

A comparative study of celiac disease in children with migraine headache and a normal control group

Soroor INALOO¹, Seyed Mohsen DEGHANI^{2,3}, Fahimeh FARZADI², Mahmood HAGHIGHAT²,
 Mohammad Hadi IMANIEH^{2,3}

¹Neuroscience, ²Gastroenterohepatology and ³Transplant Research Centers, Shiraz University of Medical Sciences, Shiraz, Iran

Background/aims: Migraine headache is one of the most frequent types of headache in children in which multiple factors, including environmental and genetic, are involved. Celiac disease is an autoimmune-mediated disease with intolerance to gluten. The clinical spectrum of celiac disease is wide. Patients may present with malabsorption symptoms or extra-intestinal involvement, or can be totally asymptomatic. The association of migraine headache and celiac disease is not well known. The aim of this study was to assess the prevalence of celiac disease in children with migraine headache, in order to detect any relationship between them. **Methods:** A total of 100 patients with migraine headache according to the International Headache Society criteria were enrolled in the study. 1500 children without history of headache or other medical diseases participating in another study for detection of the prevalence of celiac disease were selected in this study as a control group. Serum total IgA and anti-tissue transglutaminase IgA (anti-tTGA) antibodies were measured. In cases with positive serologic tests, duodenal biopsy was performed for confirmation of celiac disease. **Results:** Two of 100 patients (2%) were found to have positive serologic tests for celiac disease, compared with 30 of 1500 children (2%) in the control group who had celiac disease. **Conclusions:** The results of this study showed that the prevalence of celiac disease was not higher in patients with migraine compared with the control group. Therefore, diagnostic tests for celiac disease are not necessary as a part of the management of migraine headache.

Key words: Celiac disease, pediatric, prevalence

Migren başağrısı olan ve sağlıklı çocuklarda çölyak hastalığı sıklığının karşılaştırılması

Amaç: Migren başağrısı; patogenezinde birçok çevresel ve genetik faktörün sorumlu olduğu, çocuklarda görülen başağrısı tipleri arasında en sık karşılaşılanıdır. Çölyak hastalığı glutene intolerans ile karakterize immun sistem aracılığı ile ortaya çıkan bir tablodur. Çölyak hastalığının klinik spektrumu geniştir. Hastalar, malabsorbsiyon veya ekstraintestinal tutulum ile prezente olabilirler veya tamamiyle asemptomatik olabilirler. Migren tipi baş ağrısı ile çölyak hastalığı arasındaki ilişki iyi bilinmemektedir. Bu çalışmanın amacı migren tipi baş ağrısı olan çocuklarda çölyak hastalığı prevalansının ortaya konulması ve aralarındaki ilişkinin tespit edilmesidir. **Yöntem:** Uluslararası Başağrısı Derneği kriterlerine göre migren başağrısı olan toplam 100 hasta çalışmaya dahil edildi. Çölyak hastalığının çocuklardaki sıklığının tespit edilmesi amacı ile başka bir araştırmaya katılmış olan başağrısı veya başka sağlık sorunu olmayan 1500 çocuk kontrol grubu olarak seçildi. Serum toplam IgA ve doku transglutaminaz IgA (Anti-tTGA) antikorları düzeyleri ölçüldü. **Bulgular:** Yüz hastanın ikisinde (%2) çölyak hastalığı için serolojik olarak pozitif bulundu, buna karşılık 1500 kontrolün 30'unda (%2) çölyak hastalığı bulunmaktaydı. **Sonuç:** Bu çalışmanın sonucu göstermiştir ki, migren hastalarında çölyak hastalığı sıklığı kontrol grubuna göre artmış değildir. Bu durumda migren başağrısının değerlendirilmesinde çölyak hastalığı için tanısal testlerin gerçekleştirilmesine gerek yoktur.

Anahtar kelimeler: Çölyak hastalığı, pediatric, prevalans

INTRODUCTION

Migraine is a chronic, progressive and debilitating disorder that has important effects on people's li-

ves (1). This disorder is the most important and frequent type of headache in children. Accurate di-

Address for correspondence: Seyed Mohsen DEGHANI
 Associate Professor of Pediatric Gastroenterology,
 Shiraz Transplant Research Center, Gastroenterohepatology Research
 Center, Shiraz University of Medical Sciences,
 Shiraz, 71937-11351, Iran
 Phone: + 98 711 626 17 75 • Fax: + 98 711 647 42 98
 E-mail: dehghanism@sums.ac.ir

Manuscript received: 16.02.2010 **Accepted:** 12.04.2010

Turk J Gastroenterol 2011; 22 (1): 32-35
 doi: 10.4318/tjg.2011.0153

agnosis and proper treatment during childhood can diminish the duration of disease and improve the quality of life (2). Detection of migraine headache in children can be a particular challenge (3). Through childhood, clinical presentations of migraine vary because this disease may be expressed differently. In 1997, the International Headache Society (IHS) explained the classification and diagnostic criteria for migraine headache in children younger than 15 years (4).

