What the science tells us about Gluten Sensitivity

According to the Celiac Disease Foundation, celiac disease is a serious autoimmune disease that occurs in genetically predisposed people where the ingestion of gluten leads to damage in the small intestine. It is estimated to affect 1 in 100 people worldwide. Two and one-half million Americans are undiagnosed and are at risk for long-term health complications.

When people with celiac disease eat gluten (a protein found in wheat, rye and barley), their body mounts an immune response that attacks the small intestine. These attacks lead to damage on the villi, small fingerlike projections that line the small intestine, that promote nutrient absorption. When the villi get damaged, nutrients cannot be absorbed properly into the body. Celiac disease is hereditary, meaning that it runs in families. People with a first-degree relative with celiac disease (parent, child, sibling) have a 1 in 10 risk of developing celiac disease.

Celiac disease can develop at any age after people start eating foods or medicines that contain gluten. Left untreated, celiac disease can lead to additional serious health problems. (SOURCE)

Celiac disease (CD) is a multifactorial disorder with an estimated prevalence in Europe and USA of 1:100 and a female:male ratio of approximately 2:1. The disorder has a multifactorial etiology in which the triggering environmental factor, the gluten, and the main genetic factors, Human Leukocyte Antigen *(HLA)-DQA1* and *HLA-DQB1* loci, are well known. About 90-95% of CD patients carry DQ2.5 heterodimers, encoded by *DQA1*05* and *DQB1*02* alleles both in *cis* or in *trans* configuration, and DQ8 molecules, encoded by *DQB1*03:02* generally in combination with *DQA1*03* variant. Less frequently, CD occurs in individuals positive for the DQ2.x heterodimers (*DQA1≠*05* and *DQB1*02*) and very rarely in patients negative for these DQ predisposing markers. HLA molecular typing for Celiac disease is, therefore, a genetic test with a negative predictive value. Nevertheless, it is an important tool able to discriminate individuals genetically susceptible to CD, especially in at-risk groups such as first-degree relatives (parents, siblings and offspring) of patients and in presence of autoimmune conditions (type 1 diabetes, thyroiditis, multiple sclerosis) or specific genetic disorders (Down, Turner or Williams syndromes). (SOURCE)

The term gluten intolerance may refer to three types of human disorders: autoimmune celiac disease (CD), allergy to wheat and non-celiac gluten sensitivity (NCGS).

Gluten is a mixture of prolamin proteins present mostly in wheat, but also in barley, rye and oat. Gluten can be subdivided into three major groups: S-rich, S-poor and high molecular weight proteins.

Prolamins within the groups possess similar structures and properties. All gluten proteins are evolutionarily connected and share the same ancestral origin. Gluten proteins are highly resistant to hydrolysis mediated by proteases of the human gastrointestinal tract.

It results in emergence of pathogenic peptides, which cause CD and allergy in genetically predisposed people.

There is a hierarchy of peptide toxicity and peptide recognition by T cells. Nowadays, there are several ways to detoxify gluten peptides: the most common is gluten-free diet (GFD), which has proved its effectiveness; prevention programs, enzymatic therapy, correction of gluten pathogenicity pathways and genetically modified grains with reduced immunotoxicity.

A deep understanding of gluten intolerance underlying mechanisms and detailed knowledge of gluten properties may lead to the emergence of novel effective approaches for treatment of gluten-related disorders. (SOURCE)

ABSTRACT

Objective To determine whether infection with human enterovirus or adenovirus, both common intestinal viruses, predicts development of coeliac disease.

Design Case-control study nested within Norwegian birth cohort recruited between 2001 and 2007 and followed to September 2016.

Setting Norwegian population.

PARTICIPANTS

Children carrying the HLA genotype DR4-DQ8/DR3-DQ2 conferring increased risk of coeliac disease.

EXPOSURES

Enterovirus and adenovirus detected using real time polymerase chain reaction in monthly stool samples from age 3 to 36 months.

MAIN OUTCOME MEASURE

Coeliac disease diagnosed according to standard criteria.

Coeliac disease antibodies were tested in blood samples taken at age 3, 6, 9, and 12 months and then annually. Adjusted odds ratios from mixed effects logistic regression model were used to assess the relation between viral infections before development of coeliac disease antibodies and coeliac disease.

Results Among 220 children, and after a mean of 9.9 (SD 1.6) years, 25 children were diagnosed as having coeliac disease after screening and were matched to two controls each.

Enterovirus was found in 370 (17%) of 2135 samples and was significantly more frequent in samples collected before development of coeliac disease antibodies in cases than in controls (adjusted odds ratio 1.49, 95% confidence interval 1.07 to 2.06; P=0.02). The association was restricted to infections after introduction of gluten.

High quantity samples (>100 000 copies/μL) (adjusted odds ratio 2.11, 1.24 to 3.60; P=0.01) and long lasting infections (>2 months) (2.16, 1.16 to 4.04; P=0.02) gave higher risk estimates.

Both the commonly detected enterovirus species Enterovirus A and Enterovirus B were significantly associated with coeliac disease. The association was not found for infections during or after development of coeliac disease antibodies. Adenovirus was not associated with coeliac disease.

