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ARTICLE REVIEW

The role of nutrition in children with celiac disease

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Abstract

Celiac disease, a permanent, irreversible but treatable disease is an autoimmune disease triggered by gluten ingestion in genetically predisposed individuals, also known as celiac sprue and gluten sensitive enteropathy. The gluten fractions that are toxic are called gliadins triggers an immune reaction that leads to bowel inflammation mediated by T lymphocytes, cause damage to the small intestine and villous atrophy.

Recent findings

Intestinal inflammation and villous atrophy in small intestines by permanent intolerance to gluten in celiac disesea leads to seveare malabsorption. Around 20%-38% patients were basically nutritionally imbalance secondary malabsorption due to mucosal damage. Nutrition plays a very important role in the management of celiac disease. Gluten free diet must be balanced to cover nutrient requirements to prevent deficiencies and ensure children's health, growth and development.

Conclusion

Gluten-free diet is the only accepted and available treatment in CD. It was a life-long treatment, if not carried out with attention, it may lead to nutritional imbalance which can affect children's growth and development

Keywords celiac disease, children, gluten-free diet, growth and development

Introduction

Celiac disease (CD) is a systemic autoimmune disorder caused by permanent intolerance to gluten, such reaction leads to intestinal inflammation, villous atrophy in small intestines which leads to malabsorption.[1,2] CD is a global disease with seroprevalence of 1.4% and biopsy prevalence 0.7% worldwide, with the exception of areas showing low frequency of CD-predisposing genes and low gluten consumption (e.g., sub-Saharan Africa and Japan).[3] It is well known that CD is strongly associated with human leukocyte antigen (HLA) class II, HLA-DQ2 and HLA-DQ8 which are located on chromosome 6p21. The presence of the HLA-DQ2 allele is common in the general population, and it is present in approximately 30% of Caucasian individuals.[3,4] CD is recognized not only throughout historical CD areas such as Northern Europe and United States, but also significantly increase in new regions (Asian countries). Studies have shown that most CD cases remain undetected in the absence of serological screening due to heterogeneous symptoms and/or poor disease awareness.[3,4]

Multiple pathways are involved in the pathogenesis of CD which finally lead to the destruction of the enterocyte and subsequent atrophy of small intestinal villi. The histology of CD studies the mucosa of the small intestine, especially the submucosa, muscularis and serosa. A flat mucosa with villus shortening can be observed which is compensated for by hyperplasia and elongation of

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intestinal crypts. These changes reduce the amount of epithelial surface available for absorption.[1,2]

Gluten free diet (GFD) is the only cornerstone treatment of celiac disease. GFD involves strict lifelong avoidance of all products containing gluten, a protein known as prolamins which are protein storage in starchy endosperm of many cereal grains such as wheat, barley, rye. GFD will result in alleviation of symptoms, normalize autoantibodies and repair intestinal mucosa overtime in CD. [5,6,7] Previous study stated that as about 20%-38% CD patients were basically nutritionally imbalance secondary malabsorption due to mucosal damage of GI tract.[8] The greater small intestines mucosal atrophy also causes greater iron, copper, folate, calcium, vitamin B-12 and zinc deficiencies. [6,8] Hence, suitable GFD must be nutritionally balanced. It must cover nutrient requirements to prevent deficiencies and ensure a healthy life, especially in children where growth and development are highly depending on nutrition supply. Therefore, nutrition plays vital role in treating CD.[9] However, strict and lifelong diet is also challenging to children as major role of non-compliance due to disliking the taste of GFD and temptation. GFD compliance itself varies from 45% to 81% in children in reports by Hill et al.[10] Whereas up until now, GFD is the only treatment accepted and effective for CD, therefore this may affect long-term morbidity and mortality of children with CD.[11,12] Complete termination of gluten is nearly impossible, the gluten free indicates diet containing gluten at minimal level to be considered harmless. Recent reviews conclude less than 10 mg a day is most likely not causing any further damage to mucosal.[5] Gluten-containing foods which need to be avoided in CD patients are bread, cereals, flour and pasta in their daily diet. Two types of GFD available is naturally gluten-free or processed gluten-free that were made through purification. Several naturally GFD are rice, corn, potatoes, seeds, and legumes. Elimination of gluten through purification in processed GFD will inevitably alters macro and micronutrients composition and nutritional value in them.[6]

Methods

In this article, we aimed to provide a thorough review on the role of nutrtion in children with celiac disease. The databases EBSCOHOST, CINAHL, MEDLINE, and Web of Science were searched (2000 to present) using the following key words: pediatric, children, celiac disease, coeliac disease, gluten free diet, nutrition. An ancestry search was also used to find relevant articles.

