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The relationship between small intestinal bacterial overgrowth and irritable bowel syndrome

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Abstract. – OBJECTIVE: To explore the relationship between small intestinal bacterial overgrowth (SIBO) and irritable bowel syndrome (IBS).

PATIENTS AND METHODS: Fifty IBS patients in the hospital from January 2015 to December 2015 were assigned to the treatment group, and 50 healthy persons were assigned to the control group. Lactulose hydrogen and methane breath test were performed to measure the percentage of SIBO and oro-cecal transit time (OCTT) in treatment group and control group. These subjects were further assigned to negative SIBO group and positive SIBO group to analyze the scores of symptoms.

RESULTS: The percentage of positive SIBO in the treatment group (72%, 36/50) was significantly higher ($p<0.05$) than the control group (38%, 19/50). The scores of symptoms on the episode of IBS were not significantly different between the positive SIBO subgroup and the negative SIBO subgroup. The scores of symptoms in breath test were not significantly different between the positive SIBO subgroup and the negative SIBO subgroup. The OCTT in the treatment group (69.34±1.27 min) was significantly lower ($p<0.05$) than the control group (85.16±1.75 min). The OCTT in the positive SIBO group (88.57±4.62 min) was significantly higher ($p<0.05$) than the control group (73.42±5.25 min). The results of lactulose hydrogen and methane breath test in the treatment group were positively correlated ($r = 0.987$, $p<0.01$). The results of lactulose hydrogen and methane breath test in the control group after oral administration of lactulose were also positively correlated ($r = 0.736$, $p<0.01$).

CONCLUSIONS: SIBO was related to IBS and could prolong OCTT, yet not worsen IBS.

Key Words
Small intestinal bacterial overgrowth, Irritable bowel syndrome, Lactulose hydrogen breath test.

Introduction

Clinical manifestations of IBS include diarrhea, abdominal distention and pain, abnormal intestinal motility and change in bowel habits[1,2], thus IBS is similar to SIBO. As a result, SIBO is usually diagnosed as IBS. Currently, whether SIBO is the cause of IBS or a concomitant disease of IBS is controversial[3-5]. This is because clinical diagnosis criteria of IBS are more than that of SIBO. Different criteria may lead to different results. Direct culture of intestinal fluid is the currently gold standard of SIBO diagnosis[6]. However, this method is difficult to perform and an invasive test, which requires bacterial culture and inconvenient intubation for sampling. Therefore, the rate of false negative is high[7]. Lactulose hydrogen breath test is non-invasive, convenient to perform patient acceptability; thus widely used in the diagnosis of SIBO[8]. Our study simultaneously detects hydrogen and methane in lactulose hydrogen breath test, and analyzed the relationship between SIBO and IBS.

Patients and Methods

Patients

Fifty IBS patients in the hospital from January 2015 to December 2015 were assigned into treatment group, including 27 males and 23 females, age 21-67 years (mean age 47.8±4.2 years), 40 cases of diarrhea, 6 cases of constipation and 4 cases of mixed diarrhea and constipation. All these patients met Rome III Diagnostic Criteria. Patients with vascular and renal diseases were excluded. Another 50 healthy persons, who received physical examination, were assigned into the control group. The later including 26 males and

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24 females, age 22-66 years (mean age 48.2±4.5 years). These persons had no significant gastrointestinal symptoms, history of alcohol or cigarette consumption, previous abdominal surgery, diabetes mellitus, or neurological diseases that may affect gastrointestinal motility within 1 year. General characteristics between the treatment group and the control group were not different.

The Ethics Committee of our institution approved our research. The patients gave their informed consent.

Methods

Lactulose Hydrogen Breath Test

These patients should not use lactulose, antibiotic or other drugs that may affect gastrointestinal motility 1 month before this trial. Coloclysis was prohibited within half a month before the current trial. Hydrogen-producing food, such as dairy and wheat flour, was prohibited within 24 h before examination, satiation was also avoided. Food and water were prohibited within 12 h before examination. Brushing teeth should be performed on the day of the examination, whereas smoking was prohibited.

