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*Original Article*

# Correlation of sensitization to food allergens in Iranian patients with migraine and tension headaches

Marzieh Heidarzadeh Arani[1], Ahmad Talebian[1], Hossein Akbari[2], Alireza Ghannadian[1], Reihane Sharif[3], Hossein Motedayyen[4]

*[1]Pediatric Department, School of Medicine, Kashan University of Medical Sciences, Kashan, Iran; [2]Department of Biostatistics and Epidemiology, School of Health, Kashan University of Medical Sciences, Kashan, Iran; [3]Health Information Management Research Center, Department of Health Information Management & Technology, School of Allied Health Professions, Kashan University of Medical Sciences, Kashan, Iran; [4]Autoimmune Diseases Research Center, Kashan University of Medical Sciences, Kashan, Iran*

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**Abstract:** Objectives: Headache is one of the most common neurological disorders around the world. Previous studies have proposed associations of food allergies with headaches. Therefore, this study evaluated the frequency of sensitization to food allergens in patients with migraine and tension headaches and their correlations with these disorders. Methods: The study subjects consisted of 20 patients with migraine headache and 20 subjects with tension headache. Headache disorders were confirmed by a specialist. Food allergen sensitization was diagnosed by skin prick test (SPT) or radioallergosorbent test (RAST), clinical history, and physical examination. Results: There was no significant difference in age and gender between patients with migraine and tension headaches. Other results showed sensitization to food allergens, such as egg, wheat, fish, banana, orange, and soybean, in patients with migraine headache was similar to those in subjects with tension headache. However, patients with migraine headache significantly differed from individuals with tension headache in allergic responses to tree nut (P=0.047), peanut (P=0.028), and cow's milk (P=0.044). Conclusion: The results of this study showed that sensitization to food allergens may relate to migraine headache which their diagnosis can help to better control and manage the disease.

**Keywords:** Food allergen sensitization, migraine headache, tension headache

## Background

Headache is one of the most common neurological disorders in childhood and adolescence. Its prevalence is estimated approximately 10-20% in school children, while it increases up to 35% with the age increase from 13 to 17 years [1]. One of the most common headaches in children is migraine headache, which the average prevalence in children and adolescents is 9.1% [2]. Migraine headache is mostly severe, unilateral, and throbbing in nature [3]. It is usually accompanied by nausea, vomiting, and photo - or phonophobia [4]. Several agents are responsible for enhancing its prevalence, including stress, sleep disorders, dietary, environmental, and hormonal factors [5].

Although the starting mechanisms involved in migraine attacks are not completely understood, activation of pain factors have the key roles in promoting migraine pain [6]. Mast cells and granular immune cells are frequently observed in migraine pain location [7]. Allergens can stimulate the afferent fibers of the vagus nerve through releasing inflammatory mediators from dura mater mast cells [6]. It is reported that released vasodilator substances and cytokines from mast cells and other immune cells have important roles in the vasodilator phase of a migraine attack. Furthermore, IgE and histamine-mediated mechanisms may have the roles in the relationship between allergy and migraine [8].

Tension headache, as the most common type of headache, is characterized by pressing/tightening quality, bilateral location, and commonly milder intensity than migraine. The nausea, vomiting, photo- and phonophobia are rarely

observed in tension headache [9]. Although its etiology is not exactly identified yet, there are some reports pointing to it may relate to the activations of hyperexcitable peripheral afferent neurons and muscle tension in the head and neck [3]. It is reported that food may be considered as a trigger in the attacks of migraine and tension headaches [5]. Some studies have mentioned to cocktails, alcoholic drinks, chocolate, and cheese as the most frequent triggers of headache [10, 11].

Although numerous studies have indicated associations between allergies and headaches, the documents are insufficient and controversial to show these correlations. This study was therefore focused on determining whether the frequency of sensitization to food allergens in patients with migraine headache differ from those in individuals with tension headache. The correlation of food allergen sensitization with the development of these headaches was also evaluated.

