NON-COEILIAC GLUTEN SENSITIVITY
February 2016

Introduction

Gluten sensitivity (or “non-coeliac gluten sensitivity”) has emerged as an entity separate from coeliac disease, without a clear definition of exactly what it is. This makes diagnosis difficult. It is thought to develop as a result of a number of factors – such as human genetics, plant genetic modifications, widespread use of gluten as a food additive, contact with environmental toxins, autoimmune disease and changes in the gut microbiota.

Coeliac disease is a chronic autoimmune condition affecting the small intestine. It can be induced in susceptible individuals by the ingestion of gluten, the major storage protein of wheat, rye and barley. Current diagnosis involves serological testing followed by a confirmatory small intestinal biopsy to demonstrate the autoimmune insult typical of coeliac disease. Endogenous tissue transglutaminase is thought to deamidate the glutamine in gliadin, converting it from a neutral to a negatively charged protein. Negatively charged gliadin then induces interleukin 15 secretion in the gut enterocytes, stimulating the proliferating natural killer cells and intraepithelial lymphocytes to express NK-G2D. This leads to infiltration of the gut epithelium by lymphocytes and consequent destruction of the absorptive surface of the intestine.

The most sensitive and specific serological tests for the diagnosis of coeliac disease are based on the detection of immunoglobulin A (IgA) antibodies to human tissue transglutaminase and to the connective tissue covering smooth muscle fibres (endomysial antibodies). Genetic pre-disposition plays a large part and coeliac disease is associated with specific HLA class II genes. After one year on a gluten-free diet 80% of affected individuals will have lost their antibody response. After 5 years this figure rises to more than 90%. Also, since possibly 5% of coeliac patients are IgA deficient, determination of total IgA is required to correctly interpret the serology results.

“Wheat allergy” is a condition in which IgE antibodies to wheat develop, causing a food or contact allergy associated with nausea, urticaria and atopic reactions. There are thought to be 27 different wheat proteins that can provoke this allergy. However, wheat allergy is not thought to be caused by allergy to gluten or to the gliadin fraction of gluten and is thus a completely separate entity from coeliac disease.

On the other hand, “noncoeliac gluten sensitivity” is a relatively new definition to describe the gastrointestinal symptoms that occur in response to the inclusion of gluten in the diet in individuals who do not have coeliac disease or wheat allergy. The mechanism by which gluten causes these symptoms has not been fully elucidated. [1-4]

Gluten sensitivity in the absence of coeliac disease or wheat allergy is considered by some to be a controversial clinical diagnosis; health practitioners are accused of driving the interest in it without results from confirmatory clinical trials, since individuals with gluten sensitivity have none of the serological or histological abnormalities found in coeliac disease. However, this is a condition that is now very much more prevalent than coeliac disease and dietary exclusion of gluten in affected individuals may improve a multitude of symptoms including headaches, abdominal pain, musculoskeletal complaints and behavioural disturbances. There is also possibly an overlap between noncoeliac gluten sensitivity and inflammatory
bowel disease (IBD). Furthermore, since the 1950’s there have been consistent reports of an association between gluten ingestion and the development of schizophrenia [5].

Non-coeliac gluten sensitivity is diagnosed by excluding coeliac disease and wheat allergy

Non-coeliac gluten sensitivity was originally described in the 1970’s [6,7,8]. It is characterized by intestinal and extraintestinal symptoms after ingestion of gluten-containing food, in subjects that are not affected by either coeliac disease or wheat allergy [9,10,11]. In the absence of any reliable biomarkers, therefore, non-coeliac gluten sensitivity remains a diagnosis of exclusion. The diagnostic criteria for non-coeliac gluten sensitivity include self-reported gluten intolerance, negative coeliac disease serology (IgA tissue transglutaminase antibodies, IgA endomysial antibodies) and the absence of villous atrophy on duodenal histology whilst on a gluten-containing diet [12]. Lack of IgE antibodies to wheat proteins can be included as a part of the diagnostic criteria.

Risk factors for gluten sensitivity

Bizarro et al. estimated that for every one person with coeliac disease, there are at least six to seven with non-coeliac gluten sensitivity [2]. Of the possible risk factors, the genetic modification of wheat and the changes in baking practices over the past 50 years are possibly the most interesting. Wheat has been modified to produce higher yields in industrial farming, to have better disease resistance and create more favourable bread-making characteristics [13]. Wheat flour is preferred over flours from other grains because approximately 80% of its proteins consist of gliadins and glutenins. Dough forms when these proteins combine with water and cross-link during the manipulation of kneading through disulfide bond formation. The proteins in flours from other grains do not form dough as well as wheat flour and are therefore not preferred for producing baked products.

Gluten is important to the baking industry because it provides elasticity and shape to dough by forming a network of proteins that entrap the rising gas bubbles formed during the fermentation process, allowing it to rise. Baking then sets the shape of baked products through protein denaturation and the gelatinization of the starch component. Plant breeding over the past 50 years has been aimed at increasing the 'gluten strength' of wheat varieties, which now contain significantly less protein than older varieties, but with the same gluten strength. So as a consequence the consumption of gluten and gliadin in the Western diet has been increased substantially and "modern wheat breeding practices may have led to an increased exposure to coeliac disease epitopes" [13]. Furthermore the problem of increasing 'gluten strength' in wheat is overshadowed by the practice of using gluten, much of it imported from China [14], as a food additive in infant formula, soups, sauces, potato crisps, ice cream and many other manufactured foods. This has the effect of further increasing daily exposure to allergenic gluten, unprotected by the other components of wheat.

Conclusions

There are presently no specific tests for non-coeliac gluten sensitivity and the diagnosis is made by excluding coeliac disease and wheat allergy in subjects whose clinical condition improves on a gluten-free diet.

References


