

# Wheat desensitization treatment in patients with gluten sensitivity

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Gluten is the main structural protein of wheat and other cereals (barley, rye, etc.) and is one of the principal dietary components for most of the world population since the birth of agriculture, playing a key role in the development of human beings. On the other hand, this evolutionary trick has led to several diseases related to gluten exposure, the best studied of which is celiac disease (CD) and wheat allergy (WA). However, some individuals complain of gastrointestinal or extra-intestinal symptoms linked to the ingestion of gluten and disappearing with gluten withdrawal, even without any histological or serologic evidence of celiac disease (CD) or wheat allergy (FA). In most cases these patients consult a large number of physicians seeking the diagnosis of CD, but very often they are considered to be suffering from irritable bowel syndrome (IBS) only.

According to a recently developed consensus, the term “non-celiac gluten sensitivity” (NCGS) has been suggested for this condition, relating to “one or more of a variety of immunological, morphological or symptomatic manifestations that are induced by the ingestion of gluten in people in whom CD has been excluded” [1] and the diagnosis is possible only after exclusion of the celiac disease, food allergies or food-related disorders and the symptomatic response to a change in the diet [2]. The diagnostic “gold standard” for gluten sensitivity ought to be the double-blind placebo-controlled (DBPC) challenge, but it is a quite dangerous and time-consuming method and is therefore rarely used [3].

There are no objective findings or markers to support a diagnosis of gluten sensitivity and its pathogenesis remains obscure, although the hypothesis is based on a stimulation of the innate immune system by the gliadin. Another theory suggests that the gliadin induces a direct cytotoxic effect on enterocytes [4, 5]. However, a role for gluten proteins as the sole trigger of the associated symptoms remains to be established.

Although the patients with gluten sensitivity have a beneficial effect on their symptoms with the gluten-free diet, the same new diet reduces enormously their quality of life. For these reasons it is important not only to provide the understanding of the NCGS pathogenesis, but also how to manage this disease to enhance the quality of life of the patients.

Therefore, we present a case report about a girl with NCGS who underwent successful wheat desensitization treatment.

We report the case of a 27-year-old girl with abdominal pain, diarrhea, oral itching and throat tightness after the ingestion of wheat products. The girl had wheat allergological tests done after a previous gastroenterological evaluation to fulfill the criteria recently proposed on “gluten sensitivity” [2, 6].

She had anti-gliadin (AGA) IgA and IgG antibodies, anti-transglutaminase (anti-tTG) and anti-endomysial (EmA) IgA antibodies, esophagogastroduodenoscopy with biopsy, HLA molecular typing for celiac disease and lactulose breath test in the gastroenterological screening and wheat skin prick test, specific IgE assay and basophil activation test for the allergological evaluation.

At the end of the diagnostic tests, the patient met all the following inclusion criteria:

- IBS-like symptoms defined according to the Rome II criteria [7];
- Negative serum anti-tTG and EmA IgA antibodies;
- Negative duodenal histology (absence of intestinal villous atrophy);
- Negative wheat skin prick test and specific IgE assay [8];
- Resolution of the symptoms on gluten-free diet and reappearance on DBPC wheat challenge [9].

Since the girl presented positive HLA DQ2 haplotype and lactulose breath test, she had antibiotic and probiotic therapy for small intestinal bacterial overgrowth with a subsequent negative breath test. All allergological tests

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were negative and, as she continued to present symptoms, the patient began to avoid all products containing wheat on her own with complete disappearance of clinical manifestations.

Therefore, we did a DBPC challenge (Table 1) with wheat and she presented a systemic reaction (abdominal pains, nausea and oral itching with mucosal hyperemia) after the ingestion of 15 ml of this food.

At this point the girl underwent a wheat desensitization treatment (Table 2) and after 21 months she was able to eat about 150 gr of wheat without any adverse reaction, starting a free dietary regimen.

In the clinical practice, an emerging problem is how to manage patients who experience symptoms after wheat ingestion in the absence of the main symptoms of CD or food allergy. These subjects often start gluten-free diet on their own with a complete benefit on manifestations.

The elimination diet itself reduces quality of life, leading to social, economic, psychological problems.

Moreover, we do not know the possible complications or how strictly or for how long the diet should be adhered to. So gluten sensitivity needs further investigations before gluten-free foods are promoted as a remedy on a large scale.

In this case report we have tried to manage our patient with the same therapeutic method we use in allergic patients and we obtained good results allowing her to enlarge the diet without any restrictions.

Moreover, as in allergic diseases, in NCGS we found a very high frequency of self-reported wheat intolerance that makes the patients choose the elimination diet. The DBPC challenge is widely used to confirm the diagnosis of food hypersensitivity and therefore could be a diagnostic marker for NCGS, able to overcome the emotional component that seems to be pivotal in these patients. In this case report we have shown how the wheat DBPC test could be the “gold standard” method also to make the diagnosis in these subjects, excluding the subjective

**Table 1.** Wheat DBPC challenge (boiled semolina 40 mg/ml)

Day 1:	
Dilution 1 : 100	0.1 ml
Dilution 1 : 100	0.5 ml
Dilution 1 : 100	1 ml
Dilution 1 : 10	0.2 ml
Dilution 1 : 10	0.3 ml
Dilution 1 : 10	0.4 ml
Day 2:	
Pure solution	0.2 ml
Pure solution	0.5 ml
Pure solution	1 ml
Pure solution	2 ml
Pure solution	5 ml
Pure solution	10 ml

component that seems to prevail in this disease. Carroccio *et al.* [3] have reached the same conclusions and demonstrated that DBPC challenge confirmed the diagnosis of NCGS in a relevant percentage of patients. Although DBPC test seems to have a high diagnostic accuracy, its use is limited to the research setting because it is expensive and time-consuming [10]; therefore, a reasonable approach in clinical practice would be to perform cheaper and easier single-blind gluten challenge tests.

Although this is only a case report, our results represent a new approach in research on NCGS and could provide a future perspective of the study for its management.

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**Table 2.** Wheat desensitization treatment

Wheat	Days	Dilution	Starting dose (once a day)	Final dose (3 times a day)	Daily dose [g]
Semolina (0.02 g/ml)	1–18	$10^{-6}$	1 ml	10 ml	$0.6 \times 10^{-6}$
	19–30	$10^{-4}$	1 ml	10 ml	$0.6 \times 10^{-4}$
	31–39	$10^{-3}$	3 ml	10 ml	$0.6 \times 10^{-3}$
	40–48	$10^{-2}$	3 ml	10 ml	$0.6 \times 10^{-2}$
	49–57	$10^{-1}$	3 ml	10 ml	0.06
	58–120	Pure solution	3 ml	75 ml	4.5
Pasta (1 spagh/portion = 1.2 g)	121–144	Pure solution	1 spaghetti	4.5 spaghetti	16.2
	145–215	Pure solution	6 spaghetti	41 spaghetti	147

## Conflict of interest

The authors declare no conflict of interest.

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