## Materials and methods

### *Study populations*

The study subjects consisted of 20 patients with migraine headache (10 males and 10 females) and 20 subjects with tension headache (11 males and 9 females) who were referred to the pediatric neurology clinic of Shahid Beheshti hospital, Kashan, Iran from September 2018 to March 2019. Headache disorders were diagnosed by a specialist according to the International Classification of Headache Disorders (ICHD-3) criteria [3]. Exclusion criteria included: 1) patients with histories of allergy, chronic systemic diseases, and other neurologic conditions, which may contribute to headaches, such as cerebral palsy, stroke, trigeminal neuralgia, and seizure disorder; 2) uses of $H_1$ and $H_2$ receptor blockers, steroids, anti-leukotrienes, and other anti-allergy medicines; 3) a positive response to 2 of 6 questions regarding allergic symptoms (rhinorrhea, nasal congestion, snoring or mouth breathing, sneezing, itchy/watery eyes, and throat drainage). Inclusion criteria were: 1) patients with migraine and tension headaches; 2) individuals aged 5 to 17 years; 3) subjects without histories of allergic and other inflammatory disorders; 3) no treatment with drugs affecting immune reactions. The study was approved by the Ethics Committee of Kashan University of Medical Sciences (IR.KAUMS.MEDNT.REC.1398.020) and written informed consent was collected form all participants and legally authorized representatives of individuals prior to study initiation.

### *Diagnosis of food allergen sensitization*

Sensitization to food allergens was diagnosed based on skin prick test (SPT) or radioallergosorbent test (RAST), clinical history, and physical examination. The physical examination did not show findings consistent with allergic reactions (nasal crease, allergic shiners, nasal crease, pale or boggy turbinates, or mucous discharge in the nasal passage). SPT was performed by an allergy and immunology specialist in an allergy clinic. Some food allergens were used to diagnosis sensitization to food allergens, including tree nut, peanut, wheat, soybean, cow's milk, fish, banana, orange, and egg. All allergens were purchased from Stallergenes Greer (Antony Cedex, France). Standard doses of allergen extracts were used according to a standard technique [12]. Briefly, the marks were made on the skin of the anterior part of the forearm after cleaning with 70% alcohol. A small drop of each allergen was placed on the skin. Some scratches were gently made on the surface of the skin under each drop to penetrate the allergens into the skin. The results were evaluated after 15 to 20 minutes. Marked erythema with induration more than 3 mm diameter served as sensitization to allergens. Isotonic NaCl and histamine chloride mixed with 0.9% saline solution were used as negative and positive controls, respectively. Specific IgE antibody was analyzed by the RAST technique according to the manufacturer's protocols (ImmunoCap, Pharmacia Diagnostics, Piscataway, NJ, USA).

### *Statistical analysis*

Data were analyzed using a SPSS software (V. 19, IBM, Chicago, IL.) and are represented as the mean ± standard deviation (SD). Fisher's exact and Chi-square tests were used to evaluate the correlations. *P* value < 0.05 was considered statistically significant.

## Results

As shown in **Table 1**, gender was not associated with headache (P=0.752). Other results revealed no significant correlation between age and headache (P=0.27).

**Table 1.** Gender and mean age of the studied groups

| Headache Type | Gender | | *P* value* | Age | | *P* value** |
|---|---|---|---|---|---|---|
| | Male | Female | | Mean | SD | |
| Migraine | 10 (50%) | 10 (50%) | 0.752 | 10.5 | 2.2 | 0.27 |
| Tension | 11 (55%) | 9 (45%) | | 11.4 | 2.8 | |

*Pearson Chi-square test. **Independent samples t-test.

**Table 2.** The frequency of sensitization to food allergens and their correlation with migraine headache

| Allergen | Headache Type | | Total | *P* value* |
|---|---|---|---|---|
| | Migraine | Tension | | |
| Orange | 3 (15%) | 2 (10%) | 5 (12.5%) | 0.621 |
| Banana | 4 (20%) | 2 (10%) | 6 (15%) | 0.661 |
| Fish | 5 (25%) | 3 (15%) | 8 (15%) | 0.695 |
| Cow's milk | 7 (35%) | 1 (5%) | 8 (20%) | 0.044 |
| Egg | 3 (15%) | 1 (5%) | 4 (10%) | 0.605 |
| Soybean | 6 (30%) | 3 (15%) | 9 (22.5%) | 0.451 |
| Tree nut | 5 (25%) | 0 (0%) | 5 (12.5%) | 0.047 |
| Peanut | 8 (40%) | 2 (10%) | 10 (25%) | 0.028 |
| Wheat | 4 (20%) | 2 (10%) | 6 (15%) | 0.661 |

*The results of Fisher exact test.

