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Editorial

Screening Tests for Carbohydrate Malabsorption

Only recently has the importance of carbohydrate malabsorption been recognized in the pathogenesis of diarrhea and other intestinal symptoms. In an interesting study published in Volume 2, Number 3, Caballero, Solomons, and Torun compare various indirect tests of carbohydrate malabsorption. In 30 children, 1–3 years of age and suffering from severe protein-energy malnutrition, the authors noted a low correlation among three screening tests for carbohydrate malabsorption: postprandial breath hydrogen production, fecal reducing substances, and fecal pH. In addition, the presence of diarrhea also correlated poorly with these tests.

This lack of correlation with diarrhea is not at all unexpected. Although many of the children probably had osmotic diarrhea with carbohydrate malabsorption, some undoubtedly had secretory diarrhea without associated carbohydrate malabsorption, and negative results of these screening tests would be expected. In additon, the lack of correlation among the three screening tests also might be anticipated as each reflects a different step in the catabolism of carbohydrate by colonic bacteria. Initially, oligosaccharides are hydrolyzed to monosaccharides which, if retained intact in the fecal stream, would produce a positive Clinitest reaction for reducing substances; but most of the monosaccharides are metabolized to short-chain fatty acids, which, if retained intact in the fecal stream, would lower the fecal pH. However, the colon absorbs perhaps 80% of these fatty acids in adults. Avid absorption of fatty acids could cause a false-negative fecal pH test result in the presence of carbohydrate malabsorption. The hydrogen breath test reflects yet another metabolic step in the breakdown of carbohydrate by colonic bacteria, and thus the results may not correlate well with the presence of reducing agents and lowered pH in the stool.

Of the screening tests for carbohydrate malabsorption used by Caballero et al., the hydrogen breath test has received the most attention. Hydrogen is not produced by mammalian cells, and the presence of this gas in the breath indicates catabolism of carbohydrate in the intestinal tract, generally the colon, by coliforms and anaerobes. Although a few bacteria are present normally in the small intestine, the amount of hydrogen formed is insignificant. Colonic bacteria can form hydrogen from other nutrients, such as amino acids, but the quantity formed is inconsequential compared with the amount formed from carbohydrate. Thus, the appearance of hydrogen in the breath equates to the presence of carbohydrate in the colon. Many normal subjects have low levels of hydrogen in the breath, even after prolonged fasting, the average base-line production being 35 ml/day (1). This hydrogen is derived from the breakdown of endogenous glycoprotein present in the lumen of the gut. The formation of hydrogen after entry of carbohydrate into the colon occurs rapidly, with appearance in the breath within 5 min. An early study indicated that 14% of hydrogen formed in the colon is absorbed and appears in the breath; but more recent work has shown that the amount of hydrogen available for absorption depends on the net effect of hydrogen production and utilization by bacteria (2, personal communication). A small percentge of normal subjects excrete no hydrogen in the breath after ingestion of a nonabsorbable carbohydrate, such as lactulose. The traditional explanation for this has been lack of hydrogen production. Recent work has shown that these "nonexcreters" actually form hydrogen, but avid utilization of hydrogen by bacteria may result in no hydrogen available for absorption. In general, an increase in breath hydrogen of 20 ppm or more above the fasting level, as used in the Caballero et al. study, indicates biologically significant malabsorption. Although the appearance of hydrogen in the breath indicates carbohydrate malabsorption, this does not necessarily predict nutritional consequences because other breakdown products, such as fatty acids, may be largely absorbed from the colon.

Although the hydrogen breath test is useful in the detection of carbohydrate malabsorption, certain limitations need to be highlighted. As noted above, 5% or less of the general population excrete no hydrogen in the breath after lactulose ingestion. An

