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Relationships among Dietary Intakes and Persistent Gastrointestinal Symptoms in Patients Receiving Enzyme Treatment for Genetic Sucrase-Isomaltase Deficiency

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ABSTRACT

Background Sucrose-isomaltase deficiency (SID) remains underdiagnosed. Absent or reduced enzyme activity promotes diarrhea, abdominal bloating, and flatulence from undigested and malabsorbed disaccharides. Frequency and severity of gastrointestinal symptoms may be associated with the type of carbohydrates consumed.

Objective To characterize the dietary intakes of patients treated with sacrosidase (Sucraid; QOL Medical) for SID and determine relationships between type of carbohydrates, sacrosidase dose, and gastrointestinal symptoms.

Design A prospective 30-day observational study.

Participants/setting Forty-nine patients treated with sacrosidase for ≥3 months were recruited from the enzyme manufacturer's nationwide clinical database between November 2014 and August 2015.

Main outcome measures Dietary energy and nutrient intakes reported during 24-hour diet recall interviews, frequency and severity of gastrointestinal (GI) symptoms, and sacrosidase dose.

Statistical analyses performed Relationships between nutrient intakes, sacrosidase dose, and GI symptoms were evaluated using Spearman ρ correlation coefficients.

Results Sacrosidase dose averaged 5.2±3.1 mL/day. Participants reported 1.3±0.9 bowel movements daily. Having less frequent GI symptoms was associated with higher sacrosidase intake. Energy intakes averaged 1,562.5±411.5 kcal/day in children, 1,964.7±823.6 kcal/day in adolescents, and 1,952.6±546.5 kcal/day in adults. Macronutrient composition averaged 44% carbohydrate, 39% fat, and 17% protein. Average carbohydrate composition was 35% starch, 8% fiber, and 59% sugars. Sucrose and fructose intakes were not associated with GI symptoms. Lactose intake was associated with diarrhea. Maltose intake was associated with nausea, distension, and reflux.

Conclusions Intakes were lower in carbohydrates and higher in fat compared with the Acceptable Macronutrient Distribution Ranges. Sucrose and fructose intakes were not associated with GI symptoms. Higher maltose and lactose intakes were associated with GI symptom frequency and severity. These findings provide evidence to guide nutrition counseling for patients treated for SID.
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SUCRASE-ISOMALTASE DEFICIENCY (SID) IS MOST often an inherited disorder where genetic variants in the sucrase-isomaltase (SI) gene cause protein transport errors resulting in the absence or insufficiency of the disaccharidases sucrase and isomaltase at the brush border of the small intestine lumen. Maltase activity is also reduced because SI accounts for 60% to 80% of its activity in the brush border.[1] Consequently, these maldigested carbohydrates enter the colon, causing excess bacterial fermentation resulting in abdominal distension, cramping, pain, excessive flatulence, and osmotic diarrhea. If untreated, SID leads to inadequate growth and failure to thrive in children as well as weight loss and malnutrition in adults.[2-6]

SID is not typically part of the diagnostic algorithm for managing chronic diarrhea until more common etiologies, such as chronic nonspecific diarrhea (ie, toddler's diarrhea) or irritable bowel syndrome, are explored.[5,7,8] In addition to true congenital SID, an increasing number of patients may have secondary SI deficiency resulting from physical injury of the intestinal brush border, villus atrophy from autoimmune disorders such as celiac disease, or as a result of gastrointestinal infection.[9,10] Medical nutrition therapy using a

low-sucrose/low-starch diet is effective in reducing the frequency and severity of gastrointestinal symptoms. However, the extreme restrictiveness of the diet promotes poor long-term compliance.[5] In combination with a less-severe dietary regimen, an oral sucrase enzyme replacement, sacrosidase (Sucraid; QOL Medical), which hydrolyzes sucrose, has shown efficacy with regard to resolving abdominal cramping, bloating, gas, and watery diarrhea.[4,5,11,12]

Despite these treatment options, some patients treated for SID continue to experience gastrointestinal distress. To our knowledge, no studies have characterized the composition of typical dietary intake in patients treated for SID and whether the intake of specific foods or nutrients contributes to lingering gastrointestinal symptoms once diagnosis and combination treatment have been implemented. The purpose of the present study was to characterize the dietary intakes of children and adults who were being treated with sacrosidase for SID, identify nutrient inadequacies by comparison to the Dietary Reference Intakes, and determine relationships between the amount and types of carbohydrates consumed, sacrosidase dose, and persistent gastrointestinal symptoms.

