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SMALL INTESTINE BACTERIAL OVERGROWTH IN IRANIAN IRRITABLE BOWEL SYNDROME PATIENTS

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ABSTRACT

Irritable bowel disease (IBS) Symptoms are similar to small intestinal bacterial overgrowth (SIBO). Many studies have revealed relation between IBS and SIBO. We decided to demonstrate the glucose hydrogen breath test (GHBT) in SIBO diagnosis in IBS patients in current study.

The diagnostic interventional study was designed and 126 patients within the age limit of 18-65 years based on sample size selection who met ROME III criteria for IBS were enrolled. They were subcategorized as having IBS with diarrhea (IBS-D), IBS with constipation (IBS-C), mixed IBS (IBS-M) or unsubtyped IBS (IBS-U) based on predominant bowel habits. After that, GHBT was performed for them and frequency of SIBO based on GHBT was evaluated.

Totally, 57 cases (45.2%) had positive GHBT result. There are no significant differences in

sex and age between positive and negative GHBT patients but statistical significant differences ($p<0.05$) were declared regarding to bloating and subgroups of IBS. The positive GHBT was more frequent in patients with bloating (OR=8.17; CI95%=2.3-29.2) and it is so dependent to type of IBS in such a manner that positive GHBT was 4.8-fold in IBS-D. We used ROC analysis to estimate the accuracy of bloating for GHBT positive patients' diagnosis (area under curve was 69.5% CI95%= 59 – 80; p =0.002). Sensitivity of bloating for GHBT positivity was 93% and specificity was 34.3%.

GHBT is effective procedure for detecting SIBO in clinical practice and IBS patients. On the other hand bloating in IBS patients can be indicated SIBO in these patients.

Keywords: Bacterial Overgrowth, Bloating, Hydrogen Breath Test, Irritable Bowel Syndrome

INTRODUCTION

Irritable bowel syndrome (IBS) is a common gastrointestinal (GI) disorder which mimics abdominal pain and GI disturbance without any specific organic cause. Patients with IBS present wide range of symptoms which include both GI and extra GI complains. However the main complaints of IBS are abdominal pain and altered intestinal habits **[1**]. The prevalence of IBS in Europe and North America are estimated 10 to 15 percent **[1]**. The prevalence of IBS in Iran is much lesser than other country but it is seems to be increasing; two population-based studies have estimated it from 1.1% in 2003 to 5.8% in 2009 **[2, 3]**. The etiology of IBS is unclear yet. Some prevailing hypotheses in pathophysiology of IBS are GI motility disturbance, visceral hypersensitivity, inflammation, alterations in fecal flora, food sensitivity, bacterial overgrowth and some genetic factors **[4]**. Small intestinal bacterial overgrowth (SIBO) has been considered by researchers in pathophysiology of IBS in recent years. SIBO is excessive growth and number of bacterial in small intestine which is defined as the chronic presence of symptoms such as abdominal pain, GI disturbance and bloating which may be associated with excessive gas of small intestine due to increased production by bacterial fermentation in the gut. These are the same symptoms in IBS **[5]**. Many studies indicated a link between SIBO and IBS **[6-10]**. In contrast, some studies have refused this hypothesis **[11-13]**. Therefore, there is controversy surrounding

the proposed etiologic role of SIBO in IBS. SIBO detects with several test. Lactulose and glucose (GHBT) breath testing have been proposed as sensitive and simple tools for the diagnosis of bacterial overgrowth, because of their noninvasiveness and low cost when compared with the gold standard (culture of jejunal aspirate) **[14]**. The aim of this study aimed to investigate the relation between IBS and SIBO and some predictors of SIBO in IBS patients and evaluate the GHBT in SIBO diagnosis in IBS patients.