*The frequency of sensitization to food allergens and their associations with migraine and tension headaches*

Our data revealed that food allergens such as orange, banana, fish, egg, soybean, and wheat were not significantly correlated to both headache types (**Table 2**). Other results showed that migraine headache was significantly associated with sensitization to food allergens such as cow's milk, tree nuts, and peanut ($P < 0.05$, **Table 2**). However, there was no significant relationship between food allergen sensitization and tension headache (**Table 2**).

## Discussion

Migraine headache is one of the most common headaches that involves approximately 15% of the population around the world. The etiology of this disorder is not well determined yet [8]. It is shown that allergic reactions can participate in headaches through stimulating the afferent fibers of the vagus nerve [13]. Therefore, we evaluated the frequency of sensitization to some food allergens in Iranian patients with migraine and tension headaches and their possible impacts on the development of headaches.

The results of the present study revealed that there was no significant difference in allergic reactions to egg, wheat, fish, banana, and soybean allergens between patients with migraine and tension headaches. However, patients with migraine headache had a significant sensitization to peanut, cow's milk, and tree nut allergens compared to patients with tension headache.

Although there are some studies showing no significant impacts of food allergens on migraine development [14], the results of this study were consistent with numerous studies pointing to the effects of allergic foods on the occurrence of migraine attacks [15-19]. *Ku et al*. reported that there was a significant difference in migraine prevalence between patients with and without allergic rhinitis [20]. In a study conducted by *Grant et al*. it was demonstrated that some food allergens had fundamental roles in enhancing migraine attacks [15]. The most prevalent allergens were wheat (78%), orange (65%), egg (45%), tea and coffee (40%), chocolate and milk (37%), beef (35%), corn (35%), sugar (35%), yeast (35%), mushroom (35%), and pear (28%) [15]. *Monro et al*. had similar results in regard to the impacts of food allergens on the incidence of migraine attacks [21]. *Wilson et al*. evaluated 20 patients with migraine and SPT revealed the most prevalent foodstuffs related to migraine headache were wine, cheese, and chocolate [22]. *Eross et al*. revealed that the most common allergens caused headaches in 62% of the patients were grass and special trees (13%), dust (10%), particular foodstuffs (7.7%), cat and dog hairs (5.1%), and mold (2.6%) [23]. In another study on individuals with migraine, the most common food allergens aggravated migraine were egg, cheese, cow's milk, wheat, tomato, casein, pork, and bean [24]. In line with the effects of food allergens on headache, it is shown that wheat allergen increases the frequency of migraine but not its severity [25]. Previous studies have revealed that asthma occurrence was significantly higher in children who had mothers suffering from migraine and asthma than those who did not have [26]. Other studies have indicated that the migraine in mothers may act as a risk factor for developing rhinitis in their children [27].

In an attempt to discover the possible impacts of food allergens on tension headache, the relationship of food allergen sensitization with tension headache was studied. Our data revealed that no significant correlation of food allergen sensitization with tension headache, which is consistent with previous reports [5]. However, some studies have mentioned that dietary factors could be effective on the development of tension headache [10, 11]. This discrepancy could be attributed to the type of allergens and the age of the patients used to determine the association of food allergen sensitization with tension headache.

Regarding the fact that migraine and tension headaches may relate to the long-term activation of nociceptors, allergies may participate in migraine headache through releasing cytokines and vasodilators from mast cells and other immune cells in dura mater. These mediators result in vasodilation of vessels in central nerve system and activation of the trigeminal nerve afferent fibers [6, 8, 28, 29].

## Conclusion

Taken together, the results of this study along with previous studies showed that sensitization to some food allergens may relate to migraine headache which their diagnosis can help to better control and manage the disease. However, there are some limitations related to the present study, including a lack of evaluation of the impacts of other food allergens on migraine and tension headaches and elimination diets, such as the elimination of food allergens reported in this study from the diet, to determine their effects on migraine headache. Therefore, these limitations should be studied in future studies with larger sample sizes.

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## Disclosure of conflict of interest

None.

**Address correspondence to:** Dr. Hossein Motedayyen, Autoimmune Diseases Research Center, Shahid Beheshti Hospital, Kashan University of Medical Sciences, 5th Kilometer of Ravand Road, Kashan, Iran. ORCID: 0000-0002-4863-1771; Fax: 00983155578011; E-mail: hmotedayyen@gmail.com; Reihane Sharif, Health Information Management Research Center, Department of Health Information Management and Technology, School of Allied Health Professions, Kashan University of Medical Sciences, 5th Kilometer of Ravand Road, Kashan, Iran. E-mail: Fr.sharif@yahoo.com

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