MATERIALS AND METHODS

Written informed consent was provided and a central institutional review board along with the Vanderbilt University Medical Center Institutional Review Board approved the study protocol. From November 2014 to August 2015, 66 patients were recruited from QOL Medical's nationwide clinical database of patients being treated with sacrosidase and by study advertisement accompanying sacrosidase home shipments. All patients in the database had previously provided a waiver for Health Insurance Portability and Accountability Act authorization for research recruitment. Potential participants were screened by the study team for meeting inclusion criteria that they had been undertaking sacrosidase treatment for ≥3 months, were English speakers, and had a mobile device to enable using the Trial Guide (mProve Health, Arlington, VA) application for providing medication use and gastrointestinal symptom data electronically.

At enrollment, participants were instructed to maintain their current diet and physical activity for the 30-day observational period. Newly prescribed sacrosidase patients typically receive counseling from a registered dietitian nutritionist (RDN) to eliminate sucrose and starch from their diet for 2 weeks while starting sacrosidase therapy and then gradually reintroduce these foods to establish sucrose and starch tolerance. Demographic data (age, sex, race, height, and weight) were self-reported via an online Family Health Questionnaire during the first week of the study (Table 1). A parent or family caregiver provided primary data for participants younger than age 11 years and assisted with data collection for those aged 11 to 17 years.

During the observation period, participants completed three 24-hour diet recall interviews that included obtaining information regarding dietary supplement use. Diet recalls were conducted on 2 weekdays and 1 weekend day and were performed over the telephone by one RDN from the Vanderbilt Diet, Body Composition, and Human Metabolism Core who was trained in using the US Department of Agriculture multipass methodology.[13-15] A food amounts booklet was provided to participants at enrollment to assist with portion size estimation. For safety purposes, participants were instructed that in the case that they noticed a change in gastrointestinal symptom frequency or severity they should telephone the Vanderbilt Diet, Body Composition, and Human Metabolism Core to report their prior 24-hour intake,

Table 1. Characteristics of 49 individuals being treated for sucrase-isomaltase deficiency who participated in an observational study of dietary intake, sacrosidase use, and gastrointestinal symptoms

Characteristic	n	%	Age	BMI[a]	*z* score	Sacrosidase dose (mL/d)[b]
Sex						
Male	32	65.3	—	—	—	—
Female	17	34.7	—	—	—	—
Race/ethnicity						
White, non−Hispanic	44	89.8	—	—	—	—
Other	5	10.2	—	—	—	—
Life stage group[c]						
Age 1-3 y[d]	9	18.4	2.0±0.9	16.2±1.8	−0.07±1.4	4.0±2.1
Age 4-8 y[d]	17	34.6	5.8±1.6	16.0±2.3	−0.85±2.8	6.2±4.0
Age 9-18 y[d]	14	28.6	12.9±1.9	19.2±4.3	−0.31±1.5	6.7±2.9
Age ≥19 y	9	18.4	27.6±10.4	26.0±5.1	—	3.9±2.5

[a]BMI=body mass index.

[b]At the time of this study, Sucraid (QOL Medical) was listed in the Food and Drug Administration's Drug Shortages Database. To avoid a drug shortage, QOL Medical the Food and Drug Administration made Sucraid lots available under a consent process, requiring both the prescribing physician and the patient (or primary caregiver) to sign a consent waiver. Three of 49 participants in this study received one of the consented Sucraid lots while enrolled. None have reported adverse reactions or events.

[c]Life stage group as defined in the Dietary Reference Intakes with age ranges of 1 to 3 years, 4 to 8 years, 9 to 13 years, 14−18 years, and ≥19 years. The 9 to 13 years and 14 to 18 years age groups were collapsed into one adolescent group yielding four life stage categories due to limited sample size.

[d]A parent or family caregiver provided primary data for participants younger than age 11 years and assisted with input for those aged 11 to 17 years.

Table 2. Average energy and nutrient intake from three 24-hour diet recalls acquired from 49 individuals being treated for sucrase-isomaltase deficiency (SID) by life stage group[a]

