Gluten Free Diet for IBS

Subjects: Others
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The Gluten Free Diet is often considered as a diet therapy for Irritable Bowel Syndrome (IBS) patients, in addition to the more famous and recognized Low FODMAP Diet. Evidence on its efficacy and long-term safety is scarce, but it can still be included in therapy for selected IBS patients, on the basis of specific symptoms and dietary history.

Keywords: Gluten Free Diet ; Irritable Bowel Syndrome ; Non Celiac Gluten Sensitivity ; Diet ; Therapy ; IBS ; GFD ; FODMAP

1. Gluten Free Diet (GFD)

Gluten refers to a family of proteins known as prolamins (glutenin and gliadin), which are storage proteins in the starchy endosperm of many cereal grains such as wheat, barley and rye[1]. In a GFD, these cereals, and also their hybrids or derived cereals such as Kamut®, spelt and triticale, are not allowed. Oats are tolerated when not contaminated (however, it is necessary to check product by product). Alternatives to cereals containing gluten are rice, corn, potatoes and minor cereals or pseudocereals such as teff, millet, buckwheat, quinoa and amaranth[2]. The GFD therefore consists of a complete elimination from the diet of products containing wheat, barley and rye. This is not always simple because gluten contamination may be present in unsuspected products such as soy sauce, packet broth and malt by-products[3][4]. Table 1 reports foods that are allowed and forbidden in a GFD.

Table 1. Gluten free diet: allowed and forbidden foods.

Allowed Foods	Forbidden Foods
Corn	**Wheat**
Potatoes	**Barley**
Rice	**Rye**
Millet	**Malt**
Buckwheat	**Kamut®**
Quinoa	**Spelt**
Amaranth	**Triticale**
Teff	**Bulgur**
Oats, if free from contamination	**Beer** **Malt**

A GFD is the only recognized therapy for Celiac Disease (CD), which is an autoimmune condition characterized by a specific serological and histological profile and triggered by gluten ingestion in genetically predisposed individuals[5]. In recent years, GFD has been suggested as a possible therapy in Irritable Bowel Disease (IBS), or at least in a subgroup of IBS patients[6].

2. GFD as a diet therapy for IBS

A GFD is often suggested to patients with IBS-like symptoms (abdominal pain, diarrhea, bloating and flatulence). Indeed, Vazquez-Roque et al. showed that in these patients gluten caused a decrease in the expression of tight junction proteins in the colonic mucosa, causing an alteration of bowel barrier functions, especially in patients with HLA DQ8/2, the same as celiac patients[7]. Listed in Table 2 the studies on GFD efficacy in IBS

Table 2. Studies on Gluten free Diet (GFD) in Irritable Bowel Syndrome (IBS).