METHODOLOGY

This diagnostic interventional study was conducted in 2010 to August 2011 among 126 patients age between 18 to 65 years old who met ROME III criteria for IBS. They were included consequently and evaluated by gastroenterologist. Patients with diabetes mellitus, scleroderma, IBD, prior small intestinal surgery, under treatment with any chemical therapy among last three month and GI infections were excluded. All of them assigned written inform consent to participate in study. Demographic data, predominant symptoms and past medical history were recorded. They were subcategorized as having diarrhea-predominant IBS (IBS-D), constipation-predominant IBS (IBS-C), mixed IBS (IBS-M) or subtype IBS (IBS-U) based on predominant bowel habits. After that, patients were referred for GHBT. It required that patients had been had a low carbohydrate meal and fast for ≥12 hours before testing. Smoking and physical exercise were not allowed 1 hour before the test. Chlorhexadine mouthwash must be used immediately before the test to eliminate oral bacteria. One breath sample was obtained at baseline then 1 g/kg pure glucose dissolved in 150 ml water was ingested by patients. Then test continued after 30, 60, and 90 minutes and all peak values of hydrogen were recorded for each patients, and total excretion of hydrogen was calculated as an area-under-time concentration curve. The breath test results were considered positive for SIBO if: 1) the hydrogen peak was >20 parts per million (ppm) at baseline or, 2) the hydrogen peak increased by >20 ppm from baseline at post-glucose ingestion measures [9]. All measures were done by one hydrogen breath test (HBT) device (Micro H_2 and Hydra, Micromedical LTD Co., England). The statistical analysis was done by SPSS 15 statistical software Package (Chicago, USA). Nominal variable were compared by χ^2 test and Fischer's exact test. Evaluation of the quantitative data was

statistically analyzed by Student's t-tests. Logistic regression analysis was used to find predictors of GHBT in IBS patients. We calculated goodness-of-fit in unconditional logistic model with Hosmer-Lemeshow test. After determining prevailed factors the receiver operating characteristic analysis was used to evaluate the accuracy of bloating in positive GHBT and SIBO diagnosis. The values of $p<0.05$ were considered to be statistically significant.

The study protocol was approved by Najafabad Medical School with approval number: 15010101882045.

RESULT

From total of 126 patients with IBS who were assessed by GHBT, 29 cases (23%) were male and 97 cases (77%) were female. The mean age was 37.6±10.3 years old (range, 16-64 years). Twenty two patients (17.5%) were IBD-D, fortysix (36.5%) were IBS-C, nineteen (15%) were IBS-M and thirty nine patients (31%) had IBS-U. bloating was visited in 99 individuals (78.6%). Totally, fifty seven cases (45.2%) had positive GHBT result.

There are no differences in sex and age between positive and negative GHBT patients but statistical significant differences ($p<0.05$) were declared regarding to bloating and subgroups of IBS **(Table 1)**. Logistic regression analysis showed the positive GHBT was more frequent in patients with bloating (OR=8.17; CI95%=2.3-29.2) and it is so dependent to type of IBS in such a manner that positive GHBT was 4.8-fold in diarrhea type IBS **(Table 2)**.

We used ROC analysis to estimate the accuracy of bloating for GHBT positive patients' diagnosis. ROC analysis determined the area under curve was 69.5% (CI95%= 59 – 80; p =0.002). **Figure 1** showS the ROC diagram and area under curve. Sensitivity of bloating for GHBT positivity was 93% and specificity was 34.3%.

DISCUSSION

One of probable factors in IBS pathophysiology is SIBO. This bacterial overgrowth produces some gas in intestine and detection of gas assesses the SIBO, indirectly. In the current study we intended to assess SIBO in IBS patients with GHBT. We found 45.2% of patients had positive GHBT. The range of positive hydrogen breathing tests in different studies was varied from 23% to 54% **[7-9, 15-18]**. Differences in the population characteristics (i.e. age, geographical origin) and methodology for HBT (kind of sugar consumption for test, model of chromatograph, gases analyzed, criteria to

assess positivity to the test) may explain the discrepancy in the prevalence of SIBO across these studies **[16]**. Ford and *et al*. **[16]** demonstrated in a Meta analysis that the positive test was higher if hydrogen test was done by Lactulose. 54% with lactulose, in contrast to 31% with glucose. It seems, digestive capacity of intestine regarding to different sugars varies. Glucose is absorbed fast in the proximal small intestine. Thus detecting hydrogen in this test means SIBO in a proximal location. In contrast, lactulose can pass more through small bowl and is absorbed more distal than glucose. It justifies the high prevalence of positive hydrogen test in lactulose HBT **[5]**. In this manner, GHBT is the most commonly used test in the diagnosis of SIBO, although GHBT may be less sensitive for the diagnosis of SIBO since it is absorbed in the proximal small bowel. Its overall sensitivity in detecting SIBO was between 25% to 93% and specificity was from 34% to 96% **[5, 19]**.

On the other hand, type of IBS was affected on GHBT result. In our result positive test was higher in IBS-D than other type significantly. Many studies demonstrated that GHBT was more positive in patients with chronic non-specific diarrhea and when patients obtained ROME III criteria for IBS, SIBO based on GHBT was more frequent in diarrheal type of IBS **[15, 20]**.

