



The Role of Diet in Cognitive Impairment in Multiple Sclerosis



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Submission: May 17, 2021; Published: May 24, 2021

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Abstract

Multiple Sclerosis is a chronic inflammatory autoimmune disease that affects the CNS. It can manifest with various neurologic symptoms such as cognitive impairment. Cognitive decline in MS is crucial given that it is suggestive of a worse prognosis and quality of life. Cognitive impairment in MS has various risk factors like degree of lesions, progressive form of the disease, fatigue and depression. Up to today no medication has been useful in treating cognitive impairment in MS. Certain lifestyle modifications like modifications in the diet have shown small changes. Diet in MS is a key factor given that it can provide vitamin D supplementation and it can improve fatigue and comorbidities.

Keywords: Multiple Sclerosis; Cognitive impairment; Vitamin D; Diet; Gut microbiote; Demyelinating; autoimmune disease

Abbreviations: MS: Multiple Sclerosis; RRMS: Relapsing-Remitting Multiple Sclerosis; CIS: Clinically Isolated Syndrome; CNS: Central nervous system

Introduction

Cognitive problems are present in Multiple Sclerosis (MS) in 40-65% of cases [1]. It can appear early on the disease in preclinical cases or in advanced stages. It is more prevalent in the relapsing-remitting (RRSM) form of MS than in the Clinically isolated syndrome [2].

Cognitive impairment in MS is characterized by slowing in the processing speed and in later stages episodic and visuo-spatial memory as well as complex attention are affected [2]. It impairs quality of life as it complicates activities of daily living social and family situation. Furthermore, it has been associated to a worse prognosis of the disease [3].

Factors that have been related to cognitive abnormalities are: depression and anxiety, fatigue, the degree of lesions seen in MRI and progression and long duration of the disease [3]. Other factors that could accelerate cognitive decline are: environmental such as diet, vascular lesions, comorbidities, hereditary factors, lower physical activity and a low cognitive reserve [3, 4].

Diet has a particular importance in MS as not only has it been key in cognitive impairment due to other diseases but in MS particularly, in previous studies there has been evidence of the relationship between MS and vitamin D. Newer studies have

also commented on the possible relationship of other vitamins, specific diets and gut microbiota and MS.

Multiple Sclerosis

Multiple Sclerosis is a chronic autoimmune inflammatory disease of the Central Nervous System (CNS). It is characterized by demyelination of the brain, spinal cord and optic nerves. It has different presentations beginning with the clinically isolated syndrome, in which there has only been one event, RRSM, with more than one event with relapses and the progressive forms of the disease where there are no relapses: Primary and secondary progressive MS [5].

Multiple Sclerosis can have various manifestations like visual impairment, ataxia, hemiparesis, sensory abnormalities, autonomic and cognitive impairment. Some of these symptoms can be improved with pharmacologic interventions nevertheless cognitive impairment has not shown promising results with medication. Cognitive impairment is paramount given the effect on quality of life and the worse prognosis of the disease [3].

Vitamin D and Multiple Sclerosis

Vitamin D has been associated to Multiple Sclerosis for several years now. Vitamin D has been described as essential

for bone homeostasis yet it has an important role in regulation of immunity specifically in the CNS, where vitamin D receptors have been found in glial cells. It is a factor that not only increases the risk of presenting the disease but in patients with MS with low vitamin D levels makes them prone to relapses and a faster disease progression. In a study by Darwish et al in 2017, serum levels of 25 hydroxyvitamin D were measured in patients with MS and cognitive impairment with low levels. Cognitive testing was done at baseline and 3 months after vitamin D replacement with improvement seen in cognitive testing [6,7].

The daily requirements for vitamin D are of 600-800 IU/day according to the Institute of Medicine. Vitamin D can be found in the diet in mushrooms, egg yolk, dairy products and fatty fish. It is noteworthy, that diet can be helpful with vitamin D deficiency, still it only provides up to 400IU a day while sun exposure in a summer day can produce up to 10,000 IU of vitamin D. Oral supplementation can also be given in cases where the previous cannot be reached [6].

Other Vitamins

In addition to vitamin D, other vitamins have been involved in MS pathophysiology. Vitamin B complex has been described formerly in different neurologic conditions as it is known to have a role in remyelination. Thiamine (vitamin B1) in low levels causes depression and fatigue. In one study, the increase of consumption of thiamine in the diet was correlated to a decrease in depression, cognition was not studied in this article [8]. Niacin (vitamin 3) has demonstrated remyelination in mouse models and complex B at high doses was beneficial in a small pilot study regarding visual affection in Multiple Sclerosis. Vitamin B12 has been found at normal levels in patients with MS although more studies are required. There are no studies on vitamin B complex that have included cognition as a variable [9,10,11].

Vitamin K-dependent gene GAS 6 (Growth arrest specific gene 6) is known to assist in remyelination via oligodendrocytes as it has anti-apoptotic properties although studies have been done in murine models [12].

Specific Diets

Diet has been shown to improve neuroinflammation and mitochondrial dysfunction as well as partially preventing cognitive decline in neurologic diseases specially in cognitive conditions. Based on this premise, specific diets have been studied in MS: Caloric restriction, Mediterranean diet, low-fat diet and Ketogenic diet [13].

A study with caloric restriction followed by the Mediterranean diet revealed subjective improvement in memory and attention. Another cross-sectional study done with Mediterranean diet had similar findings [13]. Small studies in Caloric restriction diets have been done in the context of abnormal gut microbiome in MS. These have evidenced improvement in metabolome [14].

Low-fat diets have shown improvement in fatigue and metabolic biomarkers while not in relapses or EDSS score [15]. Hydration has also been linked to increased fatigue [16].

The Ketogenic diet in MS is currently in an ongoing trial in Berlin, based on a previous mouse model that showed decreased disease activity, remyelination and improvement in attention and memory [17].

Preventive Measures

Pharmacologic treatment like donepezil has not shown any improvement in cognitive decline due to MS [18]. It is important however, to treat other comorbidities if present such as: fatigue, depression and anxiety, which can worsen cognition. Supportive therapy should be given for their daily activities by occupational therapists and if required, speech therapists [19]. It is advisable to measure the vitamin D levels yet no supplementation of other vitamins is recommended at the moment. Regarding the diet, high body mass and diets high in salt and fats with limited physical activity increase cognitive decline and in patients with MS there is an increased risk of fatigue. Therefore, although further studies are required it is advisable to follow a balanced diet.

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DOI: [10.19080/GJIDD.2021.08.555735](https://doi.org/10.19080/GJIDD.2021.08.555735)

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