The breath analyzer was purchased from Quin Tron (Milwaukee , WI, USA). Both the levels of hydrogen and methane were represented by ppm. The standard curve was plotted after calibration of the breath analyzer, which detected the levels of hydrogen and methane in the breath of fasting subjects. The subjects were orally administrated with lactulose 10 ml (Abbott Healthcare Products B.V., Weesp, The Netherlands, Registry No. H20120387), then exhaled 1 time every 20 min. The levels of hydrogen and methane at different time points were measured and recorded, the profile of hydrogen level against time and the profile of methane level against time were plotted.

Diagnostic Criteria of SIBO

The diagnostic criteria of positive hydrogen breath test: one of the following criteria[9]: I- Hydrogen level in fasting breath ≥ 20 ppm, mean hydrogen level of duplicate measurements at an interval of 20 min ≥ 20 ppm; II- Classical dual peaks, i.e., small intestine peak and colon peak, were seen after oral administrated of lactulose. The level of hydrogen peak was higher than fasting level by 12 ppm, with a starting point before 90 min. Another higher peak appeared 60 min later. III- After oral administrated of lactulose, a high flat peak appeared as a starting point before 90 min, and the highest level was higher than fasting level by 20 ppm within 180 min. IV- The hydrogen level was increased by 20 ppm 90 min after oral administrated of lactulose[2]. The diagnostic criteria of positive methane breath test: one of the following criteria[10]: I- Methane level in fasting breath ≥ 10 ppm, mean methane level of duplicate measurements at an interval of 20 min ≥ 10 ppm. II- After oral administrated of lactulose, a high flat peak appeared as a starting point before 90 min, and the highest level was higher than fasting level by 10 ppm within 180 min. Those patients, who met the above criteria of positive hydrogen/methane breath test, were determined as positive SIBO.

Scores of IBS Symptoms

The intestinal symptoms and breath test of IBS patients were graded on the episode of IBS. These symptoms were graded according to severity and frequency, the combination of each symptom score was considered as a total score[10].

OCTT

The time to the increment of hydrogen level in hydrogen breath test > 10×10^{-6} was considered OCTT. The duration of increasing hydrogen level was ≥ 30 min. If dual peak appeared, the first peak was considered small intestine peak (indicating SIBO), the second peak was considered colon peak (indicating OCTT)[11].

Observational Measurements

The incidence of positive SIBO was analyzed through lactulose hydrogen and methane breath test, and the OCTT was compared between the treatment group and the control group. The patients in treatment group were further assigned to negative SIBO subgroup and positive SIBO subgroup; the scores of IBS symptoms were compared.

Statistical Analysis

SPSS 20.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Measurement data were expressed as mean±SD and analyzed by *t*-test or rank sum test. Categorical data were expressed as frequency and percentage, and analyzed by X^2 test. $p<0.05$ was considered as significant difference.

Results

Percentage of Positive SIBO

As shown in Figure 1, the percentage of positive SIBO in the treatment group (72%, 36/50) was significantly higher ($p<0.05$) than the control group

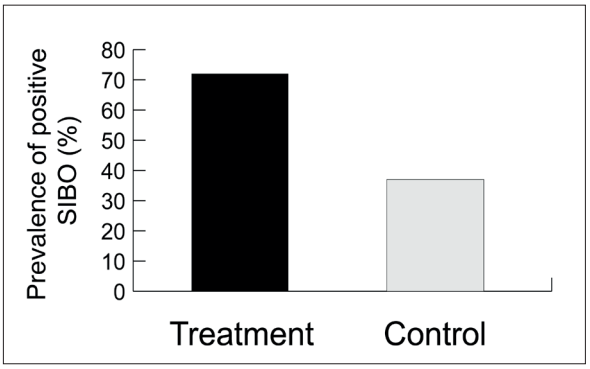

Figure 1. The prevalence of positive SIBO.

(38%, 19/50). The percentage of positive hydrogen breath test in the treatment group (68%) was significantly higher (p<0.05) than the control group (32%). The percentage of positive methane breath test in the treatment group (46%) was significantly higher (p<0.05) than the control group (32%). Only 2 IBS patients with diarrhea had negative hydrogen breath test and positive methane breath test.

Scores of Symptoms

As shown in Table I, the scores of symptoms on the episode of IBS were not significantly different between the positive SIBO subgroup and the negative SIBO subgroup. As shown in Table II, the scores of symptoms in breath test were not significantly different between the positive SIBO subgroup and the negative SIBO subgroup.

