

Patients With Irritable Bowel Syndrome Exhale More Hydrogen Than Healthy Subjects in Fasting State

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Background/Aims

Irritable bowel syndrome (IBS) is a common disorder with significant morbidity and impairment of quality of life. Most patients (26%-83%) with IBS from Asia reported bloating. Bloating may result from increased amount or distribution of gas in the gut or exaggerated perception of distension. To evaluate whether patients with IBS produce more hydrogen even in fasting state, we conducted a study with the following aims: (1) to estimate fasting breath hydrogen levels among patients with IBS as compared with healthy controls (HC) and (2) to study relationship between symptoms of IBS and stool frequency and fasting breath hydrogen levels.

Methods

Eighty-one patients with IBS (Rome III criteria) and 123 HC were included. Hydrogen breath test was performed using a gas analyzer after an overnight (12 hours) fast. Both patients with IBS and HC had similar preparation before breath hydrogen estimation.

Results

Of 93 patients with symptoms of functional gastrointestinal disorders, 81 (87.1%) met Rome III criteria and 12 (12.9%) were negative and hence, excluded from the study. Patients with IBS were comparable in age (35 ± 11.8 years vs 37.5 ± 13.1 years, $p = \text{NS}$) and gender (male 61/81 [75.3%] vs 77/123 [62.6%], $p=0.67$) with HC. Average fasting breath hydrogen was higher in patients with IBS as compared to HC (mean 10.1 ± 6.5 ppm vs 5.5 ± 6.2 ppm, $p < 0.0001$). Number of stools per week correlated with average fasting breath hydrogen excretion in patients with IBS ($r = 0.26$, $p = 0.02$).

Conclusions

In spite of similar preparation for the test, fasting breath hydrogen was higher in patients with IBS as compared to HC. Number of stools per week correlated with fasting breath hydrogen levels among patients with IBS.

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Key Words

Breath tests, Bloating, Abdominal discomfort, Diarrhea, Small intestine

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Conflicts of interest: None.

Introduction

Irritable bowel syndrome (IBS) is a common gastrointestinal disorder with significant morbidity,¹ impairment of quality of life² and work absenteeism.³ Most patients (26%-83%) with IBS from Asia reported bloating.⁴ Bloating may result from increased amount of gas or its abnormal movement in the gut or increased perception of the distension.⁵ A few studies using computerized tomography or radiographs of abdomen revealed higher amount of gas in patients with IBS.^{6,7} A study using infusion of radioactive xenon gas into small bowel revealed that patient with IBS tend to trap the gas in small bowel, which has low ability to distend compared to colon whereas, in healthy subjects the gas moved down to the colon.⁸ In another study from our center, patients with IBS complained of more symptoms than healthy subjects to a comparable level of hydrogen production following lactose load, which was likely to be related to visceral hypersensitivity.⁹ In a recent study, it was found that patients with IBS were less often methane producers compared with the healthy subjects.¹⁰ Since 4 atoms of hydrogen combine to produce 1 molecule of methane, the authors suggested that increased frequency of bloating among patients with IBS might be explained by reduced methane production among them.¹⁰ However, there is no study directly comparing fasting breath hydrogen among patients with IBS and healthy subjects and relationship between various symptoms of IBS and fasting breath hydrogen levels.

Hwang et al¹¹ suggested that methane production among patients with IBS was associated with constipation. Methane slows the gut transit, therefore, may cause constipation.¹¹ Hence, it is logical to propose that excess hydrogen production should be associated with higher stool frequency. In a recent study from our center, patients with chronic non-specific diarrhea produced more hydrogen than those with IBS and healthy subjects in response to glucose load.¹² Hence, it is interesting to evaluate whether there is any relationship between fasting breath hydrogen levels and stool frequency. Accordingly, we aimed to study: (1) fasting breath hydrogen levels among patients with IBS as compared to healthy subjects with same preparation and (2) relationship between symptoms of IBS and stool frequency and fasting breath hydrogen levels.

