Muralidhar Jatla, M.D., Ritu Verma, M.D., Series Editors

Nutritional Complications of Celiac Disease

by Jennifer Autodore, Muralidhar Jatla

Celiac disease (CD), a common immune-mediated enteropathy, primarily affects the absorptive capacity of the small intestine, leading to concern for specific nutrient deficiencies. Factors contributing to its extent include length of time prior to formal diagnosis, extent of damage to the gastrointestinal tract, and degree of malabsorption (1). Many children present with overall poor growth rate, that includes mild to severe wasting as per percentage of ideal body weight or mild to severe stunting of growth as per percent of standard height for age. Weight loss may or may not be evidenced in the pediatric population. Prior to formal diagnosis, the child may also present with food refusal, anemia, and evidence of vitamin/mineral deficiencies. Iron, calcium, and folate are key nutrients often affected in those with celiac disease, as these nutrients are absorbed in the proximal small bowel. If the disease progresses further down the small intestinal tract, malabsorption of carbohydrates, fat and fat soluble vitamins (ADEK), protein, and other nutrients may also occur (2). Secondary lactose intolerance often results as the enterocytes at the tips of blunted villi are absent to produce the enzyme lactase (3). Nutrient deficiencies require immediate correction via the addition of a gluten-free multivitamin with minerals, protein, and other vitamin/mineral supplementation as identified, along with initiation of the gluten-free diet. The effectiveness of vitamin and mineral supplementation in the pediatric celiac population has not been thoroughly studied.

Jennifer Autodore, R.D., LDN, Pediatric Clinical Dietitian, Division of Gastroenterology and Nutrition, The Children's Hospital of Philadelphia, Philadelphia, PA. Muralidhar Jatla, M.D., Attending Physician, Section of Pediatric Gastroenterology, The Children's Hospital at Scott & White, Assistant Professor of Pediatrics, Texas A&M University Health Sciences Center College of Medicine, Temple, TX.

COMMON CAUSES OF ANEMIA IN CELIAC DISEASES

The most common cause of anemia in those with celiac disease is Iron, Folate, or Vitamin B_{12} deficiency. Iron is an essential trace element necessary for the production of hemoglobin (Hgb), a substance in red blood cells that enables the transport of oxygen from the lungs throughout the body. Fe deficiency can lead to a delay in normal infant motor function/mental function, reduced work performance, impaired behavioral and intellectual performance, impaired ability to maintain body temperature in cold environments, decreased resistance to infections, increased absorption of lead, and adverse outcomes during pregnancy (4). There are two chemical structures of iron: heme and non-heme. Heme iron is readily absorbed and consumed via animal sources (red meat, fish, and poultry). Non-heme iron is not as well absorbed and is found in fruits, vegetables, grains, and eggs. Iron intake can be maximized by choosing gluten-free alternatives that are higher in iron such as amaranth, buckwheat bran, montina flour, rice bran, and quinoa flour (5). Eating a source of heme iron and non-heme iron at the same meal is recommended. Vitamin C also increases the absorption of non-heme iron. Diets that include a minimum of five servings of fruits and vegetables daily should provide adequate Vitamin C to enhance non-heme iron absorption. On the contrary, calcium, polyphenols, tannins, phytates, and some proteins found in soybeans may inhibit non-heme iron absorption. The greatest influence on iron absorption is the amount stored in the body. Iron absorption increases when body stores are low and decreases when body stores are high to protect against toxicity.

Folate

Folate is derived from the Latin word folium, meaning "leaf," and is a form of the water soluble vitamin B_9. Folate is necessary for the production and maintenance of new cells, which is important during periods of rapid cell division and growth (4). Diarrhea, loss of appetite, weight loss, weakness, glossitis, headaches, heart palpitations, irritability, and behavioral disorders are classic signs of deficiency. In addition, folate deficiency may slow growth in infants and children. Deficiency can occur when an individual's need is increased, dietary intake is inadequate, and when the body excretes more folate that usual. Above all, folic acid is absorbed in the jejunum, which can become damaged in those with active CD. Certain medications also interfere with the body's ability to use folate, such as methotrexate.

