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Frequency of Sucrase Deficiency in Mucosal Biopsies

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Carbohydrates, sugars, and starches are an important source of energy, especially for the brain, which is completely dependent on glucose for energy (1). The US Department of Agriculture recommends that carbohydrates provide 45% to 65% of daily energy units (2) and the dietary reference intakes set the adequate

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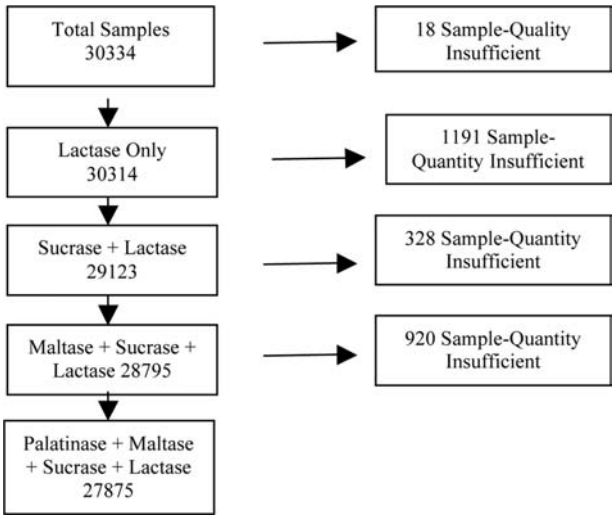

FIGURE 1. The samples varied widely in size of tissue and condition on arrival. Eighteen of the samples were insufficient or were received in a compromised state, so the assay could not be performed. For 1191 of the 30,314 samples, either a lactase-only level was ordered or the quantity was not sufficient to perform the other disaccharidase assays. Of the remaining samples, there was adequate tissue to perform the sucrase, maltase, and palatinase assays and protein level in 27,875.

intake at 60 to 130 g/day, depending on age (1). Cells can avail themselves of this energy source only when it is in the form of a simple sugar. Carbohydrates present to the gastrointestinal tract for digestion and absorption as monosaccharides, disaccharides, oligosaccharides, and polysaccharides. Initial digestion occurs via enzymes secreted into the lumen, but for absorption, carbohydrates must be in the form of a single sugar. The final digestion of disaccharidases occurs by enzymes located on the brush border of the enterocyte. The brush border contains the disaccharidases lactase, sucrase, isomaltase, and trehalase that hydrolyze lactose to glucose and galactose, sucrose to glucose and fructose, maltose to 2 glucose molecules, and trehalose to 2 glucose molecules. Deficiency in any of these enzymes results in malabsorption of the disaccharidase and can be associated with various symptoms. Deficiency can occur because of a congenital lack of the enzyme, injury to the enterocyte, or, in the case of lactase, as a normal process of aging. Congenital sucrose-isomaltase deficiency is an autosomal recessive disorder that is considered to be rare, occurring in 5% of the native populations of Greenland, Alaska, and Canada, but in only 0.02% in North Americans of European descent. Because symptoms vary from severe to mild, however, the incidence may be much higher. To assess how frequently sucrase-isomaltase deficiency is found in endoscopic biopsies, we reviewed the results of biopsies assayed for disaccharidases in a reference laboratory.

METHODS

Disaccharidase analyses were performed on small bowel biopsies according to the method of Dalqvist (3). Briefly, the tissue was homogenized and then the respective substrate, lactose, sucrose, maltose, or palatinose, was added. The amount of glucose produced was quantified with a Beckman DU 800 spectrophotometer (Beckman Coulter, Jersey City, NJ). Protein was quantified according to the method of Lowry et al (4).

The log books of all of the disaccharidase analyses performed between January 1, 2006 and July 29, 2011, were reviewed. Information on the following categories was included in the data collection and entered into a Microsoft Excel database: date of birth, date of analysis, age at time of analysis, and results of assays for lactase, sucrose, maltase, and palatinase. Data were imported from the Microsoft Excel database into the SAS software package (SAS Institute, Cary, NC). Descriptive statistics were generated using frequency tables.

RESULTS

From January 1, 2006 through July 29, 2011, the laboratory received 30,334 samples. The samples varied widely in size of tissue and condition on arrival. Of those samples, 18 were insufficient or were received in a compromised state, so the assay could not be performed. For 1191 of the 30,314 samples, either a lactase-only level was ordered or the quantity was not sufficient to perform the other disaccharidase assays. Of the remaining samples, there was adequate tissue to perform the sucrase, maltase, and palatinase assays and protein level in 27,875 (Fig. 1). The age or date of birth was not provided for 41 samples.

Table 1 shows the number of analyses performed for each of the disaccharidases, and Table 2 shows the total number of samples that were deficient in each enzyme. Disaccharidase deficiencies were found in fewer than half of the samples; most were sufficient in all of the enzymes tested. The most common deficiency was lactase, followed by pandisaccharidase deficiency. Of note, 9.3% of the patients were deficient in sucrase and maltase, but within this group, 86% had pandisaccharidase deficiency. Consistent with the literature, the classical signature activities of congenital sucrose-isomaltase deficiency, extremely low sucrose with normal lactase, were rare, occurring in 0.1% of the samples.