Materials and Methods

1. Study subjects

From December 2008 to February 2010, 93 patients with functional lower gastrointestinal disorder referred to Gastrointestinal Pathophysiology and Motility Laboratory of the Department of Gastroenterology of a tertiary referral center in the northern India for breath hydrogen testing and 123 healthy controls (HC) were included. IBS was diagnosed using Rome III criteria.¹³ IBS was classified into diarrhea predominant (D-IBS) and constipation predominant (C-IBS) on subjective feeling of bowel movement. Also, on Bristol stool form scale, stool type 1, 2 and 3 were taken as C-IBS and 5, 6 and 7 were taken as D-IBS; those who reported alternating type of stool were taken as I-IBS (indeterminate type-IBS) (Asian IBS consensus).¹⁴ HC were selected from the community or staff members of the institute excluding those fulfilling criteria for IBS on enquiry. The study protocol was approved by the Institutional Ethics committee. Informed consent was obtained from all the patients and HC. Patients who received antibiotics, proton pump inhibitors and promotility or antimotility drugs within 4 weeks before inclusion into the study were excluded.

2. Hydrogen breath test

Hydrogen breath test was performed using a breath gas analyzer (Bedfont gastrolyzer, Bedfont Scientific Ltd, ME13QX, England) after an overnight (12 hours) fast.¹⁵

3. Patient preparation

Both the patients with IBS and HC were asked to avoid slowly absorbed carbohydrates (like bread and potato) and fiber during the previous 48 hours before the test as this might lead to high basal levels of hydrogen in the breath.¹⁶ Subjects were not allowed to take fruits, vegetables, and legumes. Also, they were asked not to ingest any beans, nuts, soy or large meals, and to limit dairy intake the day before the test. Patients who were on lactulose were asked to stop it 72 hours before the test. Cigarette smoking and exercise were avoided 2 hours before and during the test, as hyperventilation can cause changes in breath hydrogen content. The subjects were then asked to brush their teeth and rinse their mouth with antiseptic mouth wash (chlorhexidine) and tap water before the test. Three values of breath hydrogen were recorded from each subject every 5-minute in fasting state and an average of these values was also taken.¹⁶

4. Clinical evaluation

Subjects were given a bowel symptom questionnaire. Symptoms included bloating, excess gas, diarrhea, constipation and abdominal pain, passage of mucus, feeling of incomplete evacuation, straining, and urgency. The patients were asked how they feel about their bowel movements (diarrhea or constipation). Western definitions of constipation (less than 3 stools per week)¹⁷ and diarrhea (more than 3 stools per day)¹⁷ were also applied. Bristol Stool Form Scale was also used to define bowel pattern.¹⁸

5. Statistical methods

Categorical and continuous data were analyzed using chi-square and Mann-Whitney U test, respectively. The time by group interaction was analyzed using repeated measures ANOVA (General linear model). Spearman rank correlation was used to evaluate the relationship between each pair of continuous variables. The p-values less than 0.05 were considered significance.

Results

1. Demographic and clinical parameters

Of the 93 patients with functional lower gastrointestinal

symptoms, 81 (87.1%) fulfilled Rome III criteria for IBS and 12 (12.9%) were negative and hence, excluded from this study. Patients with IBS were comparable in age (mean 35 ± 11.8 years vs 37.5 ± 13.1 years, $p = \text{NS}$) and gender (male 61/81 [75.3%] vs 77/123 (62.6%), $p = 0.67$) with HC (Table 1). On subjective feeling of bowel movement, of 81 patients with IBS 50 (61.7%) and 29 (35.8%) were constipation and diarrhea predominant, respectively while 2 (2.5%) patients felt neither constipation nor diarrhea. Of 81 patients with IBS, 3 (3.7%), 4 (4.9%), 18 (22.2%), 13 (16%), 15 (18.5%) and 28 (34.6%) were passing Bristol stool type 1, type 2, type 3, type 4, type 5 and type 6, respectively. Of 128 HC initially screened, 5 were excluded from the study as they fulfilled Rome III criteria for IBS.