Celiac disease (CD) is an autoimmune enteropathy due to permanent intolerance to gluten-containing cereals in some people who are genetically susceptible (5). The classic presentations of CD are diarrhea, weight loss, failure to thrive, and abdominal distention, but many patients, if not most, present with subtle symptoms without classic manifestation of malabsorption syndrome or even diarrhea. This form of CD is typical (5,6). With advancements in serologic tests, CD is more commonly realized than before.

According to the frequency of the two conditions (CD and migraine headache), the relationship of a neurologic disorder, i.e. migraine, with untreated CD is difficult to ascertain, but a few studies have been conducted to detect this relationship. These studies were performed mainly in adult celiac patients and determined a prevalence of migraine headache of about 18-21% (7). The aim of this study was to determine the association of these two conditions by detection of the prevalence of CD among children with migraine headache.

MATERIALS AND METHODS

A total of 100 children with migraine headache (59 male, 41 female) with an age range of 5-18 years (mean age: 10.6 ± 2.8 years) introduced by the Pediatric Neurology Clinic, affiliated with Shiraz University of Medical Sciences, were enrolled in this study. Diagnosis of migraine headache was according to the IHS criteria. Informed consent was obtained from each patient or their parents, and this study was approved by the Ethics Committee. For every patient, a questionnaire was prepared to explain the clinical characteristics of the migraine disease. Each patient was questioned about the duration of headache, duration of attack (hour), intensity (mild, moderate, severe), frequency (times per month), location of pain, the presence of aura, and associated autonomic features (nausea, vomiting, photophobia).

The general and neurologic physical examinations were done by a pediatric neurologist, and the child's weight and height were recorded. Then, these patients underwent laboratory testing to measure the concentration of serum total immunoglobulin (Ig)A and anti-tissue transglutaminase IgA (anti-tTGA) antibodies. Because of the co-occurrence of IgA deficiency with CD, it may be acceptable to measure total IgA level to determine the cases with IgA deficiency in order to reduce the possibility of false-negative results. Total IgA by SRID (single radial immunodiffusion) and anti-tTGA antibodies by ELISA (Diagnostics GmbH Wendelsheim- micro from ring 2) were assessed. Titers above 18 u/ml were considered to be positive. The cases with positive serology tests were referred to a pediatric gastroenterologist to obtain duodenal biopsy by endoscopy. Definite diagnosis of CD was based on histologic criteria.

A total of 1500 children without a history of headache or other medical diseases (825 male, 675 female; mean age: 9.5 ± 1.3 years) participating in another study for detection of the prevalence of CD were selected as a control group for this study. For all these children, serology tests for CD were performed and duodenal biopsy was taken in patients with positive results.

RESULTS

According to the data obtained from the questionnaires, it was found that the most frequent type of migraine headache in these children was migraine without aura, or common type (70%). Other patients (30%) had migraine with aura, or classic type, and the most common aura was the visual one. The duration of attack in 60% of children was 3-72 hours, and the great majority of these patients had moderate intensity of headache. Frequency was less than three times a month in 63% of cases. In this study, headache was localized bilaterally in the frontal lobe in 55% of cases, and 75% of these patients had a history of migraine headache in first-degree family members.

The results of serology tests determined that only 2 children among the 100 migraine patients (2%) in this study had a titer above 18 u/ml and were considered to be positive for CD. Duodenal biopsy confirmed the diagnosis of CD in these patients. One of these 2 positive cases was an 11.5-year-old girl with a three-year history of headache. Characteristics of headache in this patient included duration of attack of 24-48 hours, moderate to severe

intensity, frequency of ≥ 3 times per month, and bifrontal localization of pain. Her brother also suffered from migraine headache. The other case was a 13-year-old boy with classic type migraine whose onset of headache was two years before. Characteristics of headache in this patient included duration of attack of 2-4 hours, frequency of 2 times per month and mild intensity. For these two patients, weight and height were plotted on growth charts according to age, and both had weight and height below the 5th percentile. After six months on a gluten-free diet, headache had improved in these patients.

In the control group, of 1500 children with a mean age of 9.5 ± 1.3 years, 30 children had positive serology tests for CD (2%).

