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Relationship Between Methane Production and Breath Hydrogen Excretion in Lactose-Malabsorbing Individuals

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Recent studies have shown reduced breath hydrogen (H_2) excretion in methane (CH_4)-producing healthy individuals following ingestion of lactulose. This questions the reliability of the breath hydrogen test (BHT) in CH_4 excretors, but the relationship between CH_4 and H_2 excretion in other clinical applications of the BHT is not known. We reviewed BHT results in two groups of subjects: (1) 385 children tested for lactose malabsorption in a hospital setting, and (2) 109 lactose-malabsorbing patients tested with a home kit. The percentage of lactose malabsorbers in group 1 (51%) was the same regardless of CH_4-producing status ($P = 0.97$). The BHT data from group 2 showed a positive correlation ($r = 0.6$, $P < 0.000001$) between the magnitude of the rise in CH_4 and H_2 concentrations, and the H_2 excretion curves were significantly higher in the CH_4-producing individuals. We conclude that attention to CH_4-producing status is not necessary in the interpretation of the lactose BHT.

KEY WORDS: hydrogen; methane; breath; lactulose; lactose malabsorption.

The breath hydrogen test (BHT) is commonly used in the diagnosis of carbohydrate malabsorption. Hydrogen gas (H_2) is produced by intestinal bacteria during fermentation of malabsorbed sugars, and a portion of the gas is excreted in breath (1). The remainder of the H_2 is excreted in flatus or metabolized by colonic bacteria through methanogenesis, sulfate reduction, or acetogenesis (2). Several factors such as colonic pH (3) and sulfate availability (2) interact to determine which of these mechanisms predominates in an individual. In general, methane (CH_4) production appears to be the most important pathway for H_2 consumption in the colon, and 30–50% of the adult Caucasian population are breath CH_4 excretors (4).

Recent studies in healthy adult volunteers (5, 6) have shown that breath CH_4 excretors have lower breath H_2 production following ingestion of test doses of the nonabsorbable sugar lactulose than non-CH_4 producers. The results suggest that the H_2 produced from lactulose fermentation in these subjects is utilized for CH_4 production, thereby reducing the amount of H_2 available for excretion in the breath. This may be relevant in the interpretation of clinical tests that utilize lactulose as a substrate, such as measurement of mouth-to-cecum transit time. Methane production has been associated with slow colonic transit in one study (7), and significantly longer mouth-to-cecum transit times in CH_4 excretors were found by other investigators (6). Whether the difference is truly determined by decreased motility in these individuals or is attributable to conversion of H_2 to CH_4 remains to be

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elucidated. Different patterns of H_2 excretion related to CH_4-producing status have also been reported during evaluation of starch malabsorption (8). However, the relationship between CH_4 production and breath H_2 excretion in common clinical applications of the BHT, such as the lactose BHT for diagnosis of lactose malabsorption, has not been examined. One study in adult French subjects (9) reported a decreased prevalence of CH_4 production in lactose malabsorbers, suggesting that the inverse relationship between CH_4 and H_2 production is similar following ingestion of lactose.

The purpose of this study was to investigate whether different criteria should be used for the interpretation of the lactose BHT in CH_4 producers. We reasoned that a retrospective review of our patient data would show decreased breath H_2 excretion and a lower incidence of lactose malabsorption in CH_4-producing subjects if the relationship between CH_4 production and H_2 excretion were the same as in the previously reported studies utilizing lactulose as a substrate.

MATERIALS AND METHODS

We reviewed data from 385 lactose breath hydrogen tests (group 1) performed in our laboratory from November 1984 to February 1991. The majority of the patients were children of diverse ethnic backgrounds from Maryland or Pennsylvania who had been referred for evaluation of gastrointestinal complaints such as abdominal pain and diarrhea. The age range was 3 months to 21 years. All of the tests were performed in the hospital, where the ambient CH_4 concentration is <3 parts per million. The dose of lactose used was 2 g/kg (maximum 50 g). Breath was sampled at 30-min intervals for 3 hr and collected using a nasal prong system (10). Samples were analyzed for H_2 and CH_4 concentration on a Quintron model DP Microlyzer (Quintron Instrument Co., Inc., Milwaukee, Wisconsin), and the results expressed as parts per million (ppm). The CO_2 content was analyzed on a Beckman CO_2 Monitor LB-3 (SensorMedics Corp., Anaheim, California) and the values used to normalize the H_2 concentration in the expired air to an alveolar concentration (11). The data available for review on these patients were baseline and peak H_2 concentration, peak CH_4 concentration, and interpretation of the lactose BHT as positive or negative, but complete H_2 and CH_4 excretion curves were not available. A positive test was defined as a rise in H_2 concentration greater than 10 ppm from the baseline value within the first 120 min of the test or a rise greater than 20 ppm at any time. Patients were classified as CH_4 producers if their breath CH_4 concentration was higher than 4 ppm (ie, >1 ppm above ambient CH_4 concentration).