Result and Discussions

Risk of GFD

A collaborative study investigated different composition of gluten free products (GFP) and gluten-containing products. GFP were mainly high in fat, mainly saturated fat, and low in protein and carbohydrate which leads to lower energy content. Additionally, GF products also had more sodium and less fiber.[13] Some commercially available GFP are also have lower content of micronutrients and minerals. Specifically, vitamin A, thiamine, riboflavin, niacin, vitamin B6, vitamin B12, folate, biotin, vitamin D, pantothenate, magnesium, sodium, iron, cupper, iodine, chlorine, manganese and selenium intakes were lower in GFP.[9,14]As a consequence, life-long therapy of GFD rise concerns about its impact on a patient's anthropometric parameters and its nutritional adequacy.

Nutritional inadequacy consequences in GFD

GFD, the only treatment for CD, is indeed reduces risk of increase mortality and adverse events in CD.[13,14] However, GFD itself is not risk-free, as it may cause further nutritional complication as a result of poor nutrients quality of GFD products described above.[6,9]

Numerous studies revealed imbalance diet contributed by GFD in children with CD. Macro and micronutrient imbalance were found in children consuming GFP. A study conducted by Elliot, examined nutritional quality of package GFP in children and showed packaged GF food have poor nutritional quality compared to regular products containing gluten (88% vs 97%: $p<0.01$). Products with a GF claim had lower levels of protein, sodium, total fat, and saturated fat compared with products without a GF claim. A higher proportion of the GF products had high levels of fat and trans-fat. Calories from sugar in GFD compared with child-targeted products without a GF claim were similar. [15]

Öhlund et al. conducted a study by using 5-day food record of 25 CD children age 4-17 years on CFD. Thirteen over 25 children did not meet recommended energy intake (below new nordic nutrition recommendation). The dietary intake for CD children on GFD were inadequate regarding quality of macronutrients, mineral and vitamins. Sucrose and saturated fat were higher than recommendation, paradoxically with low fiber, polyunsaturated fatty acids, vitamin D and magnesium contain in GFP.[14] Study conducted by Zucotti et al in assessing dietary intake of 18 CD children age 4-10 years old on GFP with 18 healthy children in Italy. Energy intake in CD children on GFD was significantly higher than that of non-celiac children. The percentage lipid-derived energy was lower while carbohydrate derived energy was higher in CD compared to healthy children.[16] Kulai T et al also assessed nutritional adequacy in packaged GFP in Canada, the study showed comparable calories between GF and regular foods. Although the total calories were comparable, the GF breads were significantly higher in total fat and lower in protein and iron content compared with regular breads. While GF pasta was higher in carbohydrates, but lower in protein, fiber, sugars, iron, and folate content.[17] Gluten-free cereal foods are made using refined gluten-free flour or starch not enriched or fortified, so they are found to be rich in carbohydrates and fats only and low in fiber.[18]

Overall, GFD effects on intake of macronutrient and energy was more fat-derived energy than carbohydrate with higher saturated fatty acid than PUFA. While inadequate fiber was also observed in GFD. However, recent GFP made from pseudo-grains and alternative gluten-free grains like quinoa and buckwheat have equivalent fiber content with glutted contained product. Vitamin and minerals intake in GFD including B vitamin (thiamine, riboflavin, niacin) and folic acid were also did not meet the recommendation intake. While micronutrients intake such as iron were usually added to enrich GFP knowing iron deficiency is a common manifestation of untreated CD.[19] **Table 1** summarizes common nutrient deficiency concerns in CD and the diet.[20]

GFD effects on body antrophometry

Complete elimination of gluten in GFD enables small intestine mucosa to heal and resolving symptoms also nutritional deficiencies. But contrasting results were observed in CD subjects undergone CFD. Normalizaton of body antropometric were found in CD patients compliant with GFD.[9,21,22] A study in Brasil assessed nutritional profile of 31 CD patients followed GFD for at least one year showed no significant differences in weight, height, total body fat percentage, total muscle mass, and body mass index observed compared to healthy groups ($p > 0.05$).[23] CD children on GFP were less frequently obese than healthy control subjects and most of them (77%) reached a normal weight during GFD and none of the underweight subjects became overweight or obese.[24]