When educating the newly diagnosed celiac patient, consumption of green leafy vegetables like spinach, dried beans and peas, fortified gluten-free cereal products/snack bars, sunflower seeds, cranberries, peanuts, and bananas should be promoted. A variety of gluten-free flours are available to aid in maximizing folate consumption such as corn flour, chestnut flour, soy flour, and garbanzo bean flour (5).

Vitamin B_{12}

Cyanocobalamin, vitamin B_{12}, along with folate is required for the formation and maturation of red blood cells and the synthesis of DNA (4). Vitamin B_{12} is necessary for normal nerve function and is absorbed in the ileum. In order to be absorbed, the vitamin must combine with intrinsic factor. Without intrinsic factor, vitamin B_{12} will pass through the intestine to be excreted in the stool (9). Deficiency occurs following inadequate consumption or when the body does not absorb or store enough of the vitamin. Mucosal changes are considered the major cause of B_{12} deficiency in the celiac population (6,7).

Vitamin B_{12} deficiency results in anemia, leading to paleness, weakness, fatigue, and sometimes shortness of breath and dizziness. Anemia may not develop until three to five years after the deficiency begins because a large amount of vitamin B_{12} is stored in the liver. Loss of sensation in the hands and feet, muscle weakness, loss of reflexes, difficulty walking, and confusion may also result. Signs of vitamin B_{12} deficiency in infancy include failure to thrive, movement disorders, and delayed development (8). Gluten-free sources of Vitamin B_{12} include meat, fish, poultry, eggs, and dairy products. One can maximize intake by incorporating clams, salmon, tuna, ground beef, yogurt, and milk into their diet (9).

In a study conducted by Haapalahti, et al, adolescents with celiac disease differed from healthy control subjects by having lower whole blood folate, serum ferritin and prealbumin concentrations, but higher serum transferrin receptor concentration (11). Almost fifty-percent of their celiac subjects had at least one abnormality in nutritional markers to include low serum ferritin, whole blood folate or serum vitamin B_{12}. One third of the celiac subjects had an elevated TfR-F Index, indicating a progression to anemia (11). This study reminds us that true deficiencies are difficult to demonstrate because of the complex association between ferritin, folic acid, and vitamin B_{12}. Folic acid can correct the anemia that is caused by vitamin B_{12} deficiency as serum ferritin is able to catabolize folate, resulting in decreased intracellular folate concentration (12). Folate requires vitamin B_{12} for activation, and low folate concentrations may attribute to vitamin B_{12} deficiency.

OTHER NUTRITIONAL DEFICIENCIES IN CD

There may also be deficits of fat-soluble vitamins (A, D, E, and K), as they are absorbed in the terminal ileum. This is due to the underlying fat malabsorption present with untreated or undiagnosed CD, along with poor dietary intake secondary to abdominal pain associated with eating. One may also experience excess losses of calcium, magnesium, zinc, and electrolytes in the stool if severe diarrhea and fat malabsorption are present. Recommended repletion doses vary based on age and severity of deficiency. Some fat is required in the diet to help the body absorb these vitamins. Vitamin A promotes healthy surface linings of the eyes, respiratory, urinary, and intestinal tracts. When those linings break down, it becomes easier for bacteria to enter the body and cause infection. Vitamin A also helps the skin and mucous membranes function as a barrier to bacteria and viruses. Animal sources of vitamin A include liver, beef, chicken, fortified milk, and cheese. Plant sources of vitamin A include carrot juice, carrots, spinach, cantaloupe, and kale (13). If vitamin A deficiency is identified, one must obtain a serum zinc level as zinc is required to make retinol binding protein, which is required in the transport of vitamin A from the liver to body tissues (4,13).

Vitamin D

Vitamin D is essential for promoting calcium absorption in the gut and maintaining adequate serum calcium and phosphate concentrations to enable normal mineralization of bone and prevent hypocalcemic tetany (14). It is also needed for bone growth and bone remodeling. Vitamin D deficiency may also lead to rickets in children. Very few foods naturally contain vitamin D. Salmon, tuna, mackerel and fish liver oils are among the best (14). Small amounts of vitamin D are also found in beef liver, cheese, fortified orange juice and egg yolks.