We additionally reviewed the lactose BHT results of 109 lactose-malabsorbing patients (group 2) tested at home or in a physician's office for whom we had available all data on H_2 and CH_4 excretion for 3 hr. Eighty-nine of these subjects were children (81.6%), with a mean age of 8.6 years (range 1–16), and 20 were adults (mean age 43.2). The patients or their caretakers were taught to self-test using the nasal prong technique and to store the specimens in special nonsterile vacutainers, in which stability of both H_2 and CH_4 has been documented (10). The samples were then mailed to our laboratory where they were analyzed using the same methods described above.

Statistical analysis of data was done using table analysis (χ^2), linear regression analysis, and paired Student's *t* test.

TABLE 1. RELATIONSHIP BETWEEN CH_4-PRODUCING STATUS AND INTERPRETATION OF LACTOSE BREATH HYDROGEN TEST RESULTS

	CH_4 producer	*Nonproducer*	*Total*
Positive	36 (9%)	160 (42%)	196 (51%)
Negative	34 (9%)	155 (40%)	189 (49%)
Total	70 (18%)	315 (82%)	385 (100%)

RESULTS

Seventy of the 385 patients tested in the hospital (group 1) were CH_4 producers (18%). Fifty-one percent of the total population had a positive BHT following lactose. Chi-square analysis showed that these variables were independent of each other ($P = 0.97$), as the percentage of lactose malabsorbers was almost the same regardless of the CH_4-producing status (Table 1).

In the 109 lactose malabsorbers tested at home (group 2), there was a positive correlation ($r = 0.60$, $P < 0.000001$) between the magnitude of the CH_4 rise from baseline and the magnitude of the H_2 rise (Figure 1). Additionally, the average breath H_2 val-

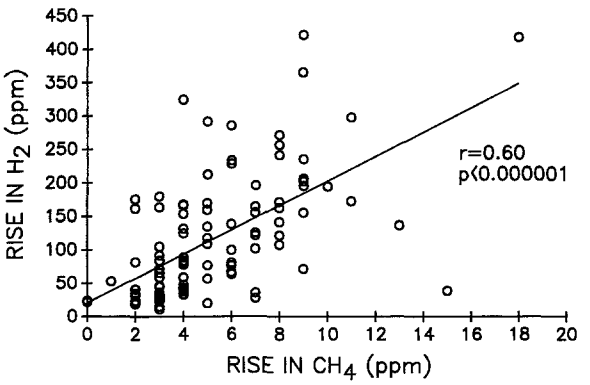

Fig 1. Correlation between the magnitude of the rise in CH_4 and H_2 concentrations in 109 lactose malabsorbers during a 3-hr lactose breath hydrogen test.

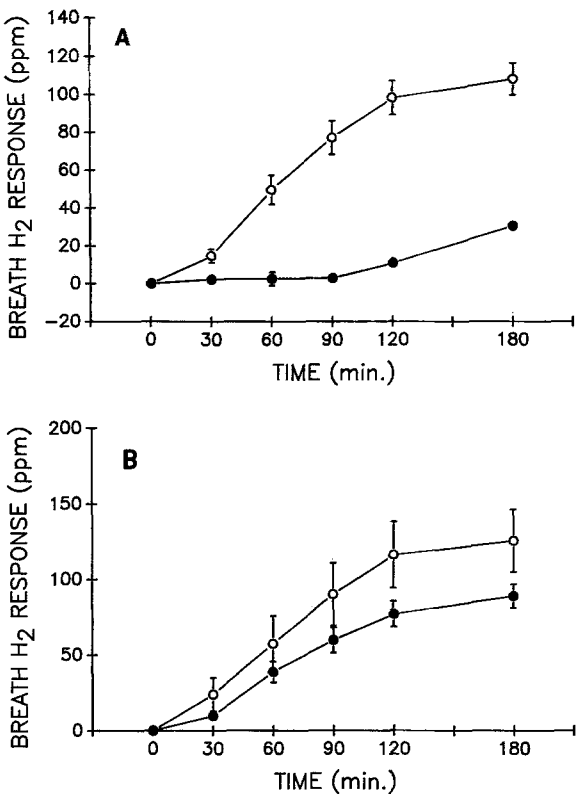

Fig 2. (A) Comparison of mean breath H_2 responses (difference between the values at each time point and the baseline) during lactose breath hydrogen tests in 109 lactose malabsorbers. Average values for CH_4 producers (>4 ppm) are represented by the open circles and nonproducers by the closed circles. Values are expressed as the mean ± SEM. (B) Comparison of mean breath H_2 responses (difference between the values at each time point and the baseline) during lactose breath hydrogen tests in 109 lactose malabsorbers. Average values for CH_4 producers (when >11 ppm of CH_4 is used as the definition) are represented by the open circles and nonproducers by the closed circles. Values are expressed as the mean ± SEM.