2. Fasting breath hydrogen in IBS and HC

Average fasting breath hydrogen concentration was higher in patients with IBS as compared to HC (mean 10.1 ± 6.5 ppm vs 5.5 ± 6.2 ppm, $p < 0.0001$; Fig. 1). There was significant difference in fasting breath hydrogen excretion at different time in patients with IBS as compared to HC (Type III sum of squares = 31.366, $p = 0.041$; Fig. 2). 12/123 (10%) HC and 20/81 (25%) patients with IBS had fasting breath hydrogen value more than 16 ppm. There was no difference in excretion of fasting breath hydrogen among patients with D-IBS and C-IBS (either

Table 1. Demographic and Clinical and Laboratory Parameters of Patients With IBS and Healthy Controls

Parameters	IBS (n = 81)	HC (n = 123)	p-value
Age (yr)	35.0 ± 11.8	37.5 ± 13.1	NS
Gender (male, n [%])	61 (75.3)	77 (62.6)	0.67
Hemoglobin (g/dL)	13.5 ± 1.9	—	—
ESR (mm/hr)	18.2 ± 13.9	—	—
Symptoms			
Abdominal pain	68 (84.0%)	5 (4.1%)	< 0.0001
Abdominal discomfort	81 (100.0%)	5 (4.1%)	< 0.0001
Abdominal distension/bloating	78 (96.3%)	13 (10.6%)	< 0.0001
Passage of mucus	54 (66.7%)	0	—
Feeling of incomplete evacuation	54 (66.7%)	17 (13.8%)	< 0.0001
Abdominal pain/discomfort relieved after defecation	73 (90.1%)	5 (4.1%)	< 0.0001
Urgency to pass stool	26 (32.1%)	0	—
Loose stool at onset of pain	77 (95.1%)	3 (2.4%)	< 0.0001
Straining during defecation	73 (90.1%)	0	—
Number of stool/week (mean \pm SD)	25 (2-56)	7 (7-14)	< 0.0001
Relief of pain with bowel movement	77 (95.1%)	5 (4.1%)	< 0.0001
More frequent stools at onset of pain	68 (84.0%)	5 (4.1%)	< 0.0001

IBS, irritable bowel syndrome; HC, healthy control; ESR, erythrocyte sedimentation rate.

Values within parenthesis indicate percentage. Continuous data is presented as mean and SD. The categorical and continuous data were compared using chi-square test, and Student's *t* test, respectively.

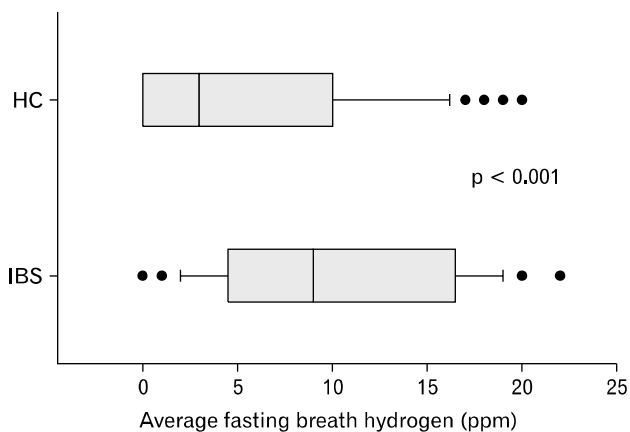


Figure 1. Comparison of fasting breath hydrogen level in patients with irritable bowel syndrome and healthy controls. IBS, irritable bowel syndrome; HC, healthy controls.

by subjective feeling or by Bristol stool form).

3. Correlation between stool frequency and fasting breath hydrogen excretion

There was a positive correlation between number of stools per week and average fasting breath hydrogen excretion in patients with IBS ($r = 0.26$, $p = 0.02$). There was positive correlation between frequency of stools per week and average fasting breath hydrogen excretion in patients with IBS who reported subjective feeling of diarrhea ($r = 0.45$, $p = 0.01$) and D-IBS (according to Bristol Stool Form Scale, $r = 0.35$; $p = 0.02$). In contrast, there was no correlation between frequency of stools per week and average fasting breath hydrogen excretion in patients with IBS who reported subjective feeling of constipation and C-IBS (according to Bristol stool type).