OCTT

As shown in Figure 2, the OCTT in the treatment group (69.34±1.27 min) was significantly lower (p<0.05) than the control group (85.16±1.75 min). As shown in Figure 3, the OCTT in the positive SIBO group (88.57±4.62 min) was significantly higher (p<0.05) than the control group (73.42±5.25 min).

Table I. The scores of symptoms in patients with positive SIBO and patients with negative SIBO on the episode of IBS.

Group	Defecation frequency	Feces properties	Percentage of abnormal feces properties	Abdominal pain	Abdominal discomfort	Abdominal distension	Belching	Bowel sound	Intestinal exhaust	Total
Positive SIBO group (n=36)	1.25±0.42	1.93±0.63	2.74±0.86	3.06±1.26	3.53±1.64	2.97±1.51	1.01±0.55	1.13±0.71	1.04±0.85	16.63±6.84
Negative SIBO group (n=14)	1.21±0.45	1.88±0.57	2.81±0.91	3.12±1.38	3.44±1.53	3.05±1.42	1.12±0.64	1.08±0.86	1.01±0.91	16.52±6.27
p	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05

Table II. The symptom scores of breath test in positive SIBO group and negative SIBO group.

Group	Defecation frequency	Feces properties	Percentage of abnormal feces properties	Abdominal pain	Abdominal discomfort	Abdominal distension	Belching	Bowel sound	Intestinal exhaust	Total
Positive SIBO group (n=36)	0.57±0.16	1.32±0.43	1.76±0.76	2.65±1.34	2.47±1.03	2.36±1.12	0.53±0.45	0.98±0.84	0.82±0.73	13.48±5.85
Negative SIBO group (n=14)	0.56±0.25	1.29±0.38	1.84±0.82	2.73±1.25	2.38±0.97	2.43±1.25	0.61±0.52	0.87±0.77	0.76±0.68	13.36±6.02
p	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05

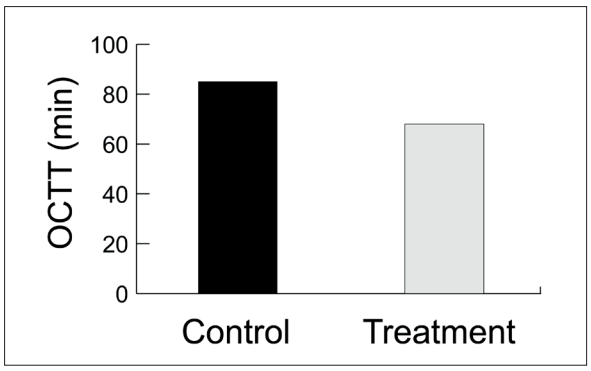

Figure 2. OCTT in treatment group and control group.

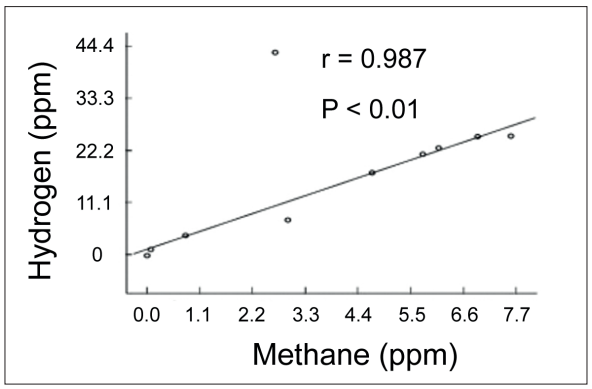

Figure 4. The relationship between hydrogen breath test and methane breath test in treatment group.

The Relationship Between Lactulose Hydrogen and Methane Breath Test

As shown in Figure 4, the results of lactulose hydrogen and methane breath test in the treatment group were positively correlated (r = 0.987, $p<0.01$). As shown in Figure 5, the results of lactulose hydrogen and methane breath test in the control group after oral administrations of lactulose were also positively correlated (r = 0.736, $p<0.01$).