	Patients	Methods	Evaluated Parameters	Results
Wahnschaffe et al.[8]2001	IBS-D = 26	6 months GFD	Stool frequency IgA anti-gliadin IgA anti-tTG IEL count HLA DQ2	Improved stool frequency in patients with HLA DQ2.
Wahnschaffe et al.[9] 2007	IBS-D = 41	6 months GFD	Stool Frequency IBS symptoms questionnaire (Likert) HLA DQ2	Stool frequency and GI symptom score returned to normal values in 60% of IBS patients who were positive and in 12% who were negative for HLA DQ2.
Biesiekierski et al. [10]2011	IBS = 34	6 weeks gluten or placebo containing bread with GFD	HLA DQ2/8 IBS symptoms questionnaire (VAS)	56% having HLA DQ2/8. 68% in the gluten group reported that symptoms were not adequately controlled compared with 40% on placebo.
Vazquez-Roque et al. [7] 2013	IBS-D = 45	4 weeks gluten containing diet or GFD	Bowel function Small bowel and colonic transit Lactulose and mannitol excretion HLA DQ2/8	The gluten containing diet increased bowel frequency in HLA DQ2/8 patients and was associated with higher intestinal permeability.
Aziz et al. [11] 2015	IBS-D = 41	6 weeks GFD	IBS-SSS HADS FIS SF-36 HLA DQ2/8	GFD reduced IBS-SSS by ≥50 points in 71%. HLA DQ2/8 positive subjects had a greater reduction in depression score and increase in vitality score.
Shahbazkhani et al. [12]2015	IBS = 72	6 weeks GFD + 6 weeks gluten powder or placebo	IBS symptoms questionnaire (VAS)	Improvement was statistically different in the gluten containing group compared with placebo group in 25% and 83% patients, respectively.
Zanwar et al. [13] 2016	IBS = 60	4 weeks GFD + 4 weeks washout + 4 weeks DBPC rechallenge	IBS symptoms questionnaire (VAS)	Gluten group scored significantly higher in abdominal pain, bloating and tiredness and their symptoms worsened within 1 week of the rechallenge.
Barmeyer et al. [14] 2017	IBS-D/M = 35	4 months GFD	SGA IBS-SSS IBS-QoL EQ-5D HLA DQ2/8	HLA DQ2/8 was not associated with wheat sensitivity. 34% of the patients reported considerably or completely relieved symptoms on the GFD.
Paduano et al. [15] 2019	IBS = 42	4 weeks LFD + 4 weeks GFD + 4 weeks Mediterranean diet	Bristol stool scale IBS-SSS IBS-QoL IBS symptom questionnaire (VAS) SF-12	After GFD, improvement in symptoms, in particular, VAS bloating, VAS pain and IBS-SSS, with a smaller improvement in bloating compared to the low FODMAP diet, but with an adherence index of only 11%.
Pinto-Sanchez et al. [16] 2020	IBS = 50	4 weeks GFD	GI transit Birmingham IBS questionnaire Bristol Stool Scale HADS STAI-TAY PHQ-15 PGWB Anti-gliadin	After the GFD, patients with anti-gliadin reported less diarrhea. IBS symptoms improved in 75% of the patients with anti-gliadin and in 38% without the antibodies. GI transit normalized in a higher proportion of patients with anti-gliadin.

DBPC: Double-Blind Placebo-Controlled; EQ-5D: European Quality of Life-5 Dimensions; FIS: Fatigue Impact Scale; GFD: Gluten Free Diet; GI: Gastrointestinal; HADS: Hospital Anxiety and Depression Scale; HLA: Human Leukocyte Antigens; IBS: Irritable Bowel Syndrome; IBS-D: Irritable Bowel Syndrome Diarrhea; IBS-M: Irritable Bowel Syndrome Mixed; IBS-QoL: Irritable Bowel Syndrome Quality of Life; IBS-SSS: Irritable Bowel Syndrome Symptom Severity Score; IEL: Intraepithelial Lymphocytes; IgA: Immunoglobulin A; LFD: Low Fermentable Oligo-, Di- and Mono-saccharides And Polyols (FODMAP) Diet; PGWB: Psychological General Well-Being; PHQ-15: Patient Health Questionnaire; SF-12: Short Form 12; SF-36: Short Form 36; SGA: Subject's Global Assessment; STAI-TAY: State-Trait Anxiety Inventory; tTG: Tissue Transglutaminase; VAS: Visual Analogue Scale.

In 1978, the term "Non-Celiac Gluten Sensitivity (NCGS)" was coined by Ellis and Linaker[17]. It is a clinical entity which seems often to overlap with IBS. It is characterized by gastrointestinal (GI) and extra-GI symptoms (headache, foggy mind, chronic fatigue, joint pain, tingling or numbness of the extremities, eczema) associated with gluten ingestion (occurring hours or days after the ingestion) in individuals in whom CD and wheat allergy have been excluded[18]. The diagnosis of certainty, according to the Salerno Expert consensus, is based on a close and standardized monitoring of the patient during elimination and reintroduction of gluten, in the absence of specific biomarkers[19]

However, the debate is still open as to whether the gluten is the culprit[20][21][22]. Indeed, also in non-gluten free food there are other molecules potentially responsible for the symptoms such as Wheat Germ Agglutinins (WGA), which induce the release of pro-inflammatory cytokines and act on the intestinal barrier, amylase trypsin inhibitors (ATIs), pest resistance molecules and activators of innate immune responses in human and murine models. Moreover, wheat also contains fructans, which are FODMAPs.

