Role of hydrogen and methane breath testing in gastrointestinal diseases

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Abstract

The hydrogen and methane breath test represents a very simple, cheap, non-invasive diagnostic procedure to evaluate intraluminal events occurring in the gastrointestinal tract. Its clinical applications are, first of all, lactose malabsorption and small bowel bacterial overgrowth, but it has also been used to evaluate mouth-to-cecum transit time, sweetener malabsorption and intestinal mucosa integrity. Methodological aspects should be better evaluated and an improvement of its accuracy should be obtained through the adoption of new protocols.

Keywords: Functional bowel disorders; Hydrogen breath test; Lactose malabsorption; Methane

1. Introduction

The hydrogen (H₂) and methane (CH₄) breath test represents a fascinating diagnostic procedure to evaluate intraluminal events occurring in the gastrointestinal tract [1]. The test is very simple, cheap, non-invasive and, consequently, widespread use was evident. Its clinical applications are first of all lactose malabsorption [2] and small bowel bacterial overgrowth [3,4] but it has also been used to evaluate mouth-to-cecum transit time [5], sweetener malabsorption [6,7], and intestinal mucosa integrity [8]. However, on methodological grounds, many aspects are not yet completely clear and many efforts are being made to expand our knowledge in order to improve test protocols and reach a satisfactory level of accuracy.

2. Lactose malabsorption and intolerance

Lactose malabsorption is a widespread condition characterized by a highly variable prevalence, ranging from 5% in northwest Europe to almost 100% in some Asian populations [9]. A high prevalence figure has also been described in the Italian population, ranging from 51% in the North to 71% in the South [10]. Intolerance symptoms, such as bloating, diarrhea, flatulence, and abdominal pain, are only present in a subgroup of patients with lactose malabsorption. This symptom pattern resembles that of many other gastrointestinal disorders and, due to the high prevalence of lactose malabsorption, it is possible that in an organic patient with a coexisting lactose malabsorption without intolerance symptoms, lactose malabsorption shown by a positive lactose breath test might be wrongly considered as being responsible for patient symptoms, inducing a delay in the right diagnosis. It has also previously been shown that patient awareness of the condition of lactose intolerance is very poor: in a group of 30 patients who considered themselves severely intolerant to lactose, 9 of them proved to be lactose absorbers at a lactose breath test [11]. Hence, anamnestic evaluation of lactose absorption is very misleading, as the patient very frequently expresses a wrong opinion. Accordingly, we need an objective test that can discriminate between absorbers and malabsorbers. The clinical value of the lactose breath test is, therefore, mainly represented by the possibility of excluding that lactose intake is definitely accompanied by symptom onset. In short, we consider the negative predictivity of the test,
rather than its positivity for lactose malabsorption, to be pivotal in clinical practice. Unfortunately, the accuracy of the test has proved to be good when a prolonged monitoring of H₂ excretion, up to 7 hours, is performed [12,13] and an alternative test for the detection of genetic polymorphism of the lactase gene was therefore suggested [14]. However, the agreement between the two tests was excellent in adult age, but poor in the age range up to the third decade, thus suggesting that it should be not considered as the new gold standard for lactose malabsorption [15].

3. Small bowel bacterial overgrowth and breath test

Small bowel bacterial overgrowth is largely dealt with in another paper of this Supplement (see article by Parodi et al.). Its definition is based on the microbiological test, as it refers to the number of bacteria in the jejunal aspirate [4,16]. However, this procedure is invasive, cumbersome and, therefore, not widely available. H₂ breath tests were, consequently, suggested as alternative tests due to their simplicity. Lactulose [17] and glucose [18] were used, but both substrates revealed some pitfalls. Lactulose is a non-absorbable carbohydrate and it is difficult to discriminate between small bowel or colonic fermentation of the substrate particularly in the event of accelerated transit [19,20]. On the contrary, glucose is an avidly absorbed sugar and may not reach a distal site of overgrowth. The extreme pathophysiological polymorphism of small bowel bacterial overgrowth makes it impossible to believe that one test is characterized by good diagnostic accuracy and it is, instead, foreseeable that the best test should be tailored on the single patient. This approach obviously involves difficulties in terms of standardization and, consequently, reproducibility of the results.

In order to improve the diagnostic accuracy of the glucose breath test for bacterial overgrowth, we have recently tested whether a glucose capsule characterized by a pH-controlled release may offer some advantage [21] and the results showed that it is possible to foresee a substrate-controlled release at a more distal level than water solution.