3-d Averages	Life Stage Group											
	Age 1-3 y			Age 4-8 y			Age 9-18 y			Age ≥19 y		
Nutrients	Mean±SD[b]	EAR[c]	RDA[d]	Mean±SD	EAR	RDA	Mean±SD	EAR	RDA	Mean±SD	EAR	RDA
Energy (kcal)	1,259.9±366.6			1,722.7±544.9			1,964.7±823.6			1,952.6±546.5		
Total fat (g)	55.6±17.2		ND[e]	74.5±30.5		ND	96.4±64.0		ND	355.3±42.0		ND
Total carbohydrate (g)	142.8±68.1	100	130	200.8±68.2	100	130	204.1±98.6	100	130	193.0±46.1	100	130
Total protein (g)	54.8±26.4		13	69.9±34.0		19	80.0±51.4		34-52	84.9±33.4		46-56
Calories from fat (%)[f]	39.9±9.5		30-40	37.0±9.0		25-35	41.0±12.7		25-35	39.3±11.3		20-35
Calories from carbohydrate (%)[f]	42.0±12.1		45-65	46.4±9.2		45-65	42.4±17.3		45-65	39.4±8.7		45-65
Calories from protein (%)[f]	18.1±7.5		5-20	16.6±5.6		10-30	16.6±8.9		10-30	18.0±6.2		10-35
Total dietary fiber (g)	9.0±5.6		19[g]	14.0±8.1		25[g]	17.5±9.2		25-38[g]	17.3±6.6		25-38[g]
Soluble dietary fiber (g)	2.8±2.2			4.4±2.7			4.7±2.7			4.3±1.9		
Insoluble dietary fiber (g)	6.3±3.9			9.6±5.8			12.8±7.5			12.7±5.8		
Starch (g)	16.6±20.0			75.4±50.0			80.4±59.4			55.9±30.5		
Total sugars (g)	109.0±67.9			98.7±54.2			88.2±48.7			95.4±42.0		
Added sugars (g)	56.6±61.1			37.8±32.6			42.2±40.4			47.8±28.4		
Calories from added sugars (%)[f]	18.0		≤25	9.0		≤25	9.0		≤25	10.0		≤25
Total grains (oz equivalents)	1.2±1.5			5.3±4.6			5.4±4.8			3.0±1.8		
Whole grains (oz equivalents)	0.4±0.6			1.0±1.4			1.3±1.3			0.4±0.6		
Refined grains (oz equivalents)	0.8±1.0			4.3±4.5			4.2±4.1			2.6±1.8		
Sucrose (g)	16.1±15.5			27.5±19.9			24.3±16.1			27.0±20.3		
Glucose (g)	42.6±54.8			26.9±22.5			25.9±20.7			31.8±25.4		
Fructose (g)	19.0±14.8			19.1±14.9			23.9±20.7			19.8±14.6		
Lactose (g)	30.0±35.6			16.8±18.2			9.2±15.0			10.5±12.2		
Galactose (g)	0.2±0.3			5.3±10.5			1.4±3.2			2.2±5.3		

(*continued on next page*)

Table 2. Average energy and nutrient intake from three 24-hour diet recalls acquired from 49 individuals being treated for sucrase-isomaltase deficiency (SID) by life stage group[a] (*continued*)

3-d Averages	Life Stage Group											
	Age 1-3 y			Age 4-8 y			Age 9-18 y			Age ≥19 y		
Nutrients	Mean±SD[b]	EAR[c]	RDA[d]	Mean±SD	EAR	RDA	Mean±SD	EAR	RDA	Mean±SD	EAR	RDA
Maltose (g)	2.6±5.0			2.3±2.2			4.4±4.1			3.7±5.5		
Potassium (mg)	1,711.6±370.9		3,000[g]	2,262.0±982.9		3,800[g]	2,400.4±1003.4		4,500-4,700[g]	2,781.6±451.8		4,700[g]
Calcium (mg)	1,067.3±376.4	500	700	1,194.1±715.9	800	1,000	889.2±522.7	1,100	1,300	1,131.1±503.2	800-1,000	1,000-1,200
Folate (μg)	175.4±45.7	120	150	322.0±107.1	160	200	305.7±136.0	250-330	300-400	312.9±106.7	320	400
Magnesium (mg)	158.1±43.4	65	80	247.6±132.2	110	130	283.7±136.3	200-340	240-410	300.5±69.3	255-350	310-420
Vitamin B-6 (mg)	1.0±0.2	0.4	0.5	1.5±0.8	0.5	0.6	1.6±0.5	0.8-1.1	1-1.3	1.8±0.4	1.1-1.4	1.3-1.7
Vitamin B-12 (μg)	4.4±1.3	0.7	0.9	4.5±2.8	1.0	1.2	4.5±3.9	1.5-2.0	1.8-2.4	4.4±1.6	2.0	2.4
Iron (mg)	9.8±6.0	3.0	7	11.1±4.9	4.1	10	12.2±4.1	5.7-7.9	8-15	12.3±6.9	5-8.1	8-18
Thiamin (mg)	0.8±0.2	0.4	0.5	1.4±0.6	0.5	0.6	1.3±0.7	0.7-1.0	0.9-1.2	1.2±0.3	0.9-1.0	1.1-1.2
Vitamin C (mg)	67.2±44.8	13	15	57.3±38.8	22	25	60.4±43.0	39-63	45-75	114.4±72.6	60-75	75-90
Vitamin D (mg)	8.6±3.7	10	15	7.3±5.8	10	15	6.0±7.2	10	15	8.2±5.6	10	15-20