It is therefore up to the clinician to understand which category each patient most likely belongs to and which diet will benefit him/her the most. This decision is fundamentally whether the patient is a NCWS patient with IBS-like symptoms responding to a GFD or is an IBS patient not sensitive to wheat or sensitive not only to wheat, for whom a Low FODMAP Diet (LFD) may be more suitable.

In conclusion, a GFD could be useful for those IBS patients who report extraintestinal symptoms or have biomarkers suggesting specific symptoms (i.e., increased duodenal mucosal lymphocytes in a duodenal biopsy or serum anti-gliadin antibodies).

References

1. Niland, B.; Cash, B.D. Health Benefits and Adverse Effects of a Gluten-Free Diet in Non-Celiac Disease Patients. Gastroenterol. Hepatol. (N. Y.) 2018, 14, 82–91.
2. Saturni, L.; Ferretti, G.; Bacchetti, T. The gluten-free diet: Safety and nutritional quality. Nutrients 2010, 2, 16–34.
3. Jones, A.L. The Gluten-Free Diet: Fad or Necessity? Diabetes Spectr. 2017, 30, 118–123.
4. Falcomer, A.L.; Santos Araújo, L.; Farage, P.; Santos Monteiro, J.; Yoshio Nakano, E.; Puppin Zandonadi, R. Gluten contamination in food services and industry: A systematic review. Crit. Rev. Food Sci. Nutr. 2020, 60, 479–493.
5. Caio, G.; Volta, U.; Sapone, A.; Leffler, D.A.; De Giorgio, R.; Catassi, C.; Fasano, A. Celiac disease: A comprehensive current review. BMC Med. 2019, 17, 142.
6. Catassi, C.; Alaedini, A.; Bojarski, C.; Bonaz, B.; Bouma, G.; Carroccio, A.; Castillejo, G.; De Magistris, L.; Dieterich, W.; Di Liberto, D.; et al. The Overlapping Area of Non-Celiac Gluten Sensitivity (NCGS) and Wheat-Sensitive Irritable Bowel Syndrome (IBS): An Update. Nutrients 2017, 9, 1268.
7. Vazquez-Roque, M.I.; Camilleri, M.; Smyrk, T.; Murray, J.A.; Marietta, E.; O'Neill, J.; Carlson, P.; Lamsam, J.; Janzow, D.; Eckert, D.; et al. A controlled trial of gluten-free diet in patients with irritable bowel syndrome-diarrhea: Effects on bowel frequency and intestinal function. Gastroenterology 2013, 144, 903–911.e3.
8. Wahnschaffe, U.; Ullrich, R.; Riecken, E.O.; Schulzke, J.D. Celiac disease-like abnormalities in a subgroup of patients with irritable bowel syndrome. Gastroenterology 2001, 121, 1329–1338.
9. Wahnschaffe, U.; Schulzke, J.D.; Zeitz, M.; Ullrich, R. Predictors of clinical response to gluten-free diet in patients diagnosed with diarrhea-predominant irritable bowel syndrome. Clin. Gastroenterol. Hepatol. 2007, 5, 844–850.
10. Biesiekierski, J.R.; Newnham, E.D.; Irving, P.M.; Barrett, J.S.; Haines, M.; Doecke, J.D.; Shepherd, S.J.; Muir, J.G.; Gibson, P.R. Gluten causes gastrointestinal symptoms in subjects without celiac disease: A double-blind randomized placebo-controlled trial. Am. J. Gastroenterol. 2011, 106, 508–515.