ues subtracted from the baseline at each time point of the test (breath H_2 response) were higher for breath CH_4 excretors (defined as CH_4 >4 ppm) than for non-CH_4 excretors ($P < 0.02$ for paired means; Figure 2A). Ambient CH_4 values were not available for these subjects, who were tested at home, making the classification of subjects as CH_4 excretors less certain than in group 1. The median peak CH_4 value in these patients (8 ppm) was higher than in the patients tested in group 1 (3 ppm). Accordingly, application of the traditional definition of a CH_4 producer as one who has a CH_4 concentration in breath >1 ppm above ambient air (12) could have resulted in classifying an excessive number of subjects as CH_4 producers. Nonetheless, the relationship in Figure 2A held true regardless of the cutoff point used to define CH_4 producers. Although the excretion curves approximated each other, the difference was still seen when higher CH_4 values were used to define a CH_4 producer. For example, taking a cutoff of 11 ppm (mean + 1 SEM), which would classify 21% of the study population as CH_4 producers (a similar proportion to that of hospital-tested patients), resulted in a similar statistical difference in H_2 values ($P < 0.01$ for paired means; Figure 2B).

DISCUSSION

Eighteen percent of our study population were CH_4 producers, which is lower than the prevalence reported in Caucasian adults. Several studies (4, 5, 13, 14) have shown variability in both H_2 and CH_4 production among populations from different geographic areas and ethnic backgrounds, and the prevalence of lactose malabsorption is similarly influenced by ethnicity (15). Since our subjects were racially heterogeneous and referred because of gastrointestinal symptoms, conclusions as to prevalence of CH_4-producing status or lactose malabsorption in our general population can not be made.

Our data show that the results of lactose breath hydrogen testing are independent of a child's CH_4-producing status. The prevalence of CH_4 production in lactose-malabsorbing and lactase-sufficient subjects was identical in this large group, and the same proportion of subjects (51%) were lactose malabsorbers regardless of their CH_4-producing status. Adjusting the thresholds of H_2 concentration by which a test is considered positive according to CH_4-producing status, as suggested by Cloarec et al (6), does not appear necessary in this setting. Additionally, in a heterogeneous population of lactose-malabsorbing children and adults, H_2 and CH_4 production are directly proportional. The higher breath CH_4 values in patients tested outside of the hospital in our study are probably due to contamination of ambient air such as caused by cigarette smoke (5). To control for this variable, we looked at the magnitude of the rise in the CH_4 concentration during the lactose BHT. Our findings contrast sharply with the observations of Bjorneklett and Jensen (5) and Cloarec et al (6), who found either no correlation or a negative correlation between H_2 and CH_4 excretion parameters following lactulose ingestion. In these studies there were no subjects with both high H_2 and high CH_4 excretion. In another study by Cloarec et al (9) that examined the prevalence of

lactose malabsorption in 102 healthy French adults, the prevalence of CH_4 production in the 24 lactose-malabsorbing subjects (25%) was lower than in lactase-sufficient subjects (47.4%). However, these subjects did not have a history of gastrointestinal symptoms, and only 12 developed symptoms associated with lactose malabsorption. Additionally, quantitative relationships between CH_4 and H_2 excretion were not investigated.

The remarkable discrepancy between these previous reports and our observations may be due to the differences in the study populations. Adaptative changes in the colonic flora in patients who are chronically fermenting malabsorbed carbohydrate, such as lactose malabsorbers, may alter the metabolic capabilities when compared to the flora of normal subjects challenged acutely with lactulose. One possibility is that lactose-malabsorbing individuals may have an active CH_4-producing flora in the proximal colon that is less pH sensitive, contrary to what has been observed in healthy adults (16). Another explanation for the discrepancy between the studies using lactulose and lactose is the difference in the magnitude of H_2 production following ingestion of the carbohydrates. For example, the mean maximum rise in H_2 concentration in one study using 10 g of lactulose was 60 ppm (SD = 41) (6), whereas 50 of our patients (46%) had H_2 rises greater than 100 ppm. When we analyzed the relationship between breath H_2 and CH_4 excretion only in those subjects with H_2 rises lower than 100 ppm, the correlation was poor ($N = 59$, $r = 0.25$, $P = 0.05$). It is possible that at lower intracolonic H_2 concentrations, CH_4 production is relatively greater and can significantly reduce breath H_2 excretion. This effect may disappear at higher H_2 concentrations, where excretion of both gases becomes directly proportional. Factors such as relative gas pressures and location of the various gas-producing flora in the colon may play a role.

Our experience suggests that attention to methane-producing status is not necessary in the interpretation of lactose breath hydrogen tests in children. This conclusion is likely to be applicable to adult subjects as well. Although CH_4-producing status could be important in those subjects who have a borderline negative lactose BHT, our data overall do not suggest this. Further research is needed to determine the mechanisms responsible for the different breath H_2 excretion patterns in CH_4-producing subjects who malabsorb lactose, in contrast to normal individuals fed a single dose of a nonabsorbable sugar.

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