[a]Life stage group as defined in the Dietary Reference Intakes with age ranges of 1 to 3, 4 to 8, 9 to 13, 14 to 18, and ≥19 years. The 9 to 13 years and 14 to 18 years age groups were collapsed into one group yielding four life stage categories due to limited sample size.
[b]SD=standard deviation.
[c]EAR=Estimated Average Requirements.
[d]RDA=Recommended Dietary Allowances.
[e]ND=not determined.
[f]AMDR=Acceptable Macronutrient Distribution Ranges.
[g]Adequate Intake.

sacrosidase use, and symptom information. Dietary intake data were entered into Nutrition Data System for Research version 2014 (University of Minnesota Nutrition Coordinating Center) for analysis.

On the same days as the diet recalls, participants and caregivers were interviewed by the study RDN regarding dose, time, and frequency of sacrosidase intake. Gastrointestinal symptoms were assessed using a questionnaire developed for this study by adapting questions from other previously validated bowel symptom questionnaires.[16,17] The gastrointestinal symptom questionnaire consisted of eight items (abdominal pain, bowel movements, burping, gas, bloating, vomiting, nausea, and reflux) measured on a scale where zero=none and 10=severe. Stool consistency was assessed using the Bristol Stool Formation Scale that incorporates age-appropriate pictures to determine consistency on a 7-point scale.[18]

Statistical Analysis

Analyses were performed using SPSS software version 23.[19] Participants' descriptive data (eg, age, sex, weight, and body mass index) and gastrointestinal data were analyzed for means and frequencies by life stage category as defined in the Dietary Reference Intakes with age ranges of 1 to 3 years (young child group), 4 to 8 years (child group), 9 to 13 years (young adolescent group), 14 to 18 years (adolescent group), and ≥19 years (adult group).[20] The 9 to 13 years and 14 to 18 years age groups were collapsed into one adolescent group, yielding four life stage categories due to limited sample size. The diet recall data was averaged for comparison to the Estimated Average Requirements and Recommended Daily Allowances or Adequate Intake by sex and life stage group.[20] Relationships between nutrient intakes, sacrosidase dose, and gastrointestinal symptoms were assessed by Spearman ρ correlation coefficients with significance set at $\alpha<.05$.

RESULTS

Of 66 potential participants being treated with sacrosidase for SID, 12 failed the screening criteria. This resulted in 54 enrolled participants. Of the 54, five participants were discontinued because they could not meet deadlines for completion of diet recall interviews and gastrointestinal symptom questionnaires. Thus, data were analyzed for 49 patients (26 children, 14 adolescents, and nine adults) who completed the study protocol (Table 1).

Comparison of participants' reported energy and nutrient intakes to recommended values are presented in Table 2. Energy intakes averaged 1,259.9±366.6 kcal/day in young children, 1,722.7±544.9 in children, 1,964.7±823.6 kcal/day in adolescents, and 1,952.6±546.5 kcal/day in adults. Of calories consumed, carbohydrate intake ranged from 39.4% to 46.4% of calories and fat intake ranged from 37.0% to 41.0% of calories. Of total carbohydrate intakes, sucrose comprised 11.3% in the young child group, 13.7% in the child group, 11.9% in the adolescent group, and 14% in the adult group (see the Figure). Added sugars ranged from 7% to 18% of energy intakes, with the highest percentage of added sugars intake in the child group. Total dietary fiber intake was low based on AI values for all life stage groups, with only 22% of the young child group, 18% in the child group, 14% in the adolescent group, and 22% in the adult group having met recommended intakes (Table 2). Overall, refined grains were being consumed two to four times as much as whole grains. Almost all (96%) participants had inadequate intakes for potassium. In addition, analysis of diet and supplement intakes showed that fewer than half of adolescent and adult participants had adequate intakes of calcium, magnesium, and folate based on the Estimated Average Requirement and Recommended Daily Allowances values.