Discussion

The present study showed that in spite of similar preparation for the test, fasting breath hydrogen excretion was higher in patients with IBS as compared to HC. Also, number of stools per week correlated with fasting breath hydrogen levels among patients with IBS. But, there was no difference in fasting breath hydrogen excretion in patients with D-IBS and C-IBS.

Chami et al¹⁹ reported that comparison between the quantity of bowel gas of patients with IBS and HC using plain abdominal radiographs resulted in a marked difference in measured values. However, our study is perhaps the first study documenting increased breath hydrogen in patients with IBS compared to HC.

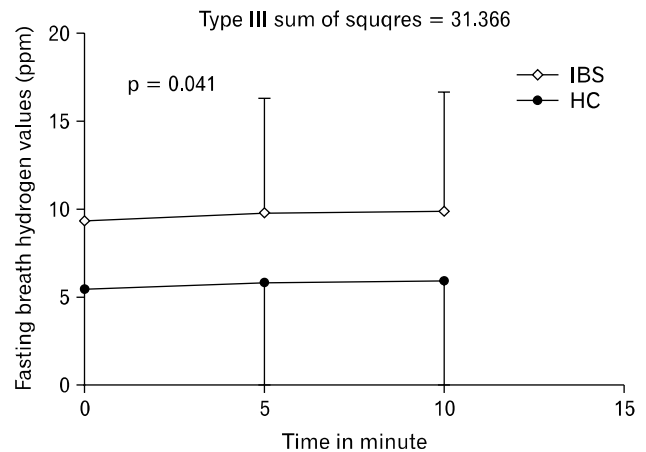


Figure 2. Comparison of fasting breath hydrogen level in patients with irritable bowel syndrome and healthy controls at different time interval using repeated measures of ANOVA. IBS, irritable bowel syndrome; HC, healthy controls.

In a recent study, methane production was found commoner among HC (34.6%) than patients with IBS (14.5%).¹⁰ Since 4 atoms of hydrogen combine to produce 1 molecule of methane, the authors suggested that increased frequency of bloating among patients with IBS might be explained by reduced methane production among them.¹⁰ In another study, Peled et al²⁰ also reported methane production to be commoner among controls (50.0%) than patients with IBS (34.4%). Since methane production is expected to have an inverse relationship with hydrogen levels, these studies support our finding of increased breath hydrogen among patients with IBS than HC. Since as high as 96% of our patients had abdominal bloating, increased hydrogen gas production, at least partly might explain abdominal bloating in IBS.

Fasting breath hydrogen levels were comparable among patients with IBS and controls in a study by Bratten et al²¹ from United States of America (5 vs 7 ppm, respectively). However, the 2 groups were not comparable as control population was 10-year younger than the IBS population.²¹ Furthermore, in that study, baseline hydrogen level was significantly lower among methane producing IBS than those without methane production.²¹ Interestingly, in this study, patients with IBS (20%)²¹ were more often methane producer than control population (15%),²¹ though not significant statistically; this in contrast to a large study that found methane production to be less common among IBS than controls.¹⁰ Hence, contradictory result in the study by Bratten et al²¹ as compared with the present study might be related to non-comparable IBS and control group and

bias in selection of IBS patients.

In another study by Riordan et al²² from Australia, median fasting breath hydrogen among 45 controls was 5 ppm (range, 1-19). This is in accordance with the results in our control population. In that study, the upper 95% confidence limit (mean + 2 standard deviation) of square root of fasting breath hydrogen value was 4 ppm, corresponding to a measured value of fasting breath hydrogen of 16 ppm. Hence, the authors considered > 16 ppm as abnormal and considered it to be diagnostic of small intestinal bacterial overgrowth (SIBO) with a sensitivity and specificity of 22% and 75%, respectively considering the result of quantitative bacterial culture of distal duodenal aspirate as the gold standard. 10% HC and 25% patients with IBS had fasting breath hydrogen value more than 16 ppm in our study. This is in discordance with our previous studies that showed 8.5% to 13% IBS had SIBO compared with 2% HC using glucose hydrogen breath test^{9,12,23}; these data, therefore, further substantiate that fasting breath hydrogen alone should not be used as a criterion for diagnosis of SIBO as reported by some authors previously.^{24,25} Poor performance of fasting breath hydrogen in diagnosis of SIBO has been shown by Riordan et al²² too.

