Vitamin B12 and Omega 3 Fatty Acid Interventions for Cognition in Elderly Avoicetrial

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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 alphalinolenic 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.

Keywords – *Vitamin B12, Omega 3, Mci*

INTRODUCTION

Ageing leads to endless forms and difficulties in addressing them. Since time immemorial, humans have been continuously trying to find answers by conducting studies on the repercussions of ageing as a whole. In all world regions, population ageing is proceeding gradually, but the populations of many low- and particularly middle-income countries are ageing faster than any other country in the past; two-thirds of the world's elderly live in low- and middle-income countries (LMICs), growing to 80% by 2050 (United Nations 2009). There are about 900 million people living worldwide aged 60 years and over. The number of older people

living in high-income countries is expected to grow by 56% between 2015 and 2050, compared to 138% in upper middle-income countries, 185% in lower middle-income countries, and 239% in low-income countries (Alzheimer's Disease International 2015). Although morbidities mediate the relationship between population ageing and social costs, chronological age relationships are complex and potentially likely to be affected by interventions in public health, health, and social care (Lloyd-Sherlock et al 2012). Globally, the incidences of neurodegenerative diseases that take the toll of human life are rising significantly. Central and peripheral nervous system diseases are neurological disorders. In other words, the brain, the spinal cord, the cranial nerves, the peripheral nerves, the roots of the nerves, the autonomic nervous system, the muscles and neuromuscular junctions. These conditions involve epilepsy, Alzheimer's disease and other dementias, stroke, migraine and other pain disorders, multiple sclerosis, Parkinson's disease, neuroinfections, brain cancers, traumatic nervous system disorders such as brain trauma, and malnutrition-related neurological disorders (World Health Organization 2014).

In almost all developed countries, the global burden of neurodegenerative diseases is expected to be the largest. Among them, there is a vital concern regarding Alzheimer's disease and dementia. Increased life expectancy leads to rapid numerical changes and is related to an increased incidence of chronic disorders such as dementia (Alzheimer's Disease International 2015). 47.5 million people have dementia worldwide, with just over half (58 percent) living in countries with low and middle incomes. There are 7.7 million new cases each year. At a given time, the average proportion of the general population aged 60 and over with dementia is between 5 and 8 per 100 individuals. The estimated number of dementia sufferers is expected to grow to 75.6 million in 2030 and almost triple to 135.5 million by 2050. The growing number of people with dementia living in low- and middle-income countries is responsible for much of this rise (WHO 2015). In 2015, there will be 9.9 million new dementia cases around the world, one every 3 seconds. 46.8 million people worldwide are estimated to be living with dementia in 2015. Every 20 years, this figure will almost double, reaching 74.7 million in 2030 and 131.5 million in 2050. According to updated 2015 figures, East Asia is the country with the most dementia sufferers in the world (9.8 million), followed by Western Europe (7.4 million). In 2015, more than a million people with dementia live in ten countries at country level: China (9.5 million), the United States (4.2 million), India (4.1 million), Japan (3.1 million), Brazil (1.6 million), Germany (1.6 million), Russia (1.3 million), Italy (1.2 million), Indonesia (1.2 million) and France (1.2 million) (Alzheimer's Disease International 2015). India had 3.5 million Alzheimer's disease/dementia patients in the year 2000, compared to 4.5 million in the United States of America (Upadhyay et al 2014). Alzheimer's disease is the most prevalent type of dementia, accounting for 60–80 percent of cases of dementia. The second most common type is vascular dementia, which occurs after a stroke, accounting for around 10 percent of cases (Alzheimer's Association 2014). The estimated cumulative worldwide cost of dementia in 2015 is US$ 818 billion in the Forbes 2015 ranking. Dementia will become a trillion dollar disease by 2018, rising to US$ 2 trillion by 2030 (International Alzheimer's Disease 2015).