However, it seems the gold standard for SIBO is direct method like culture of jejunal aspirates **[14]**. False positive rate in breath tests was higher to compare direct intestinal culture **[11]**. Many studies have examined orocecal scintigraphy to detect SIBO but it has not been effective for SIBO detection **[12, 13]**. In clinical evaluation breath tests are the best choice for clinician to evaluate SIBO in patients with GI problem, especially to differentiate IBS **[18, 21, 22]**.

One of new finding in current study was the accuracy of bloating as a symptom of IBS in diagnosis of SIBO. Bloating in IBS patients can be indicated SIBO in these patients. There were some advantages in the current study. We omitted the patients under treatment of acid reducing drugs like proton pump inhibitors and H2 blockers and other medication. To prevent the age effect on SIBO, we limited the age range of our patients from 18 to 65 years old (because the incidence of SIBO increases with age 4) **[23]**. Our study had many limitations, the

first was the no ability to measure other gas produced by bacterial fermentation like methane. Measuring methane increased the positive result of breath test **[15, 24]**. We had age limitation because age enhancement increases SIBO. We had selected individual between 18 to 65 years old.

CONCLUSION

It seems one of the etiologic factors for IBS is SIBO. Diagnosis and treatment of it can help IBS patients' health improvement. GHBT is effect procedure for detecting SIBO in clinical practice. On the other hand we found bloating was good criteria for roll-out of SIBO in IBS patients.

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Table 1: Demographic characteristics of patients with IBS distributed by GHBT result				
		IBS with +GHBT	**IBS with -GHBT**	***P* value**

sex	**Male**	**12**	**17**	**χ^2=0.226**
	Female	**45**	**52**	**p= 0.671**
Age (mean± SD)		**36.7± 10.5**	**38.7± 10.0**	**T= 1.097, p= 0. 275**
IBS subtype				
IBS-D		**15**	**7**	
IBS-C		**22**	**24**	**χ^2=9.565**
IBS-M		**4**	**25**	**p= 0.023**
IBS-U		**16**	**23**	
Blotting				
Yes		**53**	**44**	**χ^2=12.839**
No		**4**	**23**	**p<0.001**

Table 2: Risk of some factors related to positive GHBT

Variable		**Odds ratio**	**95% Confidence interval**	**P value***
sex	**Male**	**1**	**--**	**0.847**
	Female	**1.1**	**0.42- 2.84**	
Age		**1.03**	**0.99- 1.07**	**0.131**
IBS				
Subtype				
IBS-D		**4.8**	**1.34- 17.17**	**0.016**
IBS-C		**1.17**	**0.47- 2.9**	**0.734**
IBS-M		**0.58**	**0.15- 2.26**	**0.431**
IBS-U		**1**	**--**	**--**
Blotting				
Yes		**8.17**	**2.3-29.2**	**0.001**
No		**1**	**--**	

***Entered model of logistic regression with Wald test**

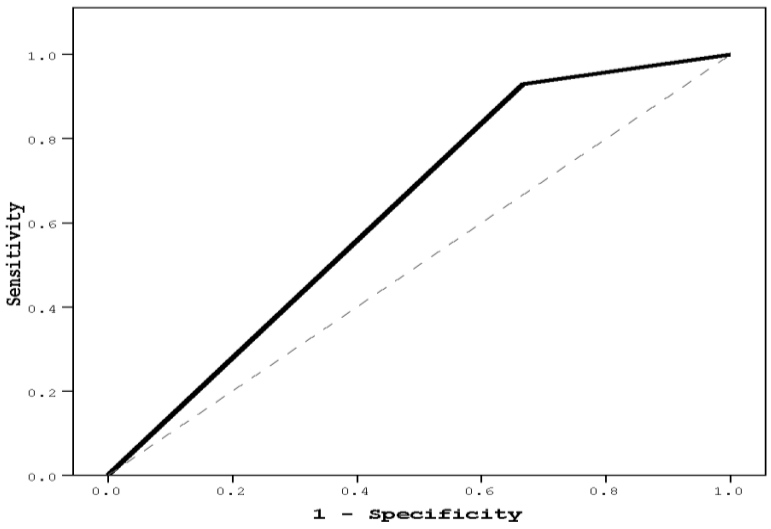

Figure 1: ROC analysis of bloating for diagnosis of positive GHBT