Vitamin E

Vitamin E is an antioxidant that protects body tissue from damage caused by free radicals that can harm cells, tissues, and organs. Existing in eight different forms, alphatocopherol is the most active form in humans (15). Vegetable oils, nuts, green leafy vegetables, and fortified gluten-free cereals are common food sources of vitamin E. More specifically, sunflower oil, sunflower seeds, almonds, corn oil, spinach, broccoli, kiwi, and mango are excellent sources (15). Vitamin K plays an important role in blood clotting. Individuals with known deficiency are usually more likely to have bruising and bleeding. Excellent food sources include cabbage, cauliflower, spinach and other green leafy vegetables, gluten-free cereals, soybeans, and other vegetables.

Calcium, Vitamin D, and Phosphorus

Calcium, vitamin D, and phosphorus are key nutrients required for the formation and maintenance of healthy bones and teeth. Deficiencies may occur as a direct result of malabsorption versus inadequate dietary intake due to secondary lactase deficiency. In most cases, lactase deficiency corrects on its own following strict adherence to the gluten-free diet over a six to eighteen month time period (1,5,6). Those diagnosed with celiac disease are considered at higher risk for developing bone disease and therefore should receive a DEXA scan (dual energy X-ray absorptiometry), quantitative CT scan, or computerized bone age estimation, along with obtaining serum calcium, alkaline phosphatase, and parathyroid hormone levels at time of diagnosis (1,17). A three-day diet record may also be obtained and run through a computerized nutrient analysis program to provide detailed macro- and micro-nutritional intake information. Along with increased Vitamin D intake, as previously discussed, one can maximize calcium intake by consuming no less than three dairy servings per day (yogurt, milk, American cheese, cheddar cheese, swiss cheese, ice cream, calcium fortified orange juice, beans, tofu, etc). General bone health guidelines also include limiting caffeine, staying active, not smoking, and adhering to a strict gluten-free diet. Not all individuals are able to meet the Recommended Daily Intake for calcium and vitamin D and therefore, may require oral supplementation (1,16,17).

Research at the Children's Hospital of Philadelphia reveals that children newly diagnosed with CD may benefit from DEXA screening for low bone mineral content (18). Patients with low BMI and those with advanced histologic damage may be at particular risk for osteopenia. Specifically, children with CD were shorter than children of similar age and sex. Spine and whole body bone mineral content for age Z-scores were significantly lower in the CD group compared to controls. When adjusted for height, significant deficits in whole-body bone mineral content persisted in CD patients. Low spine and whole bone mineral content correlated with advanced histologic grade in CD. Low BMI correlated with low whole body bone mineral content in CD.

(continued on page 39)

(continued from page 36)

A survey conducted in 2002 looked at nutrient intake and food consumption patterns of adults with CD following a GFD. Based on three-day diet records obtained and analyzed from 39 female American and eight male American adults, suboptimal quantities of fiber, iron, calcium, and grain foods were consumed (19). A somewhat similar survey was conducted in Manchester, England that analyzed three-day diet records of 49 survey respondents who were found to have overall lower caloric intake, low intake of non-starch polysaccharides, vitamin D, and calcium in comparison to the British general population. This survey also revealed that survey respondents consumed a lower amount of total calories from fat as opposed to protein calories (20). In January 2000, the Dutch Celiac Society asked 395 of its members between the ages of 12 and 25 to complete a food record and questionnaire. Nutrient intake was analyzed and compared to the general population in the Netherlands, revealing significantly lower consumption of fiber and iron. On the contrary, it showed elevated intake of saturated fat in comparison to healthy guidelines, similar to the general population (21).

CONCLUSION

In conclusion, further studies need to be conducted to evaluate nutritional adequacy in both the pediatric and adult celiac populations. Nutrition assessments and gluten-free diet education provided by registered and licensed expert dietitians should not focus only on which foods to avoid but highlight the nutritional quality of foods consumed that are important in the prevention of nutrient deficiencies. Gluten-free multivitamins with mineral supplementation may also aid in the prevention and correction of vitamin and mineral deficiencies along with oral nutritional supplementation if malnutrition is evident. Expert education will allow for the celiac population to make well informed decisions regarding nutritional intake. ■

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