Discussion

SIBO can affect human intestinal functions. For IBS patients, the presence of SIBO may determine the clinical symptoms accurately[12]. Currently, common detection of SIBO includes bacterial culture of intestinal fluid, lactulose hydrogen and methane breath test[13]. Among others, lactulose hydrogen and methane breath test are easy-to-performing and non-invasive, thus were preferred. Lactulose is difficult to digest and absorb in human intestine, and only degraded into gas by bacteria in the colon[14]. After oral administration of lactulose, if bacterial overgrew in the small intestine, lactulose will be degraded early, leading to increased hydrogen in breath. Gas may be produced again if lactulose reaches the colon, leading to SIBO-specific dual peak[15,16]. The current study demonstrated that the percentage of positive SIBO in the treatment group (72%) was significantly higher than the control group ($p<0.05$). This indicated a higher occurrence of SIBO in IBS patients, and SIBO may be associated with IBS. Hydrogen breath test could both detect SIBO and measure OCTT. In our study, the OCTT in the treatment group (69.34±1.27 min) was significantly lower ($p<0.05$) than the control group (85.16±1.75 min). The OCTT in the positive SIBO subgroup (88.57±4.62 min) was significantly higher ($p<0.05$) than the negative SIBO subgroup (73.42±5.25 min). As reported by Cuoco et al[17], SIBO could slow human intestinal transit, prolong OCTT and affect intestinal motility. Methanogens are present in human intestine, where they can transform hydrogen into methane, leading to a

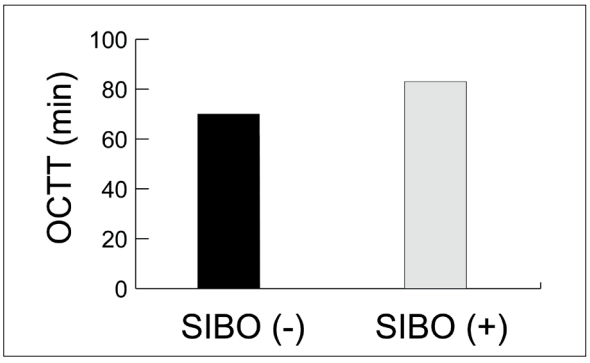

Figure 3. OCTT in positive SIBO group and negative SIBO group.

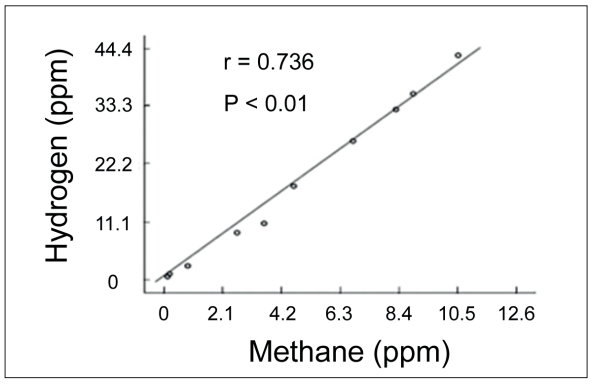

Figure 5. The relationship between hydrogen breath test and methane breath test in control group.

false negative result in hydrogen breath test. Thus, methane breath test is usually performed for subjects with negative hydrogen breath test. This can determine the presence of methanogens and allow accurate diagnosis of SIBO[18]. Lee et al[19] performed lactulose hydrogen and methane breath test in 68 IBS patients and found that 4 patients had negative hydrogen breath test yet positive methane breath test. Our study confirmed the above report and showed that 2 IBS patients with diarrhea had negative hydrogen breath test yet positive methane breath test. Further analysis found that the results of lactulose hydrogen and methane breath test in treatment group were positively correlated ($r = 0.987$, $p<0.01$). The results of lactulose hydrogen and methane breath test in the control group were also positively correlated ($r = 0.736$, $p<0.01$). This indicated that methane level was positively related to hydrogen level in the breath test of both IBS patients and healthy subjects. The diagnostic value of methane breath test for IBS patients who had negative hydrogen breath test was limited[20]. The symptoms of SIBO were similar with those of IBS[21]. We found no significant difference in the scores of IBS symptoms between positive SIBO subgroup and negative SIBO subgroup. As reported by Grover and collaborators[22], the scores of symptoms in breath test were not significantly different between positive SIBO subgroup and negative SIBO subgroup. These underscored similar symptoms between IBS and SIBO, and reflected that the etiology and pathogenesis of IBS were complicated.

Conclusions

SIBO was related to IBS. SIBO could prolong OCTT, yet not worsen IBS. This study lays the foundation for the diagnosis and treatment of IBS.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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