Fasting Breath Hydrogen Concentration in Short Bowel Syndrome Patients With Colon Incontinuity Before and After Antibiotic Therapy

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OBJECTIVE: Nutrition success in short bowel syndrome (SBS) depends on the intake nutrients and the intestinal absorption capacity. An evaluation of energy expenditure and oxidation of substrate can be obtained with indirect calorimetry by measuring O₂ and CO₂ in the respiration. Elevated colonic fermentation can occur in SBS, producing H₂ and CO₂ which can also be eliminated through respiration and as a consequence affect the results from indirect calorimetry. The objective of this study was to determine the fasting breath H₂ concentration and alterations before and after antibiotic therapy in patients with severe SBS with colon incontinuity.

METHODS: The study was conducted in two phases. In phase 1, the fasting breath H₂ concentrations were measured in 10 patients with severe SBS with colon incontinuity and a control group of 10 healthy volunteers. In phase 2, the fasting breath H₂ concentrations were re-evaluated after treatment for 7 d with antibiotics in six patients with high rates of H₂. The analyses were performed with a gas chromatograph (microanalyzer DP; Quintron Instruments, Milwaukee, WI, USA), with results of breath hydrogen and methane concentration expressed in parts per million (ppm).

RESULTS: In phase 1, the levels of fasting breath H₂ were higher in the patients with severe SBS with colon incontinuity than in the healthy controls (32.00 ± 17.77 versus 5.30 ± 3.31 ppm; P < 0.001), with 7 of 10 patients presenting levels of H₂ above the normal rate (12 ppm). The presence of an ileoceleal valve did not modify the results significantly. In phase 2, all six patients treated with antibiotics presented normalization in the levels of fasting breath H₂ (from 43.50 ± 6.90 ppm to 1.33 ± 1.03 ppm; P < 0.001) and concomitant improvement in the gastrointestinal symptoms.

CONCLUSIONS: In relation to the healthy controls, patients with SBS with colon incontinuity presented higher levels of fasting breath H₂. Antibiotic therapy normalized the levels of fasting breath H₂ and improved the gastrointestinal symptoms. We suggest that the breath H₂ test may be performed routinely in patients with SBS to diagnose elevated intestinal fermentation, prevent errors in the interpretation of the indirect calorimetry, and treat eventual associated gastrointestinal symptoms. Nutrition 2004;20:187–191. ©Elsevier Inc. 2004

KEY WORDS: short bowel syndrome, hydrogen, indirect calorimetry, carbon dioxide, colonic fermentation
obtained by IC may not be representative and lead to errors in interpretation, principally when evaluating the oxidation of the macronutrients, leading to an overestimation of the oxidation of carbohydrates and an underestimation of the oxidation of lipids.10,21 Therefore, it is necessary to verify the presence of elevated colonic fermentation when intending to evaluate the oxidation of substrate by IC.10,21

After lactulose testing in patients with SBS and remnant colon fermentation, a positive correlation was found between BH₂ and CO₂,10 which enables the use of BH₂ dosage to establish in an indirect manner the possible presence of CO₂ originating from colonic fermentation. Studies have suggested the importance of determining the BH₂ concentration while the IC is performed to correct the carbon dioxide production value in calorimetry.10,21 However, due to the non-existence of a specific formula for the correction of CO₂ originating from colonic fermentation to be used in patients with SBS, it is important to investigate the presence of elevated colonic fermentation during fasting before performing IC.

There is an association between the production of BH₂ and overgrowth of bacteria identified in small intestine culture.19,22,23 Bacterial overgrowth in the small intestine can unchain hyperfermentation and cause intestinal symptoms, malabsorption (macronutrients and vitamins), and malnutrition.1,4,18,24 These complications can compromise the recovery and prognosis of patients with SBS. Antibiotic treatment may be necessary.² It has been observed in patients with intestinal resection due to Crohn’s disease that antibiotic treatment normalizes the concentrations of BH₂ as evaluated by the lactulose test and improves gastrointestinal symptoms (pain, bloating, and soft stools).²⁵

The present study measured fasting BH₂ (FBH₂) concentrations in patients with severe SBS with colon incontinuity and the changes in these values after treatment with antibiotics. The study was performed in two phases. In phase 1, the levels of FBH₂ were evaluated in patients with severe SBS with colon incontinuity and healthy volunteer controls. In phase 2, the patients with high FBH₂ were treated with antibiotics and their FBH₂ levels were measured again.

MATERIALS AND METHODS

This study was approved by the ethics committees of the Faculdade de Medicina da Universidade de São Paulo and the Universidade Federal de São Paulo/Escola Paulista de Medicina. Informed written consent was obtained from all participants.