While study of 679 patients with GFD showed 15.8% patients moved from normal or low BMI class into overweight class and 22% of overweight patients at diagnosis gained weight after GFD. Risk of obesity of GFD is around the corner by combination of healing of intestinal mucosal which leads to better nutrition absorption and high-calorie intake of GFD mentioned above.[25]

Paradoxically, study by Ciacci et al had shown that patient following a strict gluten-free diet often suffer from various nutrient deficiencies described above. The study showed that long term strict GFD have significantly lower weight, body mass index, fat and lean body mass than control subjects.[26]

Dietary advice for children with CD

Parents' education and compliance

Life-long and strict GFD is important in pursuing mucosal healing and symptoms alleviation in CD. Strict adherence to gluten-free diet may be more challenging in children and adolescents than in adults. Non-compliance to GFD may be one of the major problem which depends not only on children but parents, notably parents knowledge. Garg et al research about predictors of compliance to GFD in CD children noted that only 65.67% children were dietary compliant to GFD. Parental influence was the main role of GFD compliance in children while environmental in adolescents age group. Parents difficulties were low level of knowledge, budget burden, and also psychological burden. While in adolescents, environmental issues were increased social interaction, increasing peer group pressure, increased outdoor activities, and need for experimentation.[11] Mother's education is a significant factor related with the compliance.[27]

Therefore, several ways to overcome these issue might be counselling aiming to increase disease knowledge (by physician) and awareness of parents regarding cheap and acceptable alternatives to wheat and easy to cook gluten-free food recipes will help ensure compliance to GFD in children (by dietician).[6] Baseline education to adolescent children undergoing peer-pressure affecting compliance is by support to children and parents.[27] Child positive behavior has significant higher degree compliance. [11,27]

Dietary composition of GFD

Ideal GFD should meet individual's nutritional needs and contain balance of macro and micronutrient. Daily recommendation for calorie intake in GFD does not differ with general population.[19] It contains 55% from complex and simple carbohydrates, 15% from dietary protein and 25%–30% or less from lipids.[6] Consumption of natural gluten free food is preferable due to balance nutrients composition, with higher nutrition value of energy, balance lipid composition and vitamin content compared to processed GFP. In GDF, main natural dietary source of protein are animal foods such as meat, milk and dairy products, eggs and fish. Plant foods sources of protein include legumes, nuts, seeds and gluten free cereals. Vegetable oils, nuts, seeds and higher fat fish including salmon, trout and herring are good source of mono saturated fats and omega-3 fatty acid.[28] Consuming iron and folic acid rich natural gluten-free food such as green vegetable, legume fish and meat are more preferable to meet micronutrient need individually.[6] To avoid micronutrient deficiencies in CD, natural source of vitamin and minerals such as fruits and vegetables should be increased. Natural gluten-free food is also cost affective which may increase GFD compliance.[29]

Pseudo-cereals and minor cereals are also frequently consumed in GFD. They are rich of minerals, such as calcium, phosphorus, sodium, potassium, chloride, and magnesium, and also iron, zinc and selenium.[30] They also are good source of carbohydrate, protein, fiber and PUFA. Superior quantity and quality of pseudo-cereals are listed in **Table 2**.

Consumption of pure oats without contamination to gluten may increase fiber, vitamin B, zinc, magnesium and iron supply in GFD.[5] Study by Størsund et al. in CD children suggested that oats may improve GFD nutritional value and compliance.[34] However, small number of people with CD may be intolerant to pure oats and develop immunological response to oat avenin (protein found in oats). Therefore, oat consumption in CD should be followed by monitor for signs and serological change.

Education should not only focus on gluten free natural food available as described above, but of special attention to commercially available GFP regarding labelling and chemical composition should also be done to parents. Since gluten-free cereal foods available are made using refined gluten-free flour or starch not enriched or fortified, so they are found to be rich in carbohydrates and fats only.[18] Thus, gluten free products should not just be gluten-free but comparable to gluten containing food in terms of nutritional profile and meet the recommended dietary allowance requirement.[29] Furthermore, some fortified GFP with vitamins and minerals are preferable than regular GFP.

