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Letter to Editor

GUT DYSBIOSIS AND ADHERENCE TO A GLUTEN FREE DIET MAINTAINING A BALANCE BETWEEN TREATMENT AND ADVERSE EFFECTS AMONG INDIVIDUALS WITH CELIAC DISEASE AND NON-CELIAC GLUTEN HYPERSENSITIVITY

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Dear Editor,

Gluten free diet is defined as a total abstinence from consuming food products that contain the protein gluten in them. Wheat, barley, and rye are the major sources of gluten in diet which is readily available to the public. According to European legislation (EU law 41/2009), GFD calls for the complete elimination of gluten-containing cereals (such as wheat, rye, barley, oats, spelt, and kamut) and only includes naturally gluten-free matrices (such as legumes, fruits and vegetables, unprocessed meat, fish, eggs, and dairy products) and/or alternatives to wheat-based foods that are made without gluten or have a gluten content of less than 20 parts per million. (1) Celiac disease is a systemic disease mainly affecting the small intestines, which is also included in the autoimmune spectrum of disorders. The pathophysiology of celiac disease stems from gliadin, which is a peptide derived from gluten, that damages the small intestine. The process results in the destruction of the small intestinal villi and causes local inflammation. The intestinal surface's diminished functionality and malabsorption follow from this destruction. The digestive system is directly impacted by inadequate nutrient absorption, but all bodily systems are indirectly affected as well. (2) non celiac gluten hypersensitivity is however a condition in which hyper Allery to gluten is present without an underlying autoimmune basis. It is a newly proposed clinical condition that, in the absence of celiac disease and wheat allergy, improves with gluten avoidance and causes both intestinal and extra-intestinal symptoms without gastrointestinal lesions. There is ongoing discussion regarding the condition's prevalence.(3)

The difference however is present in the pathogenesis of both these conditions, but they do share a common management line with avoidance of gluten and adherence to a gluten free diet is essential to overcome the adverse effects both intestinal and extra-intestinal that are brought about by these conditions. The diagnosis is mostly based on history, examination findings and investigations. The most initial investigations that help in broadly identifying celiac disease are anti-TTG antibodies which are sensitive to celiac disease and provide guidance on further investigation and treatment. However certain prerequisites need to be taken before proceeding with this investigation. These include looking for IgA deficiency and making sure that the patient is on a gluten rich diet before testing. The most specific tests include antiendomysial antibodies this test has a lower sensitivity compared to IgA class tTGA (90% vs. 98%) but shows an almost absolute specificity for CD. (4)

The upper GI endoscopy with duodenal biopsy remains the gold standard for diagnosing this condition. As for the non-celiac gluten hypersensitivity, Due to the lack of sensitive and specific biomarkers, NCGS is diagnosed based on the patient's clinical evaluation during a double- or single-blind, placebo-controlled gluten challenge, as well as the exclusion of CD and WA. The task force of the German Society of Allergology and Clinical Immunology has declared that the current diagnosis of NCGS is inappropriate due to a number of factors, including the lack of validated diagnostic criteria, the prevalence of patients self-diagnosing and self-instructing a GFD, the difficulty in identifying gluten as the primary cause, and the many variables that make it difficult to perform a clinical assessment of the patient during a GFD.(5)

As these diseases are more or less similar on the basis of gluten allergy, which is present in both these conditions, there comes a challenge on managing the symptoms and controlling the disease with balancing the adverse effects that come as a result of adhering to a strict gluten free diet, this adverse effect is mostly seen in the gut which is basically a replacement or depletion of gut microbiota and the over activity of harmful microbiota in the GI tract, this is further identified by Mazcorro et al who evaluated the gut microbiota of Mexican patients with CD (n = 6), NCG/WS (n = 12), and healthy subjects (n = 12). (6) Using ultra-high-throughput 16S rRNA gene marker sequencing, the duodenal and fecal microbiota of patients and controls were examined. After four weeks of GFD, a subgroup of patients with available paired samples were the subject of a repeat study. Overall, the gut microbiota changed in all three of the study groups after the GFD period, indicating that microbial composition may be greatly impacted by gluten withdrawal.

Another study further gives evidence that gluten free diet is associated with a decrease in the number of Lactobacillus and Bifidobacterium while increasing E. coli and Enterobacteriaceae generally linked to episodes of bacteremia.(7)

Bonder et al.[8] reported that a GFD in healthy volunteers decreased the abundance of Roseburia and increased the abundance of Victivallaceae and Clostridiaceae. (8)

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Coupled with this increase there is also a decrease in both micro and macronutrients in individuals who take up a gluten free diet and exclude all gluten products from their day-to-day meals. These changes are less evident in those individuals who take up gluten free diet to reduce weight or to adapt a healthy lifestyle as they can occasionally switch their diet and because of which these adverse effects go unnoticed in them.

The challenge comes when a person who either has celiac or a non-celiac gluten hypersensitivity starts their treatment with a long-term abstinence from gluten in their diet.

This kind of flora dysbiosis is not only limited to the intestinal tract but it extends up to the oral cavity. The oral flora of CD patients is dysbiotic. The oral cavity contains microbial flora that are connected to CD's gluten metabolism The quantity and variety of flora in saliva are far higher than those colonized in the stomach and duodenum, despite the fact that gluten-containing foods only remain in the oral cavity for a brief period of time. It is important to consider how oral flora affects gluten digestion. Researchers have discovered that the genus of Streptococcus, Neisseria, Actinomyces, and Rothia that colonized the oral cavity may have something to do with the initial metabolism of gliadin in the oral cavity (9). The saliva of CD patients contains more bacteria that can break down gluten than that of healthy individuals, a reason could be an increase in the population of lactobacillus species in the oral cavity.

On the other hand, research from the opposite perspective revealed that oral microbial enzymes break down a portion of gluten, which raises immunogenic small molecule peptide epitopes and causes additional intestinal inflammation. (10) The role of prebiotics and pro biotics in the management of symptoms is increasing due to the positive effects on symptoms of CD and Non celiac gluten hypersensitivity, namely Bifidobacteria and Lactobacilli with these organisms having the ability to restore the composition of gut microbiome and to reduce the toxic and inflammatory effects on the gut mucosa. (11)

Data and literature have led to the hypothesis that the inclusion of probiotics to a gluten free diet is both easy and cost effective, other food supplements have also shown positive results.

Beyond CD, Beaumont et al.'srandomizedtrial [89] examined the impact of a high-protein diet (HPD) on the composition of the gut microbiota, metabolic activity, and the expression of genes in the mucosa of the large intestine. According to the authors, three weeks of HPD treatment was enough to change the production of bacterial metabolites and the expression of certain genes in the rectal mucosa.(11)

More work needs to be done in this field of study as it is vital to balance the positive effects gluten free diet in patients with CD and NSGS with the adverse effects and deficiencies brought about by making this change to one's diet. In order to prevent complications and the severe progression of the disease, various dietary and supplemental strategies are being investigated to support CD patients' compliance and response to GFD. A promising therapeutic strategy for modifying the composition and function of the intestinal microbiota may be the synergistic use of prebiotics. However, there is currently not enough data to support the use of probiotics and prebiotics in standard clinical practice when it comes to CD patients. To elucidate their function in CD patients, well-designed randomized controlled trials are required in order to delineate the helpful effect of these supplements for people switching to a GFD.

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