ORIGINAL ARTICLE

Cow's milk allergy in multiple sclerosis patients

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Background: Exposure to some environmental agent such as different nutrition and contact with allergens may have a role in developing multiple sclerosis (MS). The present study was aimed to evaluate the cow's milk allergy (CMA) in MS patients compared to healthy controls. **Materials and Methods:** Between March 2012 and July 2012, 48 MS patients were selected and compared with 48 healthy subjectsto assess the frequency of CMA in MS patients compared to healthy control.Cow's milk specific immunoglobin E (IgE) was determined by Immuno CAP. Sex and the frequency of CMA were compared between study groups by Chi-square test. **Results:** Total of 96 subjects were assessed (22% male and 78% female). The mean age of the study subjects was 30.8 ± 6.6 years. Mean age of case and control groups was 30.7 (±6.9) versus 30.9 ± 6.3, respectively (*P* value = 0.83). There were no detection of cow's milk specific IgE in serum of MS patients and healthy subjects. **Conclusion:** There was no difference between MS and healthy subjects regarding CMA.

Key words: Allergy, cow's milk, multiple sclerosis

INTRODUCTION

Multiple sclerosis (MS) is achronic inflammatory demyelinating disease of the central nervous system (CNS)[1] and it is one among the common causes of neurological disability in young adults especially, women.[2] Autoimmune processes due to defects in regulatory T cells and failing of suppression auto-reactive CD4+ and CD8+ cells is suggested have a role in pathogenesis of disease.[3]

Although, the etiology of MS is unknown, there are some evidences for convolution with both genetic and environmental influences on susceptibility. Relative vitamin D deficiency,[4,5] Epstein-Barr virus,[6] and smoking[7] are among environmental factors that all have been associated with increased susceptibility to MS. Nutrition is another environmental factor thatpossibly involved in pathogenesis of MS.[8] Furthermore, dietary factors are frequently mentioned as a possible cause, there are very few clinical trials based on specific diets or dietary supplements in MS and there is no evidence in this respect.[9] Higher intake of different food compounds were considered to be associated with increased risk of MS[9] such as sweets,[10] alcohol,[11-13] smoked meat products,[10] coffee, tea,[11] and yet, none of these data were approved by subsequent studies. In 1991, in a study, it has been reported that dietary factors or food allergies may be among major causes of MS beginning and progression.[14] In the other hand, vitamin D has been implicated as being a risk-factor in MS,[15-17] and it is reported that decreased levels of 25-hydroxyvitamin D are associated with an increased risk to develop MS.[18] Furthermore, the totality of evidence for a protective role of vitamin D in MS has been supposed strong enough by some to warrant recommending vitamin D supplementation to people with MS.[19] Cow's milk allergy (CMA) has an indirect potential to cause 25-hydroxyvitamin D deficiency from affected individuals tend to avoid dairy of cow's milk products.[20]

In infancy, cow's milkis the most frequently encountered dietary allergen, and the incidence of CMA varies with age.[21] In infants and adult the reported prevalence of CMA varies between studies; however, it is clear that CMA is common allergy in early childhood, with a prevalence of 2-6%,[22] and decreases with age.[23]

It is believed that exposure to some environmental agent that occurs before puberty may begin autoimmune process and pre-dispose a genetically susceptible person to develop MS later on. Based on this fact, the hypothesis of a link between milk consumption and MS has been considered since many years ago and epidemiological studies were carried out to support this correlation.[24]

It is considered that improvement of immunological defenses effect on treatment of MS patients, therefore, detection of allergens and elimination of them from the diet could decrease disability of patients,

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The present study was aimed to evaluate the CMA in MS patients compared to healthy controls.

MATERIALS AND METHODS

Between March 2012 and July 2012, 48 MS patients (referring to MS clinic of the referral universityhospital in Isfahan) were selected and compared with 48 healthy subjects (among patients' companions and acquaintances as control group) to assess the association between CMA and MS. MS patients were diagnosed to definitely develop MS according to the McDonald Criteria.[25] Patients were eligible if they had not received corticosteroids during last month and immunosuppressants over the last 3 months. This study was investigated and approved by the ethics committee at the Isfahan University of Medical Sciences and all subjects were explained about the aim and the purposes of the study and written informed consent was obtained from all of them.

Controls were matched with the patients in regard to age and gender. To determine the allergen-specific immunoglobin E (IgE) of cow's milk, blood samples were taken from both groups of subjects and serum samples were transferred to the laboratory of Immunology.

ImmunoCAP (Phadia, Uppsala, Sweden) was used for allergen-specific IgE antibody in the serum of the subjects to be obtained. This technique is approved by Food and Drug Administration in US and has high-sensitivity and many good features[26-28] also in Iran are applicable only in the Asthma and Allergy Research Institute, Tehran University of Medical Sciences. Moreover, specific IgE antibody against cow's milk was determined and applying statistical techniques, calculations were performed and results were extracted.