Sacrosidase dose (prescribed as split dose to be taken half before meals and half during meals) averaged 4.0±2.1 mL/day in the young child group, 6.2±4.0 mL/day in the child group, 6.7±2.9 mL/day in the adolescent group, and 3.9±2.5 mL/day in the adult group. Sacrosidase was taken daily at the total dose prescribed for 89% of young child participants, 100% of child and adolescent participants, and 89% of adult participants. Participants reported an average of 1.6±0.9 bowel movements per day. Overall, a higher intake of sacrosidase was associated with having less frequent and less severe gastrointestinal symptoms (nausea severity $r=-0.76$ and $P=0.03$, distension severity $r=-0.64$ and $P=0.04$, flatulence $r=-0.41$ and $P=0.02$, and diarrhea $r=-0.44$ and $P=0.02$).

In the young child group, stomach pain was the most frequently reported symptom with an average severity score of 3.6±2.4. In the child and adolescent groups, excessive burping and flatulence were the most frequently reported symptoms. In the adult group, stomach pain, distension, and nausea were most frequently reported with severity scores of 3.9±3.1, 4.8±2.6, and 6.0±1.2, respectively. Gastrointestinal symptoms were not associated with total carbohydrate, starch, fiber, total sugars, sucrose, or fructose intakes (all P values >0.28). However, greater lactose intake was significantly associated with more episodes of diarrhea ($r=0.44$; $P=0.002$), especially in the young child group ($r=0.90$; $P=0.003$). One participant from the young child group, three from the child group, four adolescents, and three adults had diagnosed lactose intolerance. Higher intake of maltose was associated with more nausea ($r=0.58$; $P=0.007$), abdominal distension ($r=0.34$; $P=0.02$), and reflux ($r=0.75$; $P<0.001$), particularly in the adult group. The foods contributing most to maltose intakes were breakfast cereals, sweet potato chips, maple pancake syrup, tortilla, and peanut butter snack bars.

DISCUSSION

Prior information on the dietary intakes of patients treated for SID in relation to gastrointestinal symptoms and sacrosidase use has been limited.[21] Consequently, no evidence-based dietary guidelines exist for clinical practice. The findings from the present data provide novel evidence of the characteristics of typical dietary intake of patients being treated with sacrosidase and potential nutrient inadequacies. Further, several interesting relationships between dietary intakes, sacrosidase dose, and gastrointestinal symptoms were observed.

In the present study, most participants were taking their prescribed sacrosidase dose daily, which ranged from 3.9 to 6.7 mL/day. Study participants restricted dietary starch and sugars to the extent that their total carbohydrate intake on average was 42.5% of energy, lower than the recommendation of 45% to 65% of total energy intake.[20] In addition to total carbohydrate, participants' starch intake was lower than more typical American diets, ranging from only 11.6% to 39.4%

