A Case Control Study: Vitamin D Status and Sun Exposure in Multiple Sclerosis

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Abstract

Background: Vitamin D - as an environmental factor - may play a role in the etiology of Multiple sclerosis (MS). Vitamin D intake and serum levels of 25 (OH) Vitamin D were compared between MS patients and healthy individuals.

Materials and methods: In this case-control study, 168 MS patients (cases) and 168 age and sex-matched apparently healthy subjects (controls) were studied in East Azerbaijan province in Iran completed the study. A validated food frequency questionnaire was completed for each subject and serum 25 (OH) D levels were assessed using Chemiluminescence Competitive Immunoassay (CLIA).

Results: There were no significant differences in weekly frequency consumption of fats and oils between the groups. Weekly frequency consumption of beef, lamb, minced meat, cream cheese, dairy products (low-fat milk, yoghurt, ice cream (pasteurized and traditional ice cream), cream, drinking chocolate milk, milk fat and curd as well as hamburger, salami, sausage and fresh mushroom in MS patients were significantly less than healthy subjects (P < 0.05). Vitamin D deficiency (<10 ng/ml) in MS patients was significantly more common than the controls (P = 0.042).

Discussion: Severe deficiency of serum vitamin D and low consumption of vitamin D - rich foods were found among MS patients and nutrition education and/or vitamin D supplementation appears to be required.

Keywords: Multiple sclerosis; Diet; Vitamin D; 25(OH)D

Introduction

Multiple sclerosis (MS) is a chronic, inflammatory and neurodegenerative disease of the central nervous system (CNS). MS is three times more common in women than men that might be related to lifestyle factors or the effect of estrogen on increasing cytokine production in females [1]. The etiology of MS is not yet fully understood, however, studies have shown that environmental and genetic factors are involved in its incidence [2,3]. Some environmental factors such as smoking [4], infection to Epstein Barr Virus [5], disorders in inflammatory cytokines (IL2, TNFα, INFγ) [6,7], high geographical latitude [8,9], and insufficiency of vitamin D [4] seems to be more important.

The onset of MS is commonly observed in ages between 20 to 40 years and its symptoms occur depend on the site of the lesions [10-12]. There is no strong evidence that directly demonstrate the role of vitamin D in MS treatment, however, clinical evidence suggests that vitamin D in MS patients has a supporting role and recent epidemiologic studies have confirmed it [13]. Vitamin D as a steroid hormone in the skin, kidneys and liver turns to its active metabolite, i.e., Calcitroel. This metabolite has been detected in tissues with specific receptors of the CNS such as skin, muscle, neutrophils, growth factors and neurotransmitters and therefore, it may play a role in inflammation. Although there is no evidence directly demonstrating the influence of vitamin D in the treatment of MS. Recent immunological studies have shown that vitamin D supplements (oral/injection) could ameliorate clinical symptoms of MS. It seems that a high serum level of vitamin D (>50 nm) could reduce the level of disability among MS patients [14,15]. In a randomized controlled trial, the effect of a 96-week period vitamin D supplementation (20,000 IU of vitamin D3 weekly) among MS patients showed that serum 25(OH) D levels were above 50 nmol/l in winter at the end of the study [16]. There are limited studies in Iran regarding dietary pattern of vitamin D and most of the studies had low sample size. For example, studies in Ahwaz and Isfahan have demonstrated that serum 25(OH) D deficiency (<30 nmol/L) were observed not only in MS patients but also in healthy individuals [17,18]. The prevalence and incidence of MS in the Middle East, especially in the IRAN, represents an increase in MS compared to other regions. Recent descriptive studies in different parts of the country have demonstrated increased frequency of the disease [19,20]. East Azerbaijan province is located in the North West part of Iran [21] with higher latitude (38, 06º) compared to central and southern provinces of Iran such as Isfahan (32, 65º) and Ahvaz (31, 24º). Vitamin D deficiency seems to be a common problem in this region although exact statistics is not available in these parts. MS incidence in East Azerbaijanis about 27.7/100,000 people in 2011(42 indicating much higher prevalence than the central and north parts of the Iran with MS prevalence around 35.5, 20.1/ 100000 people respectively [22-24]. As MS prevalence is increasing in Iran and there is limited evidence, particularly in East Azerbaijan because of its latitude as well as some cultural factors such skin color, this study aimed to compare dietary vitamin D intake and serum levels of 25(OH) D between MS patients and apparently healthy individuals.

Materials and Methods

Study design

This case-control study was conducted between January-February
2012 on 168 MS patients (aged 20-50 yrs) registered in MS Society of East Azerbaijan province and 168 apparently healthy subjects matched for age (± 5 yrs) and sex (110 females and 58 males) in Iran. MS was diagnosed based on McDonald standards as well as brain Magnetic Resonance Imaging (MRI) findings [25,26]. Patients with Expanded Disability Scale Score (EDSS) less than 6 were included in this study. The inclusion criteria were: willingness to participate in the study, to complete 3-day food recall, ability and tendency to give a blood sample and test and being geographically resident in the studied region.

**Assessment of sunlight exposure, dietary and serum vitamin D**

The individuals' characteristics were obtained using questionnaire and face to face interview. Dietary data was collected using a 43-food item semi-quantitative food frequency questionnaire (FFQ) including four food groups (meats, dairy products, oils and fats and miscellaneous foods and then, weekly frequency consumption of foods and food groups were estimated. A 3-day food recall questionnaire was also completed for each subject (two working days and one holiday) through interview or telephone and was used to estimate nutrient intakes using Nutritionist IV software and mean of vitamin D intake was compared with the recommended daily dietary allowances (RDA) values. Daily intake of vitamin D was classified into "severe deficiency" (<0.5 mcg), "deficiency" (5.1-10 mcg), "adequate" (10.1-15 mcg), and "high intake" (>15 mcg) [27,28]. After 12-14 hours fasting, 5 ml venous blood sample was taken from the cephalic vein and serum 25 (OH) D levels was assessed using Chemiluminescence Competitive Immunoassay (CLIA) method. Serum vitamin D levels were categorized into: "severe deficiency" (<10 ng/ml), "deficiency" (10-29 ng/ml), "normal" (30-100 ng/ml), "toxicity" (>30 ng/ml) [29].