From a few cases in a country at the beginning of the 20th century to the frequency of documenting a case every 7 seconds in the world, Alzheimer's disease (AD) has increased. It has hit the top 8 of the world's big health issues from a rare illness (Cornutiu 2015). As older populations rise dramatically around the globe, Alzheimer's disease (AD) is a growing global health and economic concern. There is currently no approved disease-modifying treatment, despite the several clinical studies performed (Sugino et al 2015). Biomarker evidence of

amyloid beta (A) accumulation is associated with functional and structural brain changes, consistent with the trends of abnormality seen in patients with mild cognitive impairment (MCI) and AD dementia, according to emerging research in clinically normal older individuals (Sperling et al 2011). It has been hypothesized that cognitively normal older people are at elevated risk of experiencing cognitive impairment over time, and that cognitive changes become noticeable at some stage during this 'preclinical' disease process (Sperling et al 2011), even if the person or his/her collateral source has not yet recorded clinical symptoms.

OBJECTIVES

1. To chalk out the prevalence of MCI in elderly attending out–patient departments in hospitals of urban Baroda through neuropsychological testing.

2. To assess socio-demographic, activity, anthropometric, biophysical, dietary and bio-chemical pattern.

Global and National prevalence of neurodegenerative disorders

Unreasonably higher rates of impairment and death are faced by people with mental illnesses. "It is essential to promptly recognize and treat mental and neurological disorders in older adults." - WHO 2016 Neurodegenerative disease is an umbrella term for the sequence of neurons affecting the human brain's primary conditions. Neurodegenerative disorders are characterized as disabling and incurable conditions characterized by loss of neuronal cell activity and frequently associated with atrophy of the central nervous system structures affected, causing progressive deterioration of the nervous system (Griffin 2006). The brain and spinal cord are found in the nervous system, where the neurons act as building blocks. Neurons, if disabled or dead, are irreproducible and irreplaceable in the human body. Alzheimer's disease, Parkinson's and Huntington's disease are examples of neurodegenerative diseases.

Neurodegenerative disorders are incurable and deteriorating conditions lead to irreversible nerve cell degeneration and/or death causing difficulties with movement (called ataxias) or mental activity (called dementias) (European Union Joint Programmer- Neurodegenerative Disease Research 2014). Dementia is a condition in which there is loss in memory, thought, actions and the capacity to perform daily tasks, according to the WHO Fact Sheet 2016. While dementia affects the elderly predominantly, it is not a common part of ageing. 47.5 million individuals have dementia worldwide and there are 7.7 million new cases per year. Alzheimer's disease is the most common cause of dementia and may lead to 60–70 percent of cases. Dementia among older people worldwide is one of the main causes of disability and dependence. It is estimated that the total number of people with dementia will grow to 75.6 million in 2030 and 135.5 million in 2050, with the majority residing in low- and middle-income countries. In terms of direct treatment costs, direct social costs and the expense of informal care, dementia has substantial social and economic consequences. In 2010, the global overall cost of dementia to society was estimated at US$ 604 billion. This corresponds to 1.0 percent of the gross domestic product (GDP) worldwide, or 0.6 percent if only direct costs are taken into account. The overall cost ranged from 0.24 percent in low-income countries to 1.24 percent in high-income countries as a percentage of GDP. The world is noticing a rapid ageing of the population. From around 12% to 22%, the proportion of older adults in the world between 2015 and 2050 is expected to almost

double. This is an estimated rise, in absolute terms, from 900 million to 2 billion people over the age of 60. The unique physical and mental health problems faced by the elderly need to be recognized. Neurological and psychiatric illnesses are linked to over 20 percent of adults aged 60 and over suffering from a mental or neurological condition (excluding headache disorders) and 6.6 percent of all disability (disability adjusted life-years-DALYs) among over 60s. In the elderly population, these disabilities account for 17.4% of years of impairment (YLDs). Dementia and depression are the most common neuropsychiatric conditions in this age group (WHO 2016). Table 2.1.1 shows the total number of DALYs associated with neurological conditions (in thousands). Globally, Alzheimer's and other dementias rose from 11.78 million in 2005 to 13.54 million in 2015 and was projected to hit 18.4 million by 2030, showing a rise of 66 percent.