Alternatively, if we are unable to find a simple test to accurately diagnose this condition, currently defined on the basis of an unavailable test, a new definition could be formulated, with the bacterial count in jejunal aspirate no longer being crucial to diagnosis. Even if this idea may at first seem provoking, like for rheumatological conditions, a new set of diagnostic criteria, based on clinical and biochemical data might be the solution to the problem.

4. Mouth-to-cecum transit time and breath test

The possibility of studying mouth-to-cecum transit time with the H₂ breath test after lactulose administration was suggested in 1975 [5]. However, the test was not shown to be characterized by good reproducibility [22]. Gastrointestinal motility is not modified towards a postprandial pattern after lactulose administration and this may make the transit value dependent on the time of occurrence of intestinal phase III. An improvement of the method, in fact, is achieved by the contemporary administration of absorbable compounds (carbohydrates or lipids) [22]. Moreover, on clinical grounds, we have no information on the correlation between mouth-to-cecum transit time of non-caloric substrates and abdominal symptoms. It is foreseeable that the standardization of a caloric substrate could make this test clinically important.

5. Sweetener malabsorption

Sweetener malabsorption is responsible for symptoms like diarrhea, bloating, flatulence, abdominal pain in a large portion of functional patients. Sweeteners are non-absorbable sugars: they maintain the ability to sweeten foods, but since they are not absorbed they have no calories. However, it has been shown that [6] by increasing the oral load of sorbitol and the concentration of a sorbitol solution, a parallel increase of malabsorbers among a group of healthy volunteers is evident. This condition is largely underestimated, precisely because there is a lack of awareness in the community that the amount of sweeteners potentially able to induce symptoms is the equivalent of two or three dietetic candies. However, the clinical value of breath test in this condition is poor, since in this case, an anamnestic evaluation could be sufficient to detect the use of sweeteners.

6. Methane and breath test

The production of CH₄ in humans was first described at the beginning of the XIX century, when Magendie reported his study on guillotined convicts suggesting the presence of this gas in the intestine [23]. Subsequently, it was shown that both H₂ and CH₄ are not produced by human cells, no production is evident in germ-free rats and the production of both gases appears after contamination of these rats [24]. Hence, these gases represent products of bacterial activity at intraluminal bowel level.

More than 200 years since its description and more than forty years since its better characterization, the true significance of CH₄ production in the human intestine is largely unknown. We know that breath CH₄ excretion is gender related, being significantly more prevalent in females [25], and there are also differences among the different ethnic origins [25]: the prevalence of methane excretors is 48% in Caucasians, 45% in Blacks, 24% in Orientals and 32% in Indians. Breath CH₄ excretion does not seem linked to specific dietary proteins, fats,
carbohydrates or dietary fibers [26] and a long-term stability of breath CH₄ excretion was recently shown in a 30-year follow up [27].

After abandoning the suggested relationship with colon cancer [28], a role in the diagnosis of carbohydrate malabsorption was hypothesized when a sudden increase of breath CH₄ excretion after oral administration of the malabsorbed carbohydrate was evident in the absence of breath H₂ excretion [29]. In subjects showing breath H₂ excretion, it was shown that the coexistence of breath CH₄ excretion is associated with a reduction of the levels of breath H₂ [30], suggesting that a portion of H₂ is condensed into the CH₄ molecule. However, even if a possible role for breath CH₄ excretion in the improvement of diagnosis of carbohydrate malabsorption was hypothesized, no diagnostic criterion is available and many different, arbitrary criteria are present in the literature.

Similarly, the role of breath CH₄ excretion in the pathophysiology of functional symptoms is largely unknown. The possibility that intraluminal CH₄ production might reduce intraluminal gas volume and, consequently, reduce gas-related symptoms is an attractive hypothesis, but no data are yet available on this topic. However, the interest in methane production at intestinal level goes beyond the pathophysiology of functional bowel disorders as intestinal fermentation is a complex metabolic pathway, able to influence sensorimotor activity of the gastrointestinal tract. In humans, it has been shown that colonic fermentation modifies fundic tone [31] and lowers esophageal sphincter tone [32], and that products of intraluminal fermentation modify ileal and colonic motility [33–35].

In conclusion, breath H₂ and CH₄ excretion represent a simple tool for monitoring intraluminal events. Methodological aspects should be better evaluated and an improvement of its accuracy should be obtained through the adoption of new protocols. A greater knowledge of intraluminal events could allow us to obtain additional information on the pathophysiology of the sensorimotor alterations of the gastrointestinal tract.

Conflict of interest statement

None declared.

References