DISCUSSION

Celiac disease (CD) is associated with certain human leukocyte antigen (HLA) types that facilitate the production of antibodies against gliadin. This triggers an autoimmune process, the main effect of which is malabsorption syndrome, but it can affect non-intestinal organs. The extra-intestinal manifestations of CD, especially the presence of neurologic disorder in these patients, have been commonly investigated (8). These investigations found that neurologic disorders were more common in children with CD (51.4%) than control groups (19.9%) (9). Furthermore, in that study, headache was the most commonly found neurologic disorder, although some literature has shown that peripheral neuropathy and ataxia were common neurologic symptoms in CD. One study in Madrid in 2001 found a higher prevalence of both migraine and tension headache in celiac patients (10).

Contrary to the studies performed for detection of neurologic disorders in CD, researches about the presence of CD in patients with extra-intestinal manifestations, such as migraine, to determine the prevalence of CD are fewer in number.

Gabrielli et al. (11) reported a higher percentage of positive serologic tests for CD in patients with migraine (4.4%) than in the control group (0.4%), and the symptoms of these patients improved with a gluten-free diet. Their study was conducted in the adult age group.

Borgna-Pignatti et al. (12) showed that a significant proportion of children with migraine had subclinical CD, and they proposed that diagnostic tests for CD should be included as a part of the management of migraine headache. Alehan (13) found a higher prevalence of anti-tTGA antibodies in children with migraine (5.5%) compared with the control group (0.6%). On the other hand, some studies determined no relationship during childhood and suggested that inclusion of CD screening in the routine diagnostic evaluation of children with migraine was not necessary (14). In our study, 2% of children with migraine were found to have CD compared with 2% in the control group ($p = 1$); thus, no association was detected. The results of this study and others showed that there were only a few reports on the association of CD and migraine headache in children. In most of these studies, the sample of children with migraine was small, so larger multicentric studies should be performed to detect this relationship.

In conclusion, although according to a few studies, a higher percentage of anti-tTGA antibodies in patients with migraine may show an association between migraine and CD in children, more research needs to be conducted. With respect to screening for CD, it is better that these expensive tests be done in children with migraine who have other associated symptoms suggestive of CD, such as low weight and height for age, and not routinely in all children with migraine headache.

Acknowledgements: *The authors would like to thank Dr. Nasrin Shokrpour at the Center for Development of Clinical Research of Nemazee Hospital for editorial assistance.*

REFERENCES

1. Bigal ME, Lipton RB. The prognosis of migraine. *Curr Opin Neurol* 2008; 21: 301-8.
2. Bille B. Migraine in school children. *Acta Paediatr* 1963; 136 (Suppl): 1-151.
3. Deubner DC. An epidemiologic study of migraine and headache in 10-20 year olds. *Headache* 1977; 17: 173-80.
4. Headache Classification Committee of the International Headache Society. Classification and diagnostic criteria for headache. *Cephalgia* 1998; 8 (Suppl): 1-96.
5. Cranney A, Zarkadas M, Graham ID, et al. The Canadian Celiac Health Survey. *Dig Dis Sci* 2007; 52: 1087-95.
6. Alaedini A, Green PH, Sander HW, et al. Ganglioside reactive antibodies in the neuropathy associated with celiac disease. *J Neuroimmunol* 2002; 127: 145-8.
7. Serratrice J, Disdier P, de Roux C, et al. Migraine and celiac disease. *Headache* 1998; 38: 627-8.
8. Farrell RJ, Kelly CP. Celiac sprue. *N Engl J Med* 2002; 346: 180-8.

9. Zelnik N, Pacht A, Obeid R, Lerner A. Range of neurologic disorders in patients with celiac disease. *Pediatrics* 2004; 113: 1672-6.
10. Roche Herrero MC, Arcas Martínez J, Martínez-Bermejo A, et al. The prevalence of headache in a population of patients with coeliac disease. *Rev Neurol* 2001; 32: 301-9.
11. Gabrielli M, Cremonini F, Fiore G, et al. Association between migraine and celiac disease: results from a preliminary case-control and therapeutic study. *Am J Gastroenterol* 2003; 98: 625-9.
12. Borgna-Pignatti C, Fiumana E, Milani M, et al. Celiac disease in children with migraine. *Pediatrics* 2004; 114: 1371.
13. Alehan F, Ozçay F, Erol I, et al. Increased risk for coeliac disease in paediatric patients with migraine. *Cephalalgia* 2008; 28: 945-9.
14. Lahat E, Broide E, Leshem M, et al. Prevalence of celiac antibodies in children with neurologic disorders. *Pediatr Neurol* 2000; 22: 393-6.