Phase 1

SUBJECTS. Twenty individuals participated in the first phase, 10 patients in the SBS group (five women and five men) and 10 healthy volunteers in the control group (five women and five men). Data regarding the gastrointestinal tract of patients are given in Table I. The mean length of the remaining small intestine was 59.20 ± 28.08 cm; all patients presented a total or partial colon incontinuity, and the ileocecal valve was present in three and absent in seven patients. The mean ages of the patients and healthy controls were 44.20 ± 12.83 y and 43.20 ± 11.75 y, respectively (P = 0.858; Table II). The patients under evaluation were chosen consecutively from the multidisciplinary short intestine outpatient clinic, Grupo de Estômago e Intestino Delgado da Disciplina de Cirurgia do Aparelho Digestivo do Departamento de Gastroenterologia do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, and healthy volunteers without medical risks were recruited from the same hospital community. Inclusion criteria for the SBS group were diagnosis of SBS with adaptation to oral feeding without home parenteral nutrition and non-use of antibiotics for a period of at least 3 mo. The control volunteers were paired with the patients with respect to age (± 5 y) and sex; none presented intestinal impairment or had used antibiotics within the previous 3 mo. Both groups were comprised of non-smokers.¹⁵

STUDY PROCEDURE. Patients and healthy controls underwent the BH₂ test after a fasting period of 10 to 13 h and without previous exercise.¹⁹,²⁰,²³

Collection of expired air for H₂ analysis was done in the morning at the hospital clinic and by the researcher. All participants were requested to brush their teeth and immediately before the collection to use a mouthwash with 15 mL of 0.12% chlorhexidine gluconate for disinfecting the oral cavity,¹⁷ because a high load of local bacteria can interfere with the result. The examination was performed in duplicate, with an interval of approximately 5 min between collections. Analyses of the gases were performed with a gas chromatograph (microanalyzer DP; Quintron Instruments, Milwaukee, WI, USA), and the values of H₂ and methane (CH₄) were recorded. Before beginning the evaluations, the chromatograph was calibrated with a mixture of H₂
Breath Hydrogen Testing in Short Bowel Syndrome

**TABLE II.**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>Age</td>
</tr>
<tr>
<td>1</td>
<td>51</td>
</tr>
<tr>
<td>2</td>
<td>45</td>
</tr>
<tr>
<td>3</td>
<td>46</td>
</tr>
<tr>
<td>4</td>
<td>67</td>
</tr>
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<td>5</td>
<td>48</td>
</tr>
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<td>29</td>
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<td>7</td>
<td>36</td>
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<td>8</td>
<td>32</td>
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<td>9</td>
<td>29</td>
</tr>
<tr>
<td>10</td>
<td>59</td>
</tr>
<tr>
<td>Mean</td>
<td>44.20</td>
</tr>
<tr>
<td>SD</td>
<td>12.83</td>
</tr>
</tbody>
</table>

* P < 0.001, with a statistically significant difference between groups (Wilcoxon signed rank test).

F, female; FBH₂, fasting breath hydrogen; M, male; ppm, parts per million; SD, standard deviation

(97%) and methane (49%), according to the manufacturer’s instructions. The reading was given in parts per million (ppm), and the results were considered a mean of the two evaluations. The analyses were performed in the Disciplina de Gastroenterologia Pediátrica do Departamento de Pediatria da Universidade Federal de São Paulo/Escola Paulista de Medicina, and the protocol for the collection of the gas was in agreement with that in our institution and adapted according to the literature. Analyses were done within 6 h after collection. Elevated values of BH₂ were considered to be those over 12 ppm.

**Phase 2**

Six patients who presented high BH₂ concentrations in phase 1 (patient nos. 1, 3, 5, 6, 7, and 9) were selected to participate in phase 2. These patients received antibiotic therapy with 500 mg of ciprofloxacin every 12 h for 7 d and were then re-evaluated. The same methodology used in phase 1 was used for the preparation of these patients, the collections, and analyses of FBH₂. In this phase, subjective information regarding symptoms also was collected: frequency of evacuation; consistency of the feces; presence of colic, flatulence, and abdominal distention; and alterations before and after antibiotic therapy.

**Statistical Methods**

All results are expressed as mean ± standard deviation. Comparisons between groups (SBS and healthy controls) and the treatment provided for the patients (before and after antibiotic therapy) were done with the paired t test, Wilcoxon signed rank test, and Fisher’s exact test. The results were considered statistically significant at P < 0.05.

**RESULTS**

**Phase 1**

The results from the evaluations of FBH₂ in group SBS were, on average, above the normal range, 32.00 ± 17.77 ppm (range, 5.00–50.50 ppm). The control group presented values within normal limits, 5.30 ± 3.31 ppm (range, 0.0–10.50 ppm), which was significantly lower than those obtained in the SBS group (P < 0.001; Table II). There was no association between the presence of an ileocecal valve and high levels of FBH₂ (Fisher’s exact test, P = 0.183). The values of expired CH₄ were insignificant in all study participants (CH₄ < 1 ppm).

**Phase 2**

The levels of FBH₂ were normalized in patients after antibiotic treatment; mean values of this subgroup fell from 43.50 ± 6.90 ppm (range, 31.00–50.50 ppm) to 1.33 ± 1.03 ppm (range, 0–3.00 ppm; P < 0.001; Table III). Gastrointestinal symptoms (colic, flatulence, and abdominal distention) were reported by all patients in this subgroup with the exception of patient no. 9. After antibiotic treatment, there was a subjective improvement in four of the five who initially presented symptoms, without modification in the consistency of the feces. The initial picture persisted in one patient (patient no. 7), and the consistency of the feces changed from semiliquid to liquid. With regard to the frequency of evacuation, there was no modification from the initial presentation in all six patients.