DISCUSSION

Disaccharidase deficiencies are clinically associated with diarrhea, bloating, flatulence, and abdominal pain. Relief of symptoms is achieved by avoidance of the disaccharide or, in the case of lactase or sucrase deficiency, concurrent ingestion of supplemental lactase or sucrase with the sugar. These supplemental enzymes are beneficial for individuals with congenital enzyme deficiencies, but

TABLE 1. Number of analyses with mean and standard deviation

Variable	No. analyses	Mean	Median	Standard deviation	Minimum	Maximum
Age, y	30,281	11.00	11.17	7.21	0	93.5
Lactase, $\mu mol \cdot min^{-1} \cdot g^{-1}$ protein	30,314	21.80	17.50	19.11	0	173
Sucrase, $\mu mol \cdot min^{-1} \cdot g^{-1}$ protein	29,123	56.49	53.40	27.77	0	241
Maltase, $\mu mol \cdot min^{-1} \cdot g^{-1}$ protein	28,795	167.59	161.80	67.63	0	767
Palatinase, $\mu mol \cdot min^{-1} \cdot g^{-1}$ protein	27,875	11.31	9.9 0	6.74	0	156.4

TABLE 2. Frequency of enzyme deficiencies

Lactase	Sucrase	Maltase	Palatinase	N	%	Mean age, y	Median age, y	Standard deviation
Normal	Normal	Normal	Normal	15,265	54	10.2	10.3	7.0
Deficient	Deficient	Deficient	Deficient	2347	8	11.1	11.4	6.5
Normal	Deficient	Normal	Normal	11	0.04	11.7	12.0	6.3
Normal	Deficient	Deficient	Normal	30	0.1	10.2	11.2	5.2
Normal	Deficient	Deficient	Deficient	149	0.5	8.9	8.9	7.0
Normal	Normal	Deficient	Normal	264	1.0	9.7	10.5	6.5
Normal	Normal	Normal	Deficient	3	0.001	5.0	2.0	5.3
Deficient	Normal	Normal	Normal	8963	32	12.6	12.6	7.5
Deficient	Normal	Deficient	Normal	662	2.3	11.9	12.1	6.5
Deficient	Deficient	Normal	Normal	17	0.06	11.3	11.7	4.6
Total sucrase deficiency				2603	9.3			

Normal = Lactase >10 μmol · min^{-1} · g^{-1} protein, sucrose >25 μmol · min^{-1} · g^{-1} protein, maltase $>160.8 \pm 62.8$ μmol · min^{-1} · g^{-1} protein, palatinase $> 11.1 \pm 6.5$ μmol · min^{-1} · g^{-1} protein. Deficient = lactase ≤ 10 μmol · min^{-1} · g^{-1} protein, sucrase ≤ 25 μmol · min^{-1} · g^{-1} protein, maltase ≤ 100 μmol · min^{-1} · g^{-1} protein, palatinase ≤ 5 μmol · min^{-1} · g^{-1} protein.

they may also offer relief for transient deficiencies such as may occur with small bowel injury.

The strengths of these data lie in the large sample size that is nationally representative and the consistent and experienced personnel who performed the analyses; the enzyme assay has been in use and has not changed in decades. The weaknesses of these data lie in the lack of clinical correlation, the selection by the endoscopists of a young age group from which samples were obtained, the inability to control for sample integrity throughout the entire process of obtaining the samples, and handling and shipping. The analyses were performed manually, and human error is always a possibility. We conclude that the most common disaccharidase deficiency is lactase followed by pandisaccharidase. Sucrase deficiency was rare in these samples.

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Phenotypic Observations by the CSID Dietary and Medical Support Group

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For 16 years, the congenital sucrase-isomaltase deficiency (CSID) parent support group has followed 7433 individuals diagnosed by small bowel biopsy with CSID: children (848 ages 0 to 2 years, 1722 ages 3 to 4 years, 1241 ages 5 to 8 years, and 2422 ages 9 to 17 years), adults (1200), and >44,000 blood-related relatives. Based on small bowel biopsy results and detailed clinical dietary history, 5 different clinical phenotypes have been proposed for which specific diet regimens have been developed. Patients following these diets report significant improvement in their symptoms. This article provides a brief overview of the proposed phenotypes and diet recommendations identified by the parent support group. Available enzyme therapies are discussed.

PROPOSED PHENOTYPES BASED ON INTESTINAL DISACCHARIDASE ACTIVITY AND DIETARY TOLERANCES

Table 1 identifies the proposed clinical phenotypes based on the reduction in small intestinal disaccharidase activities and dietary tolerance among those patients with CSID followed by the support group. The range of mucosal biopsy activities is taken from Table 2, which summarizes 3 patterns of CSID disaccharidase mucosal enzyme deficiencies described in the literature (1–7) and in this workshop (8–11) and makes a tentative correlation with the dietary tolerances in Table 1. One goal of future research is to confirm whether these 5 dietary phenotypes correlate with 3 mutant genotypes of SI. The enzymatic recognition of SCID is presently limited to biopsies with lactase activities >10 enzyme units (1–10), but there may be others within the large group of sucrase deficiencies with lactase activities falling below this level that await identification by new methods of genetic analysis (12).

DIETARY INTOLERANCES

None of the patients in any of the phenotypes can tolerate the following sweeteners: hydrogenated glucose syrup, galactose/maltose/malt sugar, acesulfame K, maltitol/maltitol syrup, brown rice syrup, NutraSweet/neotame, or Stevia/diterpene glycosides. Sucrose can be tolerated in only extremely small amounts without enzyme supplementation, whereas crystalline glucose, dextrose,

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