Data are presented as means ± standard deviation or number (%) as appropriate. Independent sample *t*-test was used to compare age between groups. Furthermore, sex and the frequency of CMA were compared between study groups by Chi-square test. All analysis was carried out by the Statistical Package for the Social Sciences (SPSS)-20 and statistical significance was accepted at $P < 0.05$.

RESULTS

A total of 96 subjects were assessed and results of all blood samples were analyzed. On the total subjects, 22% were male and 78% were female and the mean age of the study subjects was 30.8 ± 6.6 years. Table 1 shows the comparison of age, gender, and the frequency of CMA between study groups. As shown mean age of in case and control groups was similar and there was no statistical significant difference between groups (30.7 ± 6.9 vs. 30.9 ± 6.3 respectively, *P* value = 0.83). Of 22 male subjects, 50% were MS patients and 50% were controls. There was no significant difference between study groups in regard to gender composition. Results of CAP technique to determined allergen-specific IgE antibody against cow's milk in MS patients and healthy subjects showed that, there was no any positive CMA in these subjects and there was no difference between MS patients and healthy subjects.

Table 1: Comparison of subjects characteristics and results of cow's milk allergy between study groups

	Multiple sclerosispatients (*n*=48)	Controls (*n*=48)	*P* value
Age			
Year	30.7±6.9	30.9±6.3	0.83†
Sex			
Male	11 (22.9)	11 (22.9)	1*
Female	37 (77.1)	37 (77.1)	
Cow's milk allergy			
Yes	0	0	1*
No	48 (100)	48 (100)	

Data presented as mean±standard deviation and number (percent). *P* values calculated by †independent sample *t*-test and *Chi-square test

DISCUSSION

Since many years ago the effect of diet such as fat intake in MS has been postulated.[29] There is a higher extent consumption of saturated fat, dairy products, and cornflakes (cereals) and a decrease in the consumption of unsaturated fat in area with high prevalence of MS.[29]

Though, the findings of these studieswere not confirmed by a large number of case-control studies, epidemiological studies have proposed the association between MS prevalence and animal fat consumption.[11-13] Because MS is believed to have an autoimmune basis, many factors such as dietary can induce autoimmunity and myelin breakdown by molecular mimicry.[30]

It seems that molecular mimicry may disrupt immunological self-tolerance to CNS myelin antigens in genetically susceptible individuals. CMA is one of the most common food allergen in infancy. It seems that immune system identifies some of proteins of milk as harmful and makes IgE antibodies to neutralize it. IgE antibodies recognize these proteins in next contact and signal the immune system to release some chemicals.[31]

Therefore, cow's milk as a dietary protein has potential molecular mimicry with myelin autoantigens and may induce autoimmune process, so consumption of milk in MS patients may have a possible role in progression or relapse of disease. Furthermore, as mentioned earlier, vitamin D has been implicated as being a risk-factor in MS patients[18] and CMA transmits nutritional implications as affected individuals have a tendency to

evade dairy products and have been shown to be lacking in 25-hydroxyvitamin D.[20]

Measurement of specific IgE confirmed an IgE-mediated sensitivity to cow's milk and is a prognostic marker for persistence of CMA.[31]

In present study, we evaluated the cow's milk IgE to find allergy to milk in MS patients compare to control as a marker of persistence CMA. The result of study did not show positive CMA in MS group and no difference between MS patients and control subjects.

Our findings was similar to result of Ramagopalan *et al*. study.[32] Ramagopalan, in a population-based cohort in 2010, investigated whether or not childhood CMA influences the subsequent risk to develop MS.They collected data by telephone interview from mothers of 6638 MS index cases and 2509 spouse controls in Canada and compared the frequency of CMA between index cases and controls and could not find any significant differences. Therefore, author concluded that childhood CMA does not appear to be a risk-factor for MS.

Another study suggested that factors of liquid cow milk influence on the clinical appearance of MS.[25]

Although, medical interest in the influence of diet on the rate and severity of MS disease were carried out,[33] as our best knowledge, there are few studies in food allergens and MS, so further studies are suggested to be carried out to investigate food allergens, in a large number of MS patients and healthy individuals based on individuals recall, then positive responses assess using advanced technique and results compared between MS patients and healthy subjects.

In summary, findings of our study investigated that there is no difference between subjects developing MS and healthy subjects regarding CMA and we could not find any association between CMA and MS.

CONCLUSION

This study evaluated the frequency distribution of cow milk allergy in MS patients compared to healthy controls. Although, there was no significant difference between two groups, the small sample size of MS patients may effect on the association of this hypothesis.

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