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How to improve the gluten-free diet: The state of the art from a food science perspective

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ABSTRACT

The celiac disease is the most common food intolerance and its prevalence is increasing. Consequently, use of gluten-free diet has expanded, notwithstanding consumption as therapy for other gluten-related disorders or by wellbeing people without any medical prescription. Even the therapeutic efficiency has undoubtedly proven, several drawbacks mainly regarding the compliance, nutritional deficits and related diseases, and the alteration of the intestinal microbiota have described in the literature. Food science has been considered as one of the primary area of intervention to limit or eliminate such drawbacks. Efforts have approached shelf life, rheology and palatability aspects but more recently have mainly focused to improve the nutritional features of the gluten-free diet, and to propose dietary alternatives. The sourdough fermentation has shown the most promising results, also including a biotechnology strategy that has allowed the complete degradation of gluten prior to consumption.

1. Introduction

Celiac disease (CD) is a chronic immune-mediated inflammatory pathology of the small intestine triggered by dietary gluten. CD is the most common and increasing food intolerance, affecting approximately 1% of the worldwide population (Lionetti, Gatti, Pulvirenti, & Catassi, 2015). Progresses in the disease diagnosis undoubtedly decreased the number of undiagnosed cases, but also the agricultural changes, which occurred in the last century, might had given a contribution to increase the CD incidence (Tommasini, Not, & Ventura, 2011). The widespread use of refined grains and leavening by chemical and baker's yeast agents are some of the classical examples of the most recent trend. CD may develop at any time in life but is most prevalent at pediatric age with a high-expected ratio between undiagnosed and diagnosed cases (Lionetti et al., 2015). Genetics predisposes patients to CD, with ca. 30–40% of the general population having this signature. Exposure to gluten is the other indispensable requirement for the development of CD. However, while some subjects develop CD soon after the introduction of gluten into the diet, others do so in late adulthood, after having been exposed to gluten for decades (Sanz, 2015). Therefore, clinical data have established the existence of other environmental triggers such as the mode of birth, weaning way, gluten introduction, antibiotics and viral and bacterial infections, being the alteration of the intestinal microbiota one of the most important (Pagliari et al., 2015).

Besides CD, the umbrella term "gluten-related disorders" includes other pathological symptoms: non-celiac gluten sensitivity (NCGS) or non-celiac wheat sensitivity, as more recently defined, dermatitis herpetiformis, wheat allergy and gluten ataxia (Sapone et al., 2012). More in general, other chronic inflammatory conditions of the gastrointestinal tract such as inflammatory bowel diseases (IBD) also share some common genetic, immunological and environmental factors with CD (Casella et al., 2010).

Currently, the only effective therapy for CD and most of the other related disorders is the gluten-free diet (GFD). The exact amount of gluten that people may tolerate without developing deleterious effects is difficult to assess and probably varies between individuals, but less than 10 mg of daily gluten intake has considered safe and unlikely to cause significant abnormalities (Catassi et al., 2007). Although GFD is the therapeutic approach for CD patients, it has gained popularity among many persons in a state of wellbeing without CD or "gluten-related disorders". From 2013 to 2015, the gluten-free industry enjoyed a growth of 136%, far outpacing CD awareness and increases in prevalence (Norelle & Reilly, 2016). Usually, those people who are in good health consumed a GFD for the perceived benefits on health, weight loss and/or minimizing future risk of gastrointestinal diseases.

Even though dietary treatment with GFD is highly successful for CD

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and other “gluten-related disorders”, the adherence to this diet may pose sensory, nutritional, social and economic difficulties. The need for alternative therapies has repeatedly expressed by CD patients, especially to increase the quality of life and the health status (Branchi et al., 2015). After describing some drawbacks of the GFD, this review focuses on most of the recent advances in food science, with the main emphasis on the use of sourdough, which contribute to improve the quality of GFD and/or represent novel therapeutic strategies.

2. Pros and cons of the gluten-free diet (GFD)

The GFD has been recommended for the treatment of CD for more than a half-century (1940s), starting from the seminal early clinical studies by Dicke and colleagues (Dicke, 1941). Nowadays, GFD is the only available, accepted and efficient treatment for CD. Nevertheless, a recent literature has debated on several drawbacks, which seem to accompany the lifetime under GFD.

2.1. Compliance

Gluten is ubiquitous and safe avoidance of its main sources (e.g., wheat, barley and rye), especially when present as minor ingredients (e.g., sausages, instant soups and confectioneries), is very difficult. A large cohort study has estimated that ca. 7–30% of CD patients were non-responders, having persistent symptoms, despite the remission under GFD for more than one year (Rubio-Tapia, Hill, Kelly, Calderwood, & Murray, 2013). Inadvertent exposure to gluten caused this non-responsive CD (NRCD) and accounted for 35–50% of the persistent symptoms (Rubio-Tapia et al., 2013). Probably, other etiologies (e.g., lactose and FODMAPs - Fermentable Oligo-, Di- and Mono-saccharides, and Polyols – intolerances; and small intestine bacterial overgrowth - SIBO) also interfered with NRCD diagnosis. The long-term adherence to GFD has been estimated to range between not more than 17–45% of adults because of the many restrictions (Leffler et al., 2008). Anxiety, school/working and social situations, persistent clinical manifestations and changes in body composition are all situations associated with the long-term GFD (Di Sabatino & Corazza, 2009). Thus, one primary consequence of this dietary intervention is the deterioration of the quality of life (Lee & Newman, 2003), with the perception of a health status worse than that of the non-celiac population (Hallert et al., 1998). The gluten-free (GF) market is rapidly moving from pharmacy to large-scale retail distribution, in some cases national subsides are usually provided. Nevertheless, the daily GF basket is still more expensive than the gluten-containing counterparts are, and is only in part affordable for common family types (Lambert & Ficken, 2015).

