Dr Schär Institute

SHORT REPORT

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BACKGROUND AND OBJECTIVES

Following on from the first Consensus Conference held in London in 2011, the second International Expert Meeting on Gluten Sensitivity took place in Munich in late 2012. Around 30 scientists and medical experts from the USA, England, Italy, Germany, France, Spain, Austria, Argentina, Slovenia and the Netherlands attended the conference and discussed current scientific knowledge in the area of gluten-related disorders and gluten sensitivity (GS). The results presented in this report follow on from the BMC Medicine publication[1] which included a proposed diagnostic algorithm and was produced following the first Consensus Conference. Leading experts are working together to devise a way to compile and document the most up-to-date scientific information and to establish the first set of guidelines for gluten-related diseases, particularly GS. They are also aiming to coordinate and harmonise various studies, both ongoing and planned, which focus on gluten-related disorders and GS.

RESULTS

1. TERMINOLOGY

Nomenclature: Following the first Consensus Conference, the terms gluten sensitivity and non-coeliac gluten sensitivity have been used synonymously within the literature. At the last expert meeting in Munich, leading researchers in this field agreed to use the term Non Coeliac Gluten Sensitivity (NCGS) rather than gluten sensitivity. This term emphasises that NCGS can only be diagnosed if other conditions have been ruled out.

Definition: NCGS is a disorder which can only be diagnosed after ruling out other gluten-related disorders, such as coeliac disease (CD) and wheat allergy, when symptoms appear after consuming foods which contain gluten.

	COELIAC DISEASE	GLUTEN SENSITIVITY
Period from exposure to gluten and the onset of symptoms	Weeks to years	Hours to days
Pathogenesis	Autoimmune (innate and adaptive immunity)	Immunological Reaction-currently unclear
HLA	HLA DQ2/8 (approx. 95% of cases)	Unclear
Auto-antibodies	Positive (high sensitivity and specificity)	Negative*
Enteropathy	Present; Marsh 3	Absent; sometimes slightly increased IEL (Marsh 0–1)
Symptoms	Intestinal and extraintestinal	Intestinal and extraintestinal
Complications	Concomitant diseases, long-term complications	No concomitant diseases, long-term vcomplications unknown

* exceptions: IgA and/or IgG anti-gliadin antibodies (AGA)

2. CURRENT LEVEL OF KNOWLEDGE

Prevalence: At present, no epidemiological data has been published for NCGS in the UK. However, experts believe that NCGS is more common than CD. Preliminary estimates stand at approx. 6% of the population, based on clinic data.

Biomarkers: There are currently no biomarkers that are considered sufficiently sensitive or specific for diagnosing NCGS. Innate immunity has been observed as an important factor, but no research has yet been conducted to establish which factors trigger NCGS. An IgA reaction cannot be ruled out. Studies have pointed towards a correlation between first-generation anti-gliadin antibodies (AGA). Whilst it is not recommended that AGA are used in the diagnosis of CD; AGA could be helpful when considering a diagnosis of NCGS. This has been demonstrated in studies for specific patient groups, e.g. patients with irritable bowel syndrome (IBS). It also seems possible that ATIs (amylase trypsin inhibitors) could be involved. There are other gluten-correlated proteins which can also not be ruled out as possible triggers; however, no corresponding studies have yet been conducted. The prevalence of HLA-DQ2/DQ8 in patients with NCGS is lower than in patients with CD, since these genes have only been found in around 50% of cases. Anti-gliadin antibodies are also thought to occur in 50% of cases. AGA can be considered a marker for the intake of gluten and a resulting immune reaction to gluten, although as previously mentioned cannot be used in the diagnosis of CD.

Progression: The intestinal lesions in patients with NCGS correspond to Marsh 0 or 1. The number of intraepithelial lymphocytes is lower than in patients with CD. α/β lymphocytes have been found – CD patients have γ/δ lymphocytes. Usually, after a patient with NCGS consumes gluten, the symptoms both appear and disappear quickly.

Treatment: As with CD patients, there appears to be a range of sensitivity amongst patients affected by NCGS. Some may need to follow a strict gluten-free diet and check their food for cross-contamination. Other patients may have a higher tolerance threshold, meaning that they can tolerate a certain amount of gluten in the diet. More research is needed in this area.

Links with other conditions: A number of studies have investigated NCGS in IBS, with one Australian study describing NCGS as a cause of IBS in a group of patients. Further information on this relationship can be found in the Coeliac Disease, IBS and Gluten Sensitivity section of the Dr Schar Institute website. The role of NCGS in relation to the central nervous system is believed to be primarily linked to autism and schizophrenia. Both conditions are associated with genetic and environmental factors which play a part in creating the symptoms. Further research is required in relation to any link with autoimmune-associated conditions as well as looking at the possibility of a genetic predisposition.

Study design: Due to increasing interest from researchers in NCGS, participants at the Expert Meeting felt that there was a need to harmonise study design, where possible and appropriate.The study design should be double-blinded and placebo-controlled in order to rule out the possibility of a placebo effect during studies involving a gluten-free diet. This is the only correct scientific method to distinguish immune responses from placebo effects when investigating biomarkers and conducting IBS studies. It is also important to introduce similar or identical protocols for both ongoing and planned studies. A work group was assembled at the Expert Meeting in Munich for this purpose.

3. SUMMARY AND PERSPECTIVES

Known factors: NCGS

- is a wide-spread disorder.
- is presumed to be linked to dysfunctional innate immunity.
- reacts positively to a gluten-free diet.
- has behavioural effects (anxiety, depression).
- is clinically variable.

Unanswered questions:

- Which components of wheat are the toxic components?
- Are there any genetic components?
- Is there a threshold level of gluten tolerated by all patients with NCGS?
- Is it a permanent condition?
- Is there a link with malabsorption?
- Is there a link with autoimmune diseases?
- Is it possible to make a prognosis?

Awareness and clarification: There has been an increase in the number of people following a gluten-free diet; however, this is out of proportion with the estimated number of people thought to have CD. Both the general public and healthcare professionals should be aware of the difference between CD and NCGS.

SOURCES

1. Sapone A et al. Spectrum of gluten-related disorder: consensus on new nomenclature and classification. BMC Medicine 2012;10:13. www.biomedcentral.com/1741-7015/10/13

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