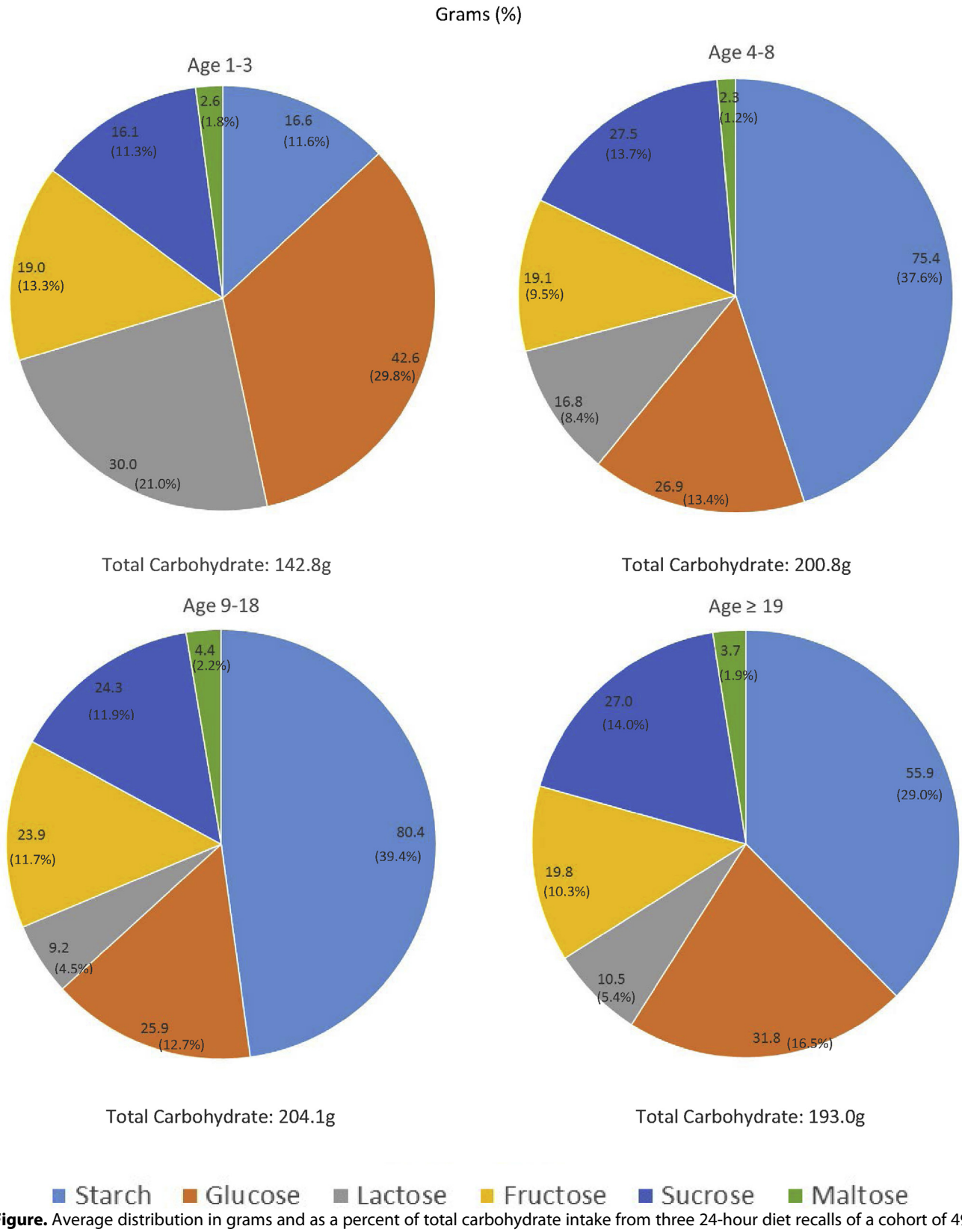

Figure. Average distribution in grams and as a percent of total carbohydrate intake from three 24-hour diet recalls of a cohort of 49 patients with sucrase-isomaltase deficiency by life stage group.

of total carbohydrates. Calculations based on National Health and Nutrition Survey data indicate starch intake usually averages 49% of total carbohydrates.[22] The lower contribution of carbohydrates to total energy intake was compensated by a higher percentage of energy from dietary fat. Participants in the young child group averaged 40% of total energy from fat and those in the other age groups averaged 39% of total energy from fat intake.[20] It is not known if the alteration in the proportion of carbohydrate to fat as a percentage of energy poses any chronic disease risk for participants. Although low-fat diets have been the cornerstone for primary prevention for much chronic disease risk reduction for many decades, more recent evidence and guidelines promote greater attention to the type (vs amount) of fat consumed.[23-25] With regard to type of fat, participants averaged a higher saturated to unsaturated fat intake ratio (0.63) compared with the general population (0.55 in those aged $\geq$2 years).[20]

The finding that sucrose intakes were not associated with gastrointestinal symptoms supports that participants were restricting their dietary intakes and taking their sacrosidase as prescribed. The present findings are also consistent with prior evidence that the combination of sacrosidase treatment with restricted sucrose and starch intake provides gastrointestinal symptom relief.[4,5,10,12] However, an unusual finding was that both maltose and lactose intakes (sugars not hydrolyzed by sacrosidase) were associated with more frequent symptoms in all life stage groups. The average maltose intake (2.9 g/day in children and 4.4 g/day in adolescents and adults) was associated with greater episodes of nausea, abdominal distention, and reflux. In general, maltose is not a large component of whole foods; thus, it derives as a byproduct of starch digestion. However, maltose is the primary sugar used in making barley malt, corn syrup, and rice syrup, which are ingredients in many processed foods.[26] Maltose is also present in some infant formulas, in malted foods and beverages, is used to make bread and brew beer, and can be added to food items to extend shelf life. Lactose intake was also associated with increased gastrointestinal symptoms, specifically diarrhea. It should be noted that 25% of study participants reported having lactose intolerance. Understanding that someone treated for SID may also have lactase deficiency should encourage clinicians to explore the possibility of pan-disaccharidase deficiency, a condition in which there is a deficiency of sucrase, maltase, lactase, and palatinase, some of which may result from acquired diffuse intestinal villous injury such as that seen in celiac disease.[10] Alternatively, because some degree of inherited lactase deficiency is a relatively common disorder in adults, the coexistence of decreased activity of sucrase, isomaltase, maltase, and lactase in patients treated for SID is also plausible.