Epidemiology of neurodegenerative diseases in India

The prevalence rates from various regions of India given approximate estimates for more than 30 million people with neurological disorders (excluding neuroinfections and traumatic injuries). This neurological condition spectrum ranged from 967 to 4,070 with an average of 2394 per 100,000 population (Gourie-Devi 2014). Few institutionalized and hospital-based studies have identified a prevalence of clinical morbidity in older adults of 49.28% (Sood et al 2006) and 8.6% in the geriatric population Similar studies found 43.32 percent psychiatric morbidity in rural seniors (Tiwari 2000), 49.2 percent in New Delhi urban areas (Chowdhury and Rasania 2008) and 19.3 percent prevalence in Lucknownow urban seniors (Tiwari and Tripathi 2009). A broad variety of figures of neurodegenerative diseases ranging from 22 to 3333 were also observed in Gururaj et al 2005. (per 1000 agespecific population). The prevalence of 95/1000 population was recorded in the previous research carried out by Shaji et al (1995) on the elderly population in their Kerala-based study on priority mental disorders. Nandi et al. (2000), meanwhile, discovered that an astonishing 61% of their research participants were 'mentally ill'. The higher incidence from these studies may probably be attributed to the study of an increasingly graying population of priority disorders. The community-based research estimates are further hindered by the non-recognition of older people's mental illness when disclosing those illnesses. In another meta-analysis study by Chandrashekhar and Isaac (1998), the prevalence of mental illnesses among the age group of 60+ years was estimated to be 31/1000.

Neuroimaging and Biomarkers for MCI detection

“Neuroimaging-biomarkers of Mild Cognitive Impairment (MCI) allow an early diagnosis in preclinical stages of Alzheimer’s disease (AD). The dynamic measures of these imaging biomarkers are used to predict the disease progression in early stages and improve assessment of therapeutic efficacy in these diseases in futute clinical trials.”

Neuroimaging

Subtle changes relevant to the pathological process may be quantified in asymptomatic or moderately symptomatic patients by evaluating humoral fluids, often cerebrospinal fluid (CSF), or by using sophisticated methods of neuroimaging. The reason for looking for biological markers in AD is, therefore, to improve diagnostic accuracy at the early stages of the disease phase. (2010 Forlenza et al). Neuroimaging is potentially an effective method for differential diagnosis and monitoring of improvements in cognitive disability. Structural (computed

tomography [CT] and magnetic resonance imaging [MRI]) and practical (single photon emission computed tomography [SPECT], positron emission tomography [PET], and magnetic resonance spectroscopy [MRS]) modalities have been used in cross-sectional and longitudinal studies in the evaluation of MCI (Jack 2010). Through using biomarkers for AD in conjunction with additional knowledge from structural magnetic resonance imaging, PIB-PET, FDG-PET and cerebrospinal fluid biomarkers, the relation of the MCI syndrome to a particular aetiology determines the certainty with which a person with MCI has the underlying AD pathology. 1) evidence of amyloid β accumulation in the brain as assessed by PET, reduced levels of amyloid β (Aβ42) in cerebrospinal fluid (CSF), and 2) evidence of neuronal damage as assessed as increased CSF tau (total and phosphorylated), brain hypo metabolism as assessed by fluorodeoxyglucose PET, and atrophy of the hippocampus from structural magnetic resonance imaging (Sachdev et al 2012). The potential prognostic benefit for possible outcomes of dementia is the utility of this classification. Subjects with a high probability of MCI due to AD are more likely to advance to AD (Roberts et al 2013).

