# Headache and celiac disease or gluten sensitivity – a review

Cefaleia e doença celíaca ou sensibilidade ao glúten – uma revisão

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#### ABSTRACT

The aim of this study is to do a review of the relationship of celiac disease (CD) or gluten sensitivity (GS) with headache. The authors conclude that there is a connection between headaches and gluten intolerance.

Keywords: Headache; Gluten; Migraine

#### RESUMO

O objetivo do estudo foi fazer uma revisão sobre a relação da doença celíaca (DC) ou sensibilidade ao glúten (GS) com as cefaleias em geral. Os autores concluem que existe associação entre cefaleia e intolerância ao glúten.

Palavras-chave: Cefaleia; Glúten; Migrânea

# INTRODUÇÃO

Celiac disease (CD) is an absence of intestinal peptidase that digest gluten protein, whose intolerance results in a total or subtotal atrophy of the proximal small intestine causing malabsorption of nutrients. Gluten, derived from the Latin *glūten* is the main ingredient for a wide variety of pastas and breads, it is an amorphous protein composed by mixing long protein chains of gliadin and glutenin.

Interaction between genetic, immunological and environmental factors account for the heterogeneity of the

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disease. It is associated with the genes of the main histocompatibility complex (MHC) and, in particular, to the HLA-DQ2 or HLA-DQ8 allelic variants. The intestinal lesion is mediated by humoral and cellular components of the immune response. The existing treatment is a diet free of prolaminas, especially gluten.

The diagnosis is established by the demonstration of the histological characteristics of the duodenum changes.<sup>(1)</sup> In gluten sensitivity (GS), there are gastrointestinal and extraintestinal symptoms, and the tests usually do not meet histological alterations of the mucous membrane of the small intestine and autoimmune antibodies [tissue transglutaminase (tTG) and endomysial (EMA)]; However, an increased level of anti-gliadinal antibodies (AGA) is frequently observed. In GS, allergy to gluten is also absent. The exact criteria for the diagnosis of this nosology is not identified, but most researchers believe that the prevalence of gluten intolerance is much higher than of celiac disease. A gluten free diet leads to the disappearance of clinical symptoms.

Population studies indicate that between 0.5% and 1% of the population of Western Europe and North America, respectively, suffer from CD. This corresponds to about three to six million people, and the largest part of them remain undiagnosed.<sup>(2)</sup>

Most complaints related to CD or GS have no familiarity in the case of headaches. None of the authors say migraine headache, they just say headache. In other words the headache, probably by homeostatic-metabolic changes of the disease, might be migraine-like. The aim of this study is to do a review of the relationship of celiac disease (CD) or gluten sensitivity (GS) with headache.

#### METHODS

The method used was searching scientific literature. We researched articles and bibliographic reference on the internet. Bireme, MedLine, Scielo, Lilacs and PubMed are websites that we used. The articles were requested in their entirety through the College Library. Bibliographic sources were cited by the Vancouver guidelines.

# RESULTS

In a German study of 72 patients (that were recruited through advertisements in the Journal of the German Celiac Society), 28% of them with CD reported migraines. In most cases there was no decrease in the frequency and intensity of migraine crises after the introduction of gluten free diet.<sup>(1)</sup>

In an Italian study taken between 2003 and 2006, there was a retrospective portion, which included patients with diagnosed CD in Bari and Catania. All patients (and their caregivers) received a questionnaire asking how their headaches were before their diagnosis. Among them, 88 (24.8%) with CD complained of headaches before the diagnosis of CD versus 16 (8%) from the control group. After introducing a gluten free diet, 77.3% showed an improvement in headaches (27.3% disappeared), and 23.9% did not improve. In almost 50% of children who did not improve, diet adherence was poor.

In the prospective study, there were 67 children with diagnosed headaches between 2002 and 2005. They were followed by the Department of Pediatrics of Catania and agreed to perform a screening for CD between 2006-2007. Only 4 of 79 children (5%) were positive TgA and EmA, and the biopsies confirmed diagnosis of CD (injury March IIIB). None complained of gastric symptoms suggestive of CD, it was impossible to identify headaches with some food or a meal. Therefore, the prevalence of CD was high in these patients with headache, 5% versus 0.6% of the population in the same geographical area, featuring comorbidity.<sup>(3)</sup>

An Israeli study conducted between 1977 and 2001 included 111 patients with DC (with biopsy) and 211 controls. The patients were an average age of 20. In both

groups the majority of patients were women (58% of the patients versus 59% in the control group). 52.5% of patients with mal absorption syndrome featured classic CD. 51.4% of patients had neurologic manifestations versus19% of the control group, the most common neurological disorder being headache at 18%. There was a predominance of female headaches (2.1: 1 F:M), and 64.5% of patients with headaches started CD later or were asymptomatic; therefore, 35.5% had classic CD during childhood. And as for the headaches, 45% meet criteria for migraine; 19.4% for tension-type headache; and 35.5% had headaches that could not be specified. In 16 patients (80%) the headaches disappeared or improved with gluten free diet.<sup>(4)</sup>

## Pathogenesis of headache in DC and GS

Association between headache and CD may be due to a long state of malnutrition, leading to vitamin deficiency and to lower levels of serotonin, a well-known cause of headache. There is a hypothesis in which an autoimmune process and immunoinflammatory disorder would induce a vascular tonus disordered (CD and migraine) this was supported by the study of positron emission tomography (PET) Scans, demonstrating the presence of abnormalities of cortical regional blood flow, improved after 6 months of gluten free diet in adult patients with CD and migraine with aura.<sup>(5)</sup>

# Where headaches related to CD/GS would enter in classification

These headaches would best be classified under item 10. Headaches attributed to homeostasis disorders, and sub-item 10.7 Headaches attributed to other homeostasis disorders.<sup>(6,7)</sup>

## CONCLUSIONS

• There is a connection between headaches and gluten intolerance;

► Headache related to CD/GS would be headache attributed to homeostasis disorder;

• CD and GS appear to be triggering factor of migraines and do not have a spurious association; and

• The highest percentage of headache in celiacs relative to the control group in most studies indicates that these entities are comorbidities.

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