A general information questionnaire was used to determine the sunlight exposure time for all subjects. In this questioner exposure to sunlight that least 20 minutes of exposure to sunlight was considered in both groups. All subjects undergo a fasting blood sampling, 5 ml venous blood sample (8-10 hours) was taken.

**Statistical tests**

For data analysis, SPSS Software 16² was applied. Distribution of quantitative variables was assessed using Kolmogorov-Smirnov test. Quantitative and qualitative variables were presented as mean ± SD and n (%), respectively. Comparison in mean dietary intake of vitamin D between the groups was performed using Mann Whitney U- and Wilcoxon tests. P less than 0.05 were considered as statistically significant [30].

**Results**

Mean age were 29.3 ± 1.2 yrs and 27.2 ± 1.3 yrs in cases and controls, respectively. Female to male ratio was 2:1 in both groups and mean BMI of quantitative variables was assessed using Kolmogorov-Smirnov test. P less than 0.05 were considered as statistically significant [30].

Weekly frequency consumption of fats and oils were not significantly different between the groups. However, weekly frequency consumption of meat group including beef, lamb, ground meat, and cream cheese (P < 0.05) and dairy products including low-fat milk, yoghurt, ice cream, pasteurized and traditional ice cream, cream, drinking chocolate milk, and milk fat curd in controls were significantly more than in MS patients. The control subjects consumed more frequently miscellaneous foods including hamburger, salami, sausage and fresh mushrooms than MS patients (P < 0.05).

After controlling the effects of age, sex, job, education level and the amount of sunlight as confounding factors significant different between minced meat, low-fat milk and fresh mushroom were showed in two groups (P < 0.05) and their intake were in patients less than healthy individuals.

Our results showed severe deficiency of vitamin D intake (0-5 mcg) exists in both group and The proportion of those with low dietary intake of vitamin D (0-5 mcg) was significantly higher among MS patients than the controls (p = 0.041) (Table 2).

**Table 2: Dietary Vitamin D status.**

<table>
<thead>
<tr>
<th>Daily intake of vitamin D (mcg)</th>
<th>Case</th>
<th>Control</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-0</td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td>10-5.1</td>
<td>79 (47.2)</td>
<td>92 (54.8)</td>
<td>0.883</td>
</tr>
<tr>
<td>15-10.1</td>
<td>43 (25.5)</td>
<td>50 (29.6)</td>
<td>0.888</td>
</tr>
<tr>
<td>&gt;15</td>
<td>10 (5.9)</td>
<td>15 (8.9)</td>
<td>0.946</td>
</tr>
</tbody>
</table>

**Figure 1:** Levels of vitamin D in two groups.

**Discussion**

Our results showed severe deficiency of vitamin D (0-5 mcg) intake exists more than three times in MS than healthy individuals.
Consumption of vitamin D-rich food including meat and dairy products were also significantly different between the cases and controls.

Other studies in Europe and America have found similar findings indicating lower dietary vitamin D intake and serum levels of 25 (OH) D in MS patients than healthy population [26-29]. Vitamin D deficiency as a risk factor for MS was first proposed over 40 years ago [29-31]. Colecalciferol (vitamin D3) is available from two sources: skin exposure to ultraviolet B radiation (UVB) in sunlight and consuming vitamin D-rich foods [32,33]. The efficiency of vitamin D intake from foods is 40 - 400 units in each serving while daily exposure to sunlight in summer for 15–20 min can provide approximately 10,000 units per minute [34]. Vitamin D intake depends on culture, age, sex, sunlight exposure, business, cloths and food pattern [35-37]. Vitamin D is available from dark and fatty fish (e.g., salmon), fortified foods (e.g., milk and juices) and vitamin supplements (Colecalciferol).

In Japan, results of the study among pre- and post- menopausal women showed fish consumption more than 4 servings/week, increased concentration of 25 (OH) D significantly than the people who intake 1-3 servings/week [38]. Effect of nutrient in MS incidence was firstly proposed by Swank et al 60 years ago and reported that high intake of fat and margarine were associated with high incidence of MS in the studied population [35]. Fish consumption is high in Norway whereas MS incidence is lower than other countries with less fish consumption [39]. The results of a prospective study on 173 nurses, vitamin D intake was estimated from 1980-2000 using a comprehensive semi quantitative FFQ revealed that decreased in MS incidence parallel to increasing vitamin D intake (p =0.03) and serum vitamin D concentration [40]. In another prospective study on 200,000 women in the USA, MS incidence was 41% lower among women who taking 400 IU/day or more from vitamin D supplements compared with those who did not take the supplements [41]. Although, it seems that dietary vitamin D intake varies in countries, consumption of vitamin D supplements (>400 IU/day) is associated with a decrease in MS risk [32]. Moreover, findings of previous epidemiological studies have revealed an increased MS risk among individuals with low serum vitamin D concentrations [37]. However, a study in Iran failed to confirm any association between egg and fish intake with circulating 25 (OH) D level among MS patients [16].

In conclusion, the present study showed that consumption of vitamin D rich foods and serum vitamin D level in MS patient are lower than the healthy subjects and therefore, nutrition education and/or vitamin D supplementation appears to be necessary.

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References