A key topic for consideration is the prognosis of the MCI subtypes. The early concept of amnestic MCI was based on the premise that patients displayed symptoms of episodic deterioration of memory at the early stages of AD and progressed linearly to full-blown dementia syndrome. A similar hypothesis was attributed to other subtypes of MCI and related (theoretical) findings (Petersen 2004) (Figure1.1). However, the correlation between MCI subtypes and particular dementia outcomes has been challenged by epidemiological and clinical research (Busse et al 2006; Fischer et al 2007). Studies indicate that people initially diagnosed with MCI can demonstrate long-term cognitive deficit stability or even return to normal norms over time (Palmer et al 2002; Loewenstein et al 2007 and Diniz et al 2009). A significant proportion of such patients may actually be reclassified as cognitively normal in a future assessment. Usually, these cases are reported as 'unstable MCI'. If a false-positive artefact of cognitive testing was the first diagnosis, or whether these people regain normal cognitive function after temporary, subtle disability still needs to be identified. Diagnostic instability is observed, as is the case, in 5% to 20% of longitudinal MCI samples (Diniz et al 2009)

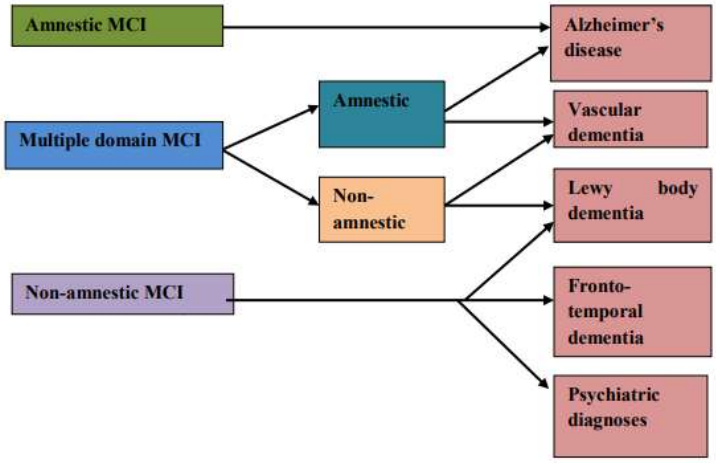

Figure 1.1: Hypothetical outcomes according to distinct mild cognitive impairment (MCI) subtypes

Search for biological biomarkers for Alzheimer's disease

A clear example of successfully transforming knowledge of main pathway physiological pathways of the disease into clinical applications is the growth of biomarker research in AD. A biomarker is a measurable function and is evaluated as an indication of processes of pathogenesis or to assess the impact of pharmacological treatments on predefined biological cascades (Wagner 2009). At least three basic criteria should be met by the ideal diagnostic marker for AD: I indicate core neurobiological changes that define the disease process; (ii) confirmed by post-mortem tests, assuming that the neuropathic conceptual results are gold standards of abnormalities affecting the same cascade; and (iii) detectable as early as possible in the continuum of the disease, preferably at p Non-invasive and easy to conduct, accurate and effective, and appropriate for large-scale screenings are additional criteria. Among several candidate markers, none of them have so far achieved universal acceptance, nor have they completely met the above requirements. In the areas of CSF and neuroimaging biomarker detection, however, substantial progress has been made towards this objective, with attention focusing on the prediction of AD in the prodromal stages of disease and in high-risk classes (Forlenza et al 2010).

CONCLUSIONS

Dementia has been considered by current estimates as an epidemic problem for low-middle-income countries, especially India. India is undeniably third today among the ten countries that are home to over a million demented individuals. Scientific bodies have trained themselves to identify novel therapeutic targets or neuro-protective nutraceuticals to curb the burgeoning hazard of cognitive impairment and effectively handle MCI by thwarting its further progression to serious disorders. Inject able doses of vitamin B12 (methylcobalamin) and flaxseeds are maintained to be incredibly promising and potentially helpful for overall health systems. Vitamin B12 and flaxseeds regulate blood pressure, weight, blood lipids and can function to increase the levels of geriatric cognition in accordance with the recent evidence collected.

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