Chatterjee et al²⁶ showed that methane production correlated with constipation in patients with IBS. This is related to slowing of gut transit by methane.²⁶ Our finding of correlation of stool frequency per week and fasting breath hydrogen level, albeit weakly, suggests fasting breath hydrogen levels might correlate with diarrhea. In another study, we found that patients with chronic non-specific diarrhea produced more breath hydrogen than those with IBS and HC.¹² Lack of significant difference in fasting breath hydrogen among patients with D-IBS and C-IBS might be related to criteria used to subtype, as it was based on Bristol stool type or subjective feeling rather than stool frequency. Also, patients with IBS with incomplete evacuation might visit toilet repeatedly resulting in spuriously increased stool frequency.

Other explanation of abdominal bloating in patients with IBS may be related to abnormal movement of gas within gut²⁷ and visceral hypersensitivity.^{5,28} Indeed, earlier studies have shown that patients with IBS had abnormal handling and tolerance of intestinal gas; when challenged with an exogenous gas load, these patients developed gas retention and symptoms.^{29,30} Further, studies have shown that this abnormality might be related to impaired transit of gas in the small bowel, rather than in the colon.^{31,32} Healthy subjects were able to propel gas from the gut when it was infused into the proximal jejunum at a rate as high as 30 mL/min.³³ Patients complaining of bloating retain gas infused

into the proximal jejunum, but the clearance of gas infused into the distal ileum and the cecum was normal.³² Furthermore, scintigraphic studies measuring transit of labeled gas showed that impaired clearance of gas from the gut was due to delayed gas transit in the small bowel.^{8,31} Also, we have shown that patients with IBS more often reported symptoms (bloating, distention, and diarrhea) following 50 g lactose load than HC in spite of a similar frequency of lactose malabsorption in the 2 groups and comparable amount of hydrogen production.⁹ In a previous study, patients with IBS more often reported symptoms following ingestion of dairy products (60% vs 27%) in spite of the same frequency of lactose malabsorption as HC.³⁴ This might be related to visceral hypersensitivity or a decreased pain threshold in patients with IBS, which is common.^{35,36}

What could be the reason for higher hydrogen production in patients with IBS? Since the preparation before the test was similar among the 2 groups, it is unlikely to be related to difference in the dietary intake. Gut flora in patients with IBS may differ from that in HC.³⁷ In a study on 20 patients with IBS, Balsari et al³⁷ showed that there was considerable homogeneity in the fecal flora, and that there was a decrease of *Coliforms*, *Lactobacilli* and *Bifidobacteria* in patients with IBS compared with HC. *Lactobacilli* are less gas producing than some other bacteria, such as *Clostridia* and *Enterobacteriaceae*.³⁸ Administration and colonization of the gut with *Lactobacilli* of patients with IBS have been associated with reduced gas related symptoms.³⁹ Thus, the abnormal gut flora in patients with IBS might cause higher excretion of fasting breath hydrogen. Small intestinal bacterial overgrowth is commoner among patients with IBS than HC.⁴⁰ Since SIBO can be associated with higher amount of hydrogen production in fasting state,⁴¹⁻⁴³ this can be another explanation for our observation.

In conclusion, the present study showed that in spite of similar preparation for the test, fasting breath hydrogen excretion was higher in patients with IBS as compared to HC. Also, number of stools per week correlated with fasting breath hydrogen levels among patients with IBS. Our finding of correlation of stool frequency and fasting breath hydrogen level, albeit weakly, suggests fasting breath hydrogen levels might correlate with diarrhea.

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