CONCLUSIONS

In this longitudinal study, a higher frequency of enterovirus, but not adenovirus, during early childhood was associated with later coeliac disease. The finding adds new information on the role of viral infections in the aetiology of coeliac disease. (SOURCE)

Gluten is among the 14 major food allergens officially recognized by Regulation (EU) No. 1169/2011. The risk to coeliac patients from gluten presence in the food products they consume is likely due to the unintentional contamination of naturally gluten-free (GF) and GF-labelled products, or to hidden sources of gluten in processed GF products. The aim of this paper is to provide a snapshot of gluten risk analysis, with emphasis on immunological methods currently used in gluten detection. The study highlights that immunoassays have some advantages over other analytical methods in gluten determination and are suitable for routine tests.

However, some factors (e.g., complexity of the food matrix, type of the applied antibody, gluten extraction procedures and lack of reference material) affect the reliability of obtained results. Hence, efforts are required at an analytical level to overcome the drawbacks of the immunological methods currently available.

Harmonization is necessary, so as to assist both consumers in making safe food choices, and the food industry in gluten risk assessment, management and communication. Genomic techniques do not target gluten proteins, but DNA or RNA which are markers indicative of the presence of gluten. They have thus attracted great attention, on the basis of several advantages. DNA has a higher stability.

DNA presents the advantage it is efficiently extracted also under harsh conditions and is not influenced by the extraction phase as proteins are. DNA analysis presents a higher sensitivity than proteins. DNA fragments can be, in fact, amplified by polymerase chain reaction (PCR) generating thousands to millions of copies in a short time.

In the case of processed foods, DNA also offers the advantage of being less subject to thermal and/or enzymatic transformations than proteins and is more stable. Genomic-based methods are thus considered a complement and/or confirmation of the protein-based methods, but somehow also a promising alternative. (SOURCE)

Gluten-related disorders have recently been reclassified with an emerging scientific literature supporting the concept of non-celiac gluten sensitivity (NCGS). New research has specifically addressed prevalence, immune mechanisms, the recognition of non-immunoglobulin E (non-IgE) wheat allergy and overlap of NCGS with irritable bowel syndrome (IBS)-type symptoms. This

review article will provide clinicians with an update that directly impacts on the management of a subgroup of their IBS patients whose symptoms are triggered by wheat ingestion. (SOURCE)

A study by Bajor et al, suggested a significant gene dose effect regarding clinical presentation: classical clinical presentation and villous atrophy are more frequent in patients with a double dose of HLA-DQB1. They were unable to prove a similar effect in terms of diarrhea at diagnosis, age at diagnosis, the degree of atrophy, and type 1 diabetes mellitus. Recent guidelines do not require HLA-typing to set up the diagnosis of CD apart from pediatric cases diagnosed without intestinal biopsy. The role of it is mainly restricted to the exclusion of CD.

Patients with high-risk HLA status may be at higher risk of severe disease course, raising concerns about the need for a stricter gluten-free diet and follow-up. However, these results should be treated with caution due to the limitations of the data available for their study. (SOURCE)

ABSTRACT

AIM

To study serological and genetic markers of gluten intolerance in children and teenagers with autism spectrum disorders (ASD) and Down's syndrome (DS).

MATERIAL AND METHODS

Thirty-three children with ASD (group 1) and 8 with DS (group 2), aged from 2.5 to 15 years, were examined. There were 27 boys and 6 girls in group1, 5 boys and 3 girls in group 2.

Most of the children were on a regular diet and only 4 children with ASD kept gluten-free diet (GFD). Using ELI method antibodies to gliadin IgG (AntiGliadin IgG), antibodies to deamidated peptides of gliadin IgA (AntiDGP IgA), immunoglobulin A (IgA) were identified. Haplotypes HLA-DQ2 and DQ8 were determined using PCR.

RESULTS

AntiGliadin IgG were identified in 12.1% (4) patients of group 1, with the exception of patients on GFD in 13.8%, and in 50% patients of group 2. One child with ASD had selective IgA

deficiency. Haplotypes predisposing to celiac disease had 41.9% of patients of group 1 and 37.5% of patients of group 2. In ASD, the distribution of genotypes was as follows: DQ2 (64.3%), DQ8 (28.6%), DQ2/DQ8 (7.1%,). In DS, all patients had haplotype DQ2. AntiDGP IgA were not identified in both groups.

CONCLUSION

The predominant form of gluten intolerance in children with ASD and DS is sensitivity to gluten, which can be identified in 40-50% of patients. Celiac disease, an autoimmune form of gluten intolerance, can be diagnosed in single cases, although predisposition to it is identified in 41.9% - 37.5% patients with ASD and DS, respectively. Before the start of GFD, laboratory tests should be made to identify forms of gluten intolerance and the use of GFD. (SOURCE)

The HLA-DQB1*02:01 allele is present in more than 90% celiac disease children. In the perspective of a widened pediatric population screening for celiac disease, a double-step process might be suggested: HLA-DQB1*02:01 might be investigated first and, only if this result is positive, children might be candidate for a prospective serologic screening, as a second step. (SOURCE)

The most important step towards achieving a diagnosis of CD is that every doctor looks for this entity and includes it in their differential process before a series of symptoms, and not only digestive but also long-term extra-intestinal usually. This is not achieved solely on the basis of clinical data and exploratory findings, but aided by analytical alterations, serological data, genetic markers and duodenal histopathological findings. If, after this process, reasonable doubts remain about its presence, it may be tentatively proposed that the patient follows a gluten-free diet (GFD) for at least six months, to assess their degree of response. (SOURCE)