11. Aziz, I.; Trott, N.; Briggs, R.; North, J.R.; Hadjivassiliou, M.; Sanders, D.S. Efficacy of a Gluten-Free Diet in Subjects With Irritable Bowel Syndrome-Diarrhea Unaware of Their HLA-DQ2/8 Genotype. Clin. Gastroenterol. Hepatol. 2016, 14, 696–703.e1.
12. Shahbazkhani, B.; Sadeghi, A.; Malekzadeh, R.; Khatavi, F.; Etemadi, M.; Kalantri, E.; Rostami-Nejad, M.; Rostami, K. Non-Celiac Gluten Sensitivity Has Narrowed the Spectrum of Irritable Bowel Syndrome: A Double-Blind Randomized Placebo-Controlled Trial. Nutrients 2015, 7, 4542–4554.
13. Zanwar, V.G.; Pawar, S.V.; Gambhire, P.A.; Jain, S.S.; Surude, R.G.; Shah, V.B.; Contractor, Q.Q.; Rathi, P.M. Symptomatic improvement with gluten restriction in irritable bowel syndrome: A prospective, randomized, double blinded placebo controlled trial. Intest. Res. 2016, 14, 343–350.
14. Barmeyer, C.; Schumann, M.; Meyer, T.; Zielinski, C.; Zuberbier, T.; Siegmund, B.; Schulzke, J.; Daum, S.; Ullrich, R. Long-term response to gluten-free diet as evidence for non-celiac wheat sensitivity in one third of patients with diarrhea-dominant and mixed-type irritable bowel syndrome. Int. J. Colorectal. Dis. 2017, 32, 29–39.
15. Paduano, D.; Cingolani, A.; Tanda, E.; Usai, P. Effect of Three Diets (Low-FODMAP, Gluten-free and Balanced) on Irritable Bowel Syndrome Symptoms and Health-Related Quality of Life. Nutrients 2019, 11, 1566.
16. Pinto-Sanchez, M.I.; Nardelli, A.; Borojevic, R.; de Palma, G.; Calo, N.C.; McCarville, J.; Caminero, A.; Basra, D.; Mordhorst, A.; Ignatova, E.; et al. Gluten-free Diet Reduces Symptoms, Particularly Diarrhea, in Patients with Irritable Bowel Syndrome and Anti-gliadin IgG [published online ahead of print, 2020 Aug 19]. Clin. Gastroenterol. Hepatol. 2020.
17. Ellis, A.; Linaker, B.D. Non-coeliac gluten sensitivity? Lancet 1978, 1, 1358–1359, doi:10.1016/s0140-6736(78)92427-3.
18. Fasano, A.; Sapone, A.; Zevallos, V.; Schuppan, D. Nonceliac gluten sensitivity. Gastroenterology 2015, 148, 1195–1204, doi:10.1053/j.gastro.2014.12.049.
19. Elli, L.; Tomba, C.; Branchi, F.; Roncoroni, L.; Lombardo, V.; Bardella, M.T.; Ferretti, F.; Conte, D.; Valiante, F.; Fini, L. Evidence for the presence of non-celiac gluten sensitivity in patients with functional gastrointestinal symptoms: Results from a multicenter randomized double-blind placebo-controlled gluten challenge. Nutrients 2016, 8, 84, doi:10.3390/nu8020084.
20. Zanwar, V.G.; Pawar, S.V.; Gambhire, P.A.; Jain, S.S.; Surude, R.G.; Shah, V.B.; Contractor, Q.Q.; Rathi, P.M. Symptomatic improvement with gluten restriction in irritable bowel syndrome: A prospective, randomized, double blinded placebo controlled trial. Intest. Res. 2016, 14, 343–350, doi:10.5217/ir.2016.14.4.343.
21. Barmeyer, C.; Schumann, M.; Meyer, T.; Zielinski, C.; Zuberbier, T.; Siegmund, B.; Schulzke, J.; Daum, S.; Ullrich, R. Long-term response to gluten-free diet as evidence for non-celiac wheat sensitivity in one third of patients with diarrhea-dominant and mixed-type irritable bowel syndrome. Int. J. Colorectal. Dis. 2017, 32, 29–39, doi:10.1007/s00384-016-2663-x.
22. Catassi, C.; Elli, L.; Bonaz, B.; Bouma, G.; Carroccio, A.; Castillejo, G.; Cellier, C.; Cristofori, F.; de Magistris, L.; Dolinsek, J.; et al. Diagnosis of Non-Celiac Gluten Sensitivity (NCGS): The Salerno Experts' Criteria. Nutrients 2015, 7, 4966–4977, doi:10.3390/nu7064966.