2.2. Nutritional imbalances

It has been strongly recommended that CD patients refer to dietitians for making sure that GFD is not only gluten deprived but also nutritionally adequate (Ludvigsson & Green, 2011). Overall, no nutritional data have supported the presumed health benefits of GFD for those individuals who do not suffer of “gluten-related disorders” (Norelle & Reilly, 2016).

Table 1 lists the main nutritional imbalances that have been attributed to the GFD. To compensate the technological properties of the deprived gluten diets, GF foods contain more carbohydrates and lipids (mainly saturated fat) compared to the gluten-containing counterparts, thus resulting in high-calorie foods (Theethira & Dennis, 2015). The lipid profiles of CD children differed from those of the reference population (Forchielli et al., 2015). Therefore, CD patients are at higher risk of overweight/obesity than the non-celiac population (Diamanti et al., 2014). An Italian multicenter cross-sectional study showed that removal of gluten from the diet increased the prevalence of overweight by 8.8%–11.5% and obesity by 5.3–8.8% (Norsa et al., 2013).

In several cases, GF products are lacking of mineral or have a less fortification with micronutrients and fibers compared to the wheat-containing counterparts (do Nascimento, Fiates, Dos Anjos, & Teixeira, 2013). Malabsorption of nutrients is frequently observed among CD patients (Botero-Lopez et al., 2011), and deficiencies of several vitamins and minerals have been shown (McGough & Cummings, 2005). Several studies described both children and adult with nutritional deficiencies regarding vitamins (Salazar et al., 2015), hemoglobin, ferritin, zinc, calcium and/or copper (Botero-Lopez et al., 2011). The intake of at least five portions of fruit and vegetables a day becomes fundamental for CD patients to enrich their diet with antioxidant compounds (Pandey & Rizvi, 2009). At the diagnosis, the deficiency of fiber intake has been related to malabsorption due to villi atrophy. During GFD, it referred to the poor nutritional quality of the GF products (Mariani et al., 1998; Martin, Geisel, Maresch, Krieger, & Stein, 2013; Wild, Robins, Burley, & Howdle, 2010). Starches and or refined flours are the main ingredients of the GF formula. Refined processes removed the outer layers of grains, which contain most of the fibers, and leave the starchy inner part (Penagini, Dilillo, Meneghin, Mameli, & Fabiano, V., & Zuccotti, G. V., 2013).

There is an emerging evidence that people consuming GF products, especially without sufficient diversity, may be at greater risk of exposure to certain mycotoxins than those who are under non-restricted dietary regime. It is well known that corn has frequently been subjected to high contamination by mycotoxins, mainly fumonisins, due to the large fungal infection in the field and during storage (Wild & Gong, 2010.). Arsenic is frequently present in inorganic form in rice, which is a very common ingredient in GF foods (Lai, Cottingham, Steinmaus, Karagas, & Miller, 2015). Serum mercury levels were four-times higher among CD adults consuming the GFD than in controls under not restricted gluten (Elli et al., 2015).

On the other hand, there is a report indicating that the nutritional quality of the Australian GF products is not significantly different compared to the gluten-containing counterparts (Staudacher & Gibson, 2015).

2.3. Nutritionally related CD comorbidity diseases associated to GFD

Long-time exposure to nutritional imbalances has also been related to the appearance of various diseases (Table 1). It has been demonstrated that the obesity risk increased in CD patients subjected to GFD because of the high glycemic index (GI) of the GF products (Lamacchia, Camarca, Picascia, Di Luccia, & Gianfrani, 2014). The GI of commercial GF breads has been estimated to vary between 74.5 and 88.3 (Rizzello, Montemurro, & Gobbetti, 2017). The absence of gluten seemed to affect the starch digestibility, thus increasing the postprandial glycemic response (Vici, Belli, Biondi, & Polzonetti, 2016). Usually, CD patients show a high risk of metabolic syndrome one year after starting the GFD (Tortora et al., 2015).

Genetic factors, participating in the regulation of the immune response and bone metabolism, contributes to CD osteopathy, which likely results as a combination among various factors such as local and systemic immunological disorders, malabsorption and malnutrition (Moreno et al., 2005). Bone alterations are the consequence of impaired calcium and vitamin D absorption and secondary hyperparathyroidism mainly resulting from the loss of villous cells in the proximal intestine, where calcium is most actively adsorbed (Krupa-Kozak, 2014). Considering that most bone mass is acquired during the first two decades of life, early diagnosis of CD is fundamental. The stratification of patients according to sex and age showed a higher prevalence of low bone mineral density (BMD) in men older than 30 years and in women of all ages. After one-year of GFD, a significant improvement has found only providing that GFD has fortified with minerals (Pantaleoni et al., 2014).

CD is associated with an increased risk of major depressive disorder, possibly due to deficiencies in micronutrients in the GFD. Patients with