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# SMALL INTESTINAL BACTERIAL OVERGROWTH IS ASSOCIATED WITH INTESTINAL INFLAMMATION IN THE IRRITABLE BOWEL SYNDROME

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#### Abstract

Background and aim. Small intestinal bacterial overgrowth is encountered in bowel disorders, including irritable bowel symptoms. Low degrees of inflammation have been recently reported in the irritable bowel syndrome. We looked for the association between intestinal inflammation and small intestinal bacterial overgrowth in irritable bowel syndrome.

Methods. Small intestinal bacterial overgrowth was assessed by the H2 glucose breath test in 90 consecutive patients with irritable bowel syndrome. A check-up of the oral cavity was carried out before the breath testing. Further on, the patients were classified into two groups, positive and negative, at the breath test. Then they were tested for intestinal inflammation with a fecal test for calprotectin. We used a semiquantitative test for this study. Both groups were compared for the association of intestinal inflammation with small intestinal bacterial overgrowth.

**Results.** A number of 24/90 (26.7%) patients with irritable bowel syndrome had small intestinal bacterial overgrowth. A positive test for intestinal inflammation was significantly more frequent in patients with irritable bowel syndrome and small intestinal bacterial overgrowth ( $chi^2$ : p < 0.05).

**Conclusions.** Small intestinal bacterial overgrowth is present in almost one quarter of patients with irritable bowel syndrome. It is significantly associated with intestinal inflammation.

**Keywords:** calprotectin, H2 breath test, irritable bowel syndrome, small intestinal bacterial overgrowth

# Introduction

Small intestinal bacterial overgrowth (SIBO) is defined as the increased number of bacteria in the small bowel [1,2]. The cut-off value is considered maximum  $10^4$  CFU/mL and SIBO is defined largely as a concentration higher than  $10^5$  [3].

SIBO was considered as a pathogenic factor in irritable bowel syndrome (IBS), because the prevalence of SIBO in IBS was considered high [4]. Later the prevalence

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value was reconsidered, but SIBO is still a factor to be assessed in patients with IBS [5,6].

On the other hand, low levels of inflammation have been reported in IBS [7,8], in contradiction with the first reports on the absence of any organic or biochemical changes in IBS [9].

In our hypothesis, the presence of bacteria in higher than normal concentration, may be related with the inflammation in the bowel. Therefore, the aim of this study was to check if SIBO may be associated with inflammation in IBS.

## Methods

#### Protocol

Consecutive patients with IBS were tested for SIBO. Consequently, they were tested for intestinal inflammation. We looked for the association between SIBO and intestinal luminal inflammation in IBS.

# Subjects

Ninety consecutive subjects with IBS diagnosed according to Rome III criteria [9] were included in this study. They were 33 males and 57 females, aged between 19 to 72 years (median age 50 years). All patients agreed to participate and offered informed consent. Patients were recommended to undergo an oral examination, performed by the same experienced dentist (AP). This examination was provided in order to detect any potential local factors of bias.

# Assessment of SIBO

We used the hydrogen breath test with glucose (GHBT). The test was performed after 12 hours fasting in each patient. After two measurements of baseline values for exhaled hydrogen, the patients were given 50 g glucose dissolved in 200 ml water. Subsequently the breath samples were collected and analyzed for hydrogen every 10 minutes for 3 hours. SIBO was suspected if a peak was detected and if the exhaled peak value was superior to 10 parts per million over baseline values [10].

# Assessment of intestinal inflammation

We used a semiquantitative fecal test, easy to use and cost-efficient [11]. Fecal calprotectin is considered a reliable surrogate marker for gut intraluminal inflammation [12]. It is routinely used for the assessment of inflammatory bowel disease (Morbus Crohn, ulcerative colitis) [13] but its levels may be slightly increased in IBS [14].

The assay used in this study was a semiquantitative one, based on the immuno-chromatographic method, to detect the presence of calprotectin in the feces (CalDetect ®, SOFAR). The test can be performed in the same day, and the result is ready immediately, like in the fecal occult blood testing. This test indicates only negative or positive results. For the positive cases, the test gives one of these values: T1 if fecal calprotectin <  $15\mu g/g$  (suggesting minimal inflammation; T2 if fecal calprotectin = 15-60  $\mu g/g$ ; T3 if fecal calprotectin >60  $\mu g/g$  [10]. We considered the value of T2 as corresponding to an inflammation in the bowel of IBS patients of low level. T3 represented severe inflammation.

## Statistics

Descriptive statistics (mean ± standard deviation) were used for parametric data. Continuous variables were compared using ANOVA or Mann-Whitney test

depending on the normal or abnormal distribution of data. An error probability of p<0.05 was considered statistically significant.

#### Results

The group of consecutive IBS patients included 33 males and 57 females. The age range varied between 19 to 72 years (median age 50 years).

Only 33 of the patients took benefit from the oral examination, the rest did not have time for appointment; 20 patients from 33 presented dental, lingual or gingival changes, but none able to influence the result of the examination. Therefore we did not stratify further the group of patients according to the dental health status.

Among the 90 subjects, we detected SIBO in 24 of them. These data indicated a prevalence of 26.7% of SIBO in patients with IBS. The main characteristics of the subjects are given in table I, according to their SIBO status: positive or negative.

**Table I.** Characteristics of the IBS patients with SIBO and without SIBO

Characteristic	SIBO positive N=24	SIBO negative N=66	Significance of difference
Age (mean+SD)	44±10	39±9	NS
Gender M/F	9/15	24/42	NS
Level of education Low/medium/high	10/7/7	31/15/20	
IBS type: C/D/M	8/4/12	29/11/26	

Legend: IBS type: C=constipation; D=diarrhea; M=mixed

Both groups had similar characteristics. All subjects gave samples of feces for the estimation of calprotectin with a semiquantitative rapid fecal test. The results are displayed in table II.

**Table II.** Numbers of patients with the result of calprotectin positive, respectively negative GHBT

	Calprotectin positive	Calprotectin negative
SIBO positive	16	8
SIBO negative	13	53

The groups were compared with the chi² test. The calculation of the significance gave a P=2.5E-0.5 and p<0.05.

The test was semiquantitative, thus each patient could have a result from T1 to T3. All our negative subjects had the value T1, all positive subjects had the value T2, in accordance to previous data [12].

# Discussion

This is to our knowledge the first study in our area

looking for the association between SIBO and endoluminal inflammation in IBS. Our study showed that a positive test for intestinal inflammation was significantly more frequent in the IBS patients who also presented SIBO (chi²: p<0.05).

The prevalence of SIBO in IBS was 26.7% in this study, higher than in another Romanian medical center [6], but compatible with data to be reported from a Romanian multicenter study (Moraru et al, submitted).

Our data are consistent with other studies reporting low degree inflammation in IBS [1,15] and contribute to the divergent values reported in different studies on the true prevalence of SIBO in IBS [16-18]. This study is not without limitations. The main one is the relatively reduced size of the sample. The subgroup of SIBO positive was especially small. However the data are consistent with those reported in similar studies and offer first data on SIBO in IBS in our area.

#### **Conclusions**

Small intestinal bacterial overgrowth is present in 26.7% of the patients with IBS. It is significantly associated to intestinal inflammation.

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