Beyond the findings related to dietary carbohydrates, this study also uncovered inadequacies in the intakes of fiber, folate, and key minerals (eg, potassium, calcium, and magnesium). In all life stage groups, dietary fiber was only half of the recommended amount. The restricted intake of starch likely explains the low fiber intake. Overall, participants were consuming two to four times as many refined grains compared with whole grains, perhaps because of better gastrointestinal tolerance to refined grains.[27] With regard to micronutrients, potassium intake was about half of the recommended intake for all age groups. It is conceivable that foods rich in potassium (eg, beans, potatoes, bananas, and orange juice) would be restricted by patients treated for SID due to their high starch or sucrose content. In addition to potassium, intakes of calcium, magnesium, and folate were also insufficient. It is likely that participants with lactose intolerance or those experiencing continued diarrhea were avoiding dairy products, which may account for the insufficient intake of calcium.

The present study has some limitations worth noting. For one, SID is categorized as a rare disease, estimated to occur in $\sim$5.5% of Americans of European descent.[10] Although definitive diagnosis by genetic testing is often not performed in daily clinical practice, recent evidence has identified several different mutations in the SI gene, suggesting that SID may be more common than previously believed.[28] In the present study, sample size was small, particularly when divided by life stage group. Although the enzyme manufacturer's clinical database used for recruitment of patients being treated for SID with sacrosidase was nationwide, there is inherent bias in using a purposive sample provided by a manufacturer. It is unclear whether the findings would differ in the case that participants were stratified by genetic diversity because current evidence has not confirmed that genetic diversity in SID produces phenotypic differences in intestinal function or gastrointestinal symptoms. Second, the study was observational in nature and dietary data collection occurred at designated time points within the study period, which did not allow evaluation over time or calculating the distribution of usual intakes typically performed in larger epidemiologic research. Although considered a reference standard for self-reported dietary intake, the potential for bias with 24-hour diet recall interviews includes under- or overestimation of intake.[29] Last, there are limited nutrient reference standards to make comparisons to other populations for the intake of starch and individual sugars.

CONCLUSIONS

Several findings from the present study may be useful to inform current standard of care because there is limited published evidence available regarding dietary intervention for individuals treated with sacrosidase for SID. The present study data support that sacrosidase therapy in combination with starch and sucrose modifications promotes normal daily gastrointestinal function. However, these data also indicate that consumption of foods high in lactose and maltose are associated with gastrointestinal symptoms and may need greater attention with regard to resolving gastrointestinal symptoms in patients treated for SID. Future research could target elucidating the role of maltose in promoting gastrointestinal symptoms, including investigation of the types of foods that produce maltose from enzymatic degradation and the maltose content of foods high in starch. Further investigation is also needed to elucidate the requirements for the individual sugars and what are the ranges of starch and sugars best tolerated by individuals being treated for SID.

References

1. Wyllie R, Hyams JS, Kay M. *Pediatric Gastrointestinal and Liver Disease*. 4th ed. Philadelphia, PA: Elsevier Saunders; 2011.
2. Antonowicz I, Lloyd-Still JD, Khaw KT, Shwachman H. Congenital sucrase-isomaltase deficiency. Observations over a period of 6 years. *Pediatrics*. 1972;49(6):847-853.