**DISCUSSION**

The objective of this study was to verify the FBH₂ levels of patients with severe SBS with colon incontinuity and to re-evaluate the levels of FBH₂ in a subgroup of patients with SBS undergoing antibiotic treatment.

High levels of BH₂ can reflect the production of CO₂ by colonic fermentation, and colonic fermentation can compromise an IC evaluation by the oxidation of macronutrients. When the BH₂ test is used to indirectly measure fermentation of carbohydrates in the colon, the existence of a constant proportion is assumed between H₂ generated in the intestine and excreted in the lungs. However, part of the hydrogen may be eliminated in the form of CH₄. Methanogenic individuals convert a great part of H₂ into CH₄. However, none of the participants in either group were shown to be methanogenic.

In the present study, more than 50% of the patients with SBS presented elevated values of FBH₂, whereas all subjects in the control group had normal values. The results obtained in this work were similar to those of other studies that performed BH₂ tests, e.g., SBS, Crohn’s disease, celiac disease, and others gastro-
intestinal diseases. In SBS elevated levels of BH$_2$ can occur due to malabsorption principally of carbohydrates and to elevated colonic fermentation. In the present investigation, patients with high levels of BH$_2$ frequently presented gastrointestinal symptoms, and after treatment with antibiotics, there was generally a normalization in the levels of BH$_2$ and an improvement in these symptoms. These data are compatible with those of Castioglione et al., who also observed such an improvement in gastrointestinal symptoms among patients with high levels of BH$_2$ after treatment with antibiotics.

Although the bacterial overgrowth in the small intestine is associated with impairment of the nutrition state, such colonic fermentation is beneficial in some patients with SBS, because this fermentation may be responsible for salvaging energy originating from carbohydrates that were not digested in the colon and for a 50% reduction in the parenteral nutrition needs of patients with SBS.

The results of the present study suggest the need to measure BH$_2$ before performing IC, principally by evaluation of the oxidation of substrate. It is a very complex task to establish the extension of the confounding error arising from bacterial fermentation in the interpretation of the gas concentrations (oxygen consumption and CO$_2$ production) obtained by the IC apparatus in this population of patients. This is because the value of CO$_2$ determined by the IC equipment reflects the sum of CO$_2$ produced by cellular oxidation and intestinal bacterial fermentation. The formulas usually used in IC do not take these aspects into consideration, and there currently is no mathematical correction available for patients with SBS. In the future, it would be interesting to determine the effect of SBS and bacterial overgrowth on the validity of IC.

The validity of IC in the evaluation of thermogenesis associated with carbohydrates fermented in humans was reviewed recently. The present work has demonstrated that, in relation to healthy controls, patients with severe SBS with colon incontinuity with or without an ileocecal valve present higher levels of FBH$_2$. Further, antibiotic therapy normalizes the levels of FBH$_2$ and improves gastrointestinal symptoms.

We suggest that the BH$_2$ test should be performed on a routine basis in patients with SBS to diagnose elevated intestinal fermentation, prevent mistakes in the interpretation of IC, and treat the eventual associated gastrointestinal symptoms.

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### REFERENCES


### TABLE III.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Sex</th>
<th>FBH$_2$ (ppm)*</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
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<tr>
<td></td>
<td></td>
<td></td>
<td>FE/d CF C FL AD</td>
<td>FE/d CF C FL AD</td>
</tr>
<tr>
<td>1</td>
<td>F</td>
<td>41.00</td>
<td>2 Pasty + + +</td>
<td>2 Pasty – – –</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>45.00</td>
<td>1 Pasty – + +</td>
<td>1 Pasty – – –</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>48.00</td>
<td>1–2 Pasty + + +</td>
<td>1–2 Pasty – – –</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>45.50</td>
<td>3–4 Liquid – + +</td>
<td>3–4 Liquid – – –</td>
</tr>
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<td>7</td>
<td>M</td>
<td>50.50</td>
<td>2–3 Semi-liquid + + +</td>
<td>2–3 Liquid + + +</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>31.00</td>
<td>2–3 Pasty – – –</td>
<td>2–3 Pasty – – –</td>
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<tr>
<td>Mean</td>
<td></td>
<td>43.50</td>
<td>1.33</td>
<td>–</td>
</tr>
<tr>
<td>SD</td>
<td></td>
<td>6.90</td>
<td>1.03</td>
<td>–</td>
</tr>
</tbody>
</table>

* FBH$_2$ BT versus FBH$_2$ AT (P < 0.001), with statistically significant difference (paired t test).

–, absent; +, present; AD, abdominal distention; AT, after treatment with antibiotics; BT, before treatment with antibiotics; C, colic; CF, consistency of feces; F, female; FE, frequency of evacuations; FL, flatulence; FBH$_2$, fasting breath hydrogen; M, male; ppm, parts per million; SD, standard deviation.

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