elevated but stable base-line excretion of hydrogen may be seen in patients with bacterial overgrowth of the small intestine and also in patients with pneumatosis cystoides intestinalis (3–5). In the former group, endogenous glycoproteins in the small intestine probably provide the necessary substrate for hydrogen production; while in the latter group, hydrogen is presumably absorbed from the cysts that contain this gas. Elevation of the fasting morning breath hydrogen also may reflect nonabsorbed carbohydrate ingested the previous evening. A subsequent decrease in this elevated base line may obscure an increase in breath hydrogen secondary to the test carbohydrate. Falsely low hydrogen excretion also may follow the use of antibiotics, although some antibiotics such as neomycin may increase hydrogen breath excretion, presumably through either selective enhancement of bacteria that produce hydrogen or selective inhibition of hydrogen-consuming bacteria (6). Laxatives and enemas also may cause a large decrease in hydrogen production (7). A recent study has shown that hydrogen production is dependent on pH; for example, a decrease in stool pH from 7.0 to 5.5 causes a decrease in hydrogen production to 24%, which is promptly reversed in minutes by increasing the pH (8). A lowered pH in the stool could cause a false-negative result of the hydrogen breath test for lactase deficiency in patients with chronic diarrhea secondary to the daily ingestion of lactose. Also, this observation could explain the lack of sensitivity of the hydrogen breath test in the detection of lactose malabsorption in children with diarrhea secondary to gastroenteritis (9). In addition, rapid transit may have an important role in causing false-negative results in these children with gastroenteritis. This effect of pH on hydrogen production also could contribute to the low correlation between fecal pH and hydrogen production noted by Caballero et. al. Additional causes of falsely low hydrogen production include hyperventilation and dilution of end tidal air (equivalent to alveolar air) with dead space air (10). These latter problems can be circumvented by measuring the CO_2 concentration and normalizing the hydrogen to the CO_2 level in the breath (11).

Falsely high hydrogen excretion may occur if the breath collection is taken shortly after smoking, because tobacco smoke contains hydrogen. Sleep also may cause elevation of hydrogen in the breath under two circumstances (12). In the fasting state, a spontaneous increase in breath hydrogen may occur during sleep, presumably secondary to the intermittent emptying of the small intestine. Also, after ingestion of nonabsorbable carbohydrate, sleep may cause a greater increase in breath hydrogen than expected, possibly secondary to hypoventilation. False elevation of hydrogen also may occur after the use of salicylates (13). The mechanism is not known, but it could be related to inhibition of prostaglandin synthesis and decreased colonic motility. After gastric surgery, patients with high activity of lactase frequently have a large increase in hydrogen after the ingestion of lactose, presumably secondary to rapid gastric emptying and fast intestinal transit (14).

Despite these limitations, the hydrogen breath test is useful not only in detecting carbohydrate malabsorption in general, as illustrated by the Caballero et al. study, but also in screening for specific disaccharidase deficiencies and bacterial overgrowth, as well as in determining small bowel transit time and quantitating carbohydrate malabsorption. The lactose hydrogen breath test is generally accepted as the most reliable screening test for lactase deficiency in both children and adults (15). Also, the sucrose hydrogen breath test seems to be a promising screening test for sucrase-isomaltase deficiency (16–19). To detect bacterial overgrowth of the small intestine, limited experience has shown some promise using glucose or lactulose as substrates (20,21). Another use of the hydrogen breath test is in determining small bowel transit time (1,20,22–24). After ingestion of a nonabsorbable carbohydrate, entry into the cecum is promptly signaled by the appearance of hydrogen in the breath. For example, the ingestion of 10 g of lactulose gives a transit time of about 90 min in normal subjects, whereas larger doses give shorter times. Clinical utility of the lactulose hydrogen breath test for small bowel transit seems to be limited. Finally, the hydrogen breath test can be used to semiquantitate the malabsorption of carbohydrate (26,27). In a given subject, equivalent amounts of hydrogen are produced from different monosaccharides and oligosaccharides, but between subjects, hydrogen production from the same amount of carbohydrate may vary many fold. Thus, for each subject, a standard curve must be constructed by plotting hydrogen production against different amounts of lactulose (for example, 6.5, 13, 26 g) (25). On the basis of the amount of hydrogen produced after the test carbohydrate, this plot can be used to quantitate the degree of carbohydrate malabsorption. This technique revealed that patients after gastric surgery malab-

sorbed 3–17% of a 100 g glucose load and normal adults malabsorbed 10–20% of 100 g of wheat flour (25,27).

In summary, each of the screening tests used by Caballero et al. to detect carbohydrate malabsorption measures a specific step in the bacterial catabolism of carbohydrate in the colon. Although all three tests have limitations, the hydrogen breath test is the most useful and versatile in evaluating various types of carbohydrate malabsorption. This test is relatively simple, sensitive, specific, noninvasive, and applicable to any age group.

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