3. Belmont JW, Reid B, Taylor W, et al. Congenital sucrase-isomaltase deficiency presenting with failure to thrive, hypercalcemia, and nephrocalcinosis. *BMC Pediatr*. 2002;2:4.
4. Treem WR, Ahsan N, Sullivan B, et al. Evaluation of liquid yeast-derived sucrase enzyme replacement in patients with sucrase-isomaltase deficiency. *Gastroenterology*. 1993;105(4):1061-1068.
5. Treem WR. Clinical aspects and treatment of congenital sucrase-isomaltase deficiency. *J Pediatr Gastroenterol Nutr*. 2012;55(suppl): S7-S13.
6. Muldoon C, Maguire P, Gleeson F. Onset of sucrase-isomaltase deficiency in late adulthood. *Am J Gastroenterol*. 1999;94(8):2298-2299.
7. Eichler E, McCallum RW, Castro-Combs J. Making sense of patients with gas and bloating of undetermined origin. *Pract Gastroenterol*; 2015:43.
8. Rahhal RM, Bishop WP. Sacrosidase trial in chronic nonspecific diarrhea in children. *Open Pediatr Med J*. 2008;2(1):35-38.
9. Gericke B, Amiri M, Naim HY. The multiple roles of sucrase-isomaltase in the intestinal physiology. *Mol Cell Pediatr*. 2016;3(1):2.
10. Cohen SA. The clinical consequences of sucrase-isomaltase deficiency. *Mol Cell Pediatr*. 2016;3.
11. Lücke T, Keiser M, Illsinger S, Lentze MJ, Naim HY, Das AM. Congenital and putatively acquired forms of sucrase-isomaltase deficiency in infancy: Effects of sacrosidase therapy. *J Pediatr Gastroenterol Nutr*. 2009;49(4):485-487.
12. Treem WR, McAdams L, Stanford L, Kastoff G, Justinich C, Hyams J. Sacrosidase therapy for congenital sucrase-isomaltase deficiency. *J Pediatr Gastroenterol Nutr*. 1999;28(2):137-142.
13. Blanton CA, Moshfegh AJ, Baer DJ, Kretsch MJ. The USDA Automated Multiple-Pass Method accurately estimates group total energy and nutrient intake. *J Nutr*. 2006;136(10):2594-2599.
14. Conway JM, Ingwersen LA, Moshfegh AJ. Accuracy of dietary recall using the USDA five-step multiple-pass method in men: An observational validation study. *J Am Diet Assoc*. 2004;104(4):595-603.
15. Conway JM, Ingwersen LA, Vinyard BT, Moshfegh AJ. Effectiveness of the US Department of Agriculture 5-step multiple-pass method in assessing food intake in obese and nonobese women. *Am J Clin Nutr*. 2003;77(5):1171-1178.
16. Pereira DI, Couto Irving SS, Lomer MC, Powell JJ. A rapid, simple questionnaire to assess gastrointestinal symptoms after oral ferrous sulphate supplementation. *BMC Gastroenterol*. 2014;14(1).
17. Talley NJ, Phillips SF, Wiltgen CM, Zinsmeister AR, Melton LJ. Assessment of functional gastrointestinal disease: The Bowel Disease Questionnaire. *Mayo Clin Proc*. 1990;65(11):1456-1479.
18. Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. *Scand J Gastroenterol*. 1997;32(9):920-924.
19. *IBM SPSS Statistics for Windows*. Armonk, NY: IBM Corp; 2015.
20. Dietary Reference Intakes: The essential guide to nutrient requirements. http://www.nap.edu/catalog/11537. Accessed December 2, 2016.
21. McMeans AR. Congenital sucrase-isomaltase deficiency: Diet assessment and education guidelines. *J Pediatr Gastroenterol Nutr*. 2012;55(suppl 2):S37-S39.
22. National Health and Nutrition Examination Survey homepage. https://www.cdc.gov/nchs/nhanes/. Accessed December 2, 2016.
23. Gow ML, Garnett SP, Baur LA, Lister NB. The effectiveness of different diet strategies to reduce type 2 diabetes risk in youth. *Nutrients*. 2016;8(8).
24. de Bock M, Lobley K, Anderson D, et al. Endocrine and metabolic consequences due to restrictive carbohydrate diets in children with type 1 diabetes: An illustrative case series [published online ahead of print April 11, 2017]. *Pediatr Diabetes*. https://doi.org/10.1111/pedi.12527.
25. Cohen E, Cragg M, deFonseka J, Hite A, Rosenberg M, Zhou B. Statistical review of US macronutrient consumption data, 1965-2011: Americans have been following dietary guidelines, coincident with the rise in obesity. *Nutr Burbank Los Angel Cty Calif*. 2015;31(5):727-732.
26. Barclay A, Sandall P, Shwide-Slavin C, Brand-Miller J. The ultimate guide to sugars and sweeteners. In: *The Ultimate Guide to Sugars and Sweeteners*. New York, NY: The Experiment, LLC; 2014:113.
27. Lin AH-M, Hamaker BR, Nichols BL. Direct starch digestion by sucrase-isomaltase and maltase-glucoamylase. *J Pediatr Gastroenterol Nutr*. 2012;55(suppl 2):S43-S45.
28. Gericke B, Amiri M, Scott CR, Naim HY. Molecular pathogenicity of novel sucrase-isomaltase mutations found in congenital sucrase-isomaltase deficiency patients. *Biochim Biophys Acta*. 2017;1863(3): 817-826.
29. Freedman LS, Commins JM, Willett W, et al. Evaluation of the 24-hour recall as a reference instrument for calibrating other self-report instruments in nutritional cohort studies: Evidence From the Validation Studies Pooling Project. *Am J Epidemiol*. 2017;186(1):73-82.

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STATEMENT OF POTENTIAL CONFLICT OF INTEREST

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