Clear labelling of GFPs and education of CD patients on how to interpret them is important to help CD subjects make safer and more informed food choices. Food labelling of processed GFP should also be noticed due to several ways of labelling; "Gluten-free", "Free of gluten", "No gluten", "Without gluten". While they all describe food: made only from ingredients which do not contain prolamins from wheat with their crossbred varieties with gluten level not exceeding 20 ppm; or consisting of ingredients from wheat, rye, barley, oats, spelt or their crossbred varieties, which have been have been processed to remove gluten; with a gluten level not exceeding 20 ppm.[6,28,30]

Nutrition requirement for CD

At the time of diagnosis, parents and children should meet with a registered dietitian who is knowledgeable about CD and the GFD. The family and child (if at an appropriate age) should be educated regarding the negative consequences of untreated CD including nutrition related complications such as osteopenia and osteoporosis, iron deficiency anemia. Little is known about the nutritional quality of the GFD in children hence, their intake should also be reviewed for nutritional adequacy. Multivitamin with minerals should be recommended due to the malabsorption that occurred prior to the diagnosis. Nutrients of particular concern include calcium, iron, folate, thiamine and riboflavin as shown in **Table 3**.[35]

Conclusion

Gluten-free diet is the only accepted and available treatment in CD. It was a life-long treatment, if not carried out with attention, it may lead to nutritional imbalance which can affect children's growth and development. Parental education and physician advisory is crucial to achieve nutritionally adequate and balanced gluten-free diet accompanied by a positive support of children environment to improve GFD compliance. Food labelling of available GFP should also be paid special attention to monitor macro and micronutrient intake of CD patients. Therefore, there is an important need to develop gluten-free products that are highly nutritious and at the same time economical. Meanwhile, performing routine follow-up is also as important as commencing GFD to observe nutritional adequacy in CD patients. Frequent follow-up by medical professionals and participation in educational activities and support groups will not only encourage compliance and prevent future complications of untreated CD, but will also improve quality of life.

Table 1. Common nutrient deficiencies in CD.[20]

At Diagnosis	GFD	GFD Products	Long-term GFD
Calorie/protein			
Fiber	Fiber	Fiber	
Iron	Iron	Iron	
Calcium	Calcium		
Vitamin D	Vitamin D		
Magnesium	Magnesium		
Zinc			
Folate, niacin, vitamin B12	Folate, niacin, vitamin B12	Folate, niacin, vitamin B12	Folate, niacin, vitamin B12
Riboflavin	Riboflavin	Riboflavin	Riboflavin

Table 2. Advantageous nutritional composition of pseudo-cereals

Nutritional Characteristics of Amaranth, Buckwheat and Quinoa[31,32,33,34]
High fiber content, 7–10 g/100 g, approximately the same as wheat fiber 9.5 g/100 g
High content of essential amino acids: lysine, arginine, histidine, methionine and cysteine.
High degree of unsaturated fatty acids, α-linolenic acid (35-50% of total fatty acid, oleic acid (25-35% of total fatty acid), and palmitic acid.
High content of folic acid: quinoa and amaranth, 78.1 µg/100 g and 102 µg/100 g, respectively, vs. 40 µg/100 g in wheat.
Source of vitamins: B, B2, B6, vitamin C and E.
Source of minerals: Calcium, magnesium and iron, twice as high as in other cereals.

Table 3. Nutrition requirement of particular concern [35]

Nutrient	Age (years)	Recommended	Sources
Calcium	1-3	500 mg	1 c. milk = 300 mg
	4-8	800 mg	2 0z cheese = 400 mg
	9-18	1300 mg	6 oz yogurt = 300 mg
			3 oz almonds = 210 mg
Iron	1-10	10 mg	3 oz beef = 1.8 mg
	11-18 (M)	12 mg	3 oz chicken = 1 mg
	11-18 (F)	15 mg	½ c. spinach = 3.2 mg
			½ c. red kidney beans = 2.6 mg
			½ c. enriched rise = 1.2 mg
			½ c. Raisins = 1. 1 mg
Folate	1-3	150 mcg	½ c. Spinach = 130 mcg
	4-8	200 mcg	½ c. Navy bean = 125 mcg
	9-18	300 mcg	½ avocado = 55 mcg
			1 orange = 45 mcg
			1 oz peanuts = 30 mcg
Thiamin	1-3	0.5 mg	3 oz beef liver = 9.2 mg
	4-8	0.6 mg	Corn tortilla = 0.2 mg
	9-13	0.9 mg	½ c. Enriched rice = 0.2 mg
	14-18 (F)	1 mg	
	14-18 (M)	1.2 mg	
Riboflavin	1-3	0.5 mg	1 c. Milk = 0,45 mg
	4-8	0.6 mg	1 c. Yogurt = 0.45 mg
	9-13	0.9 mg	1 egg = 0.27 mg
	14-18 (F)	1 mg	Corn tortilla = 0.27 mg
	14-18 (M)	1.3 mg	3 oz ground beef = 0.16 mg

Conflict of Interest

Authors declared no conflict of interest regarding this article.

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