDL,

TG/HDL, LDL/HDL and Atherogenic Index by 33.3%, 37.3%, 34% and 41.2% in the Group 2 MCI patients. Glycemic response significantly diminished to 14% and 20.3% for FBS and HbA1c in Group 2 whereas amounted to 2.6% and 3.7% for FBS and HbA1c values in Group 1. Serum vitamin B12 was significantly ($p<0.05$) and inversely associated with FBS whereas significantly ($p<0.05$) positively correlated to hip circumference. Similarly, dietary omega-3 was significantly ($p<0.05$) positively correlated to waist circumference, ACE as well as MMSE scores.

Hence, the bottom line from this study phase establishes that vitamin B12 supplementation along with 20 g roasted flaxseeds to the MCI patients for a period of six months enhanced cognitive status as substantiated from ACE, MMSE as well as MNA scoring tests, improved serum vitamin B12, lipemic, atherogenic and glycemic controls.