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Original article

Small intestinal bacterial overgrowth is common both among patients with alcoholic and idiopathic chronic pancreatitis

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A B S T R A C T

Background: Small intestinal bacterial overgrowth (SIBO) is known to occur in patients with chronic pancreatitis, particularly of alcoholic etiology. There are, however, scanty data on frequency of SIBO in patients with chronic idiopathic pancreatitis and factors associated with its occurrence.

Methods: 68 patients with chronic pancreatitis and 74 age and gender-matched healthy subjects (HS) were evaluated for SIBO using glucose hydrogen breath test (GHBT). Persistent rise in breath hydrogen 12 ppm above basal (at least two recordings) was diagnostic of SIBO.

Result: SIBO was diagnosed more often among patients with chronic pancreatitis than controls (10/68 [14.7%] vs. 1/74 controls [1.3%]; $p = 0.003$). Of 68 patients, 22 (32.3%) had alcoholic and 46 (67.6%) had idiopathic chronic pancreatitis. SIBO was as commonly detected among patients with alcoholic as idiopathic pancreatitis (3/22 [13.6%] vs. 7/46 [15.2%]; $p = 0.86$). Age, gender, body mass index (BMI), steatorrhoea, pain, analgesic use, pancreatic calcifications and use of pancreatic enzyme supplements had no relationship with the presence of SIBO. Diabetes mellitus tended to be commoner among patients with chronic pancreatitis with than without SIBO (6/10 [60%] vs. 18/58 [31%]; $p = 0.07$).

Conclusion: SIBO was commoner among patients with chronic pancreatitis, both alcoholic and idiopathic, than HS. Though presence of SIBO among patients with chronic pancreatitis tended to be commoner among those with diabetes mellitus, there was no relationship with age, gender, BMI, steatorrhoea, pain, analgesic use, pancreatic calcifications and use of pancreatic enzyme supplements.

1. Introduction

Small intestinal bacterial overgrowth (SIBO) is known to occur in patients with chronic pancreatitis, particularly of alcoholic etiology. The reported frequency of SIBO among patients with chronic pancreatitis ranges from 0 to 92% [1–6]. Such wide variation in frequency of SIBO in patients with chronic pancreatitis might be related to difference in methods of testing for SIBO and inclusion of patients with differing etiology. For example, highest frequency of SIBO of 92% was found when lactulose hydrogen breath test was used, a lower frequency was reported with glucose hydrogen breath test and an intermediate value was with jejunal aspirate culture, which is considered as the gold standard for diagnosis of SIBO. Fallaciously high frequency of SIBO in some studies might be related to the fact that early-peak criterion lactulose hydrogen breath test is often false positive. [7] Moreover, most of these studies had limitation due to small sample size, lack of control, and inclusion of patients with alcoholic pancreatitis only. Pathogenesis of SIBO in patients with chronic pancreatitis is multi-factorial, which include small bowel stasis resulting from exaggerated ileal brake induced by action of malabsorbed fat passing through ileum [8], associated diabetic autonomic neuropathy, intake of opiate and non-steroidal analgesic, reduced gut defence due to a failure of conversion of prodefensin to defensin by trypsin [9–13], and alcohol consumption [14].

Since alcohol itself can predispose to SIBO, the earlier studies that included only patients with alcoholic pancreatitis, may not give an exact estimate of frequency of SIBO occurring due to chronic pancreatitis independent to the effect of alcohol [15–17]. In India idiopathic pancreatitis is a common form of chronic pancreatitis [18]. Hence, a study including patients with idiopathic pancreatitis would help to know the frequency of SIBO in patients with chronic pancreatitis independent of alcohol. Similarly, there is scanty data on factors associated with occurrence of SIBO in patients with chronic pancreatitis.

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Accordingly, we undertook a prospective study with the following aims: (a) to study the frequency of SIBO in patients with chronic pancreatitis as compared to healthy controls using glucose hydrogen breath test, (b) to compare the frequency of SIBO in patients with chronic idiopathic and alcoholic pancreatitis, and (c) to study factors associated with occurrence of SIBO in patients with chronic pancreatitis.

2. Methods

68 patients attending a tertiary care centre in northern India and diagnosed having chronic pancreatitis during a 2-year period (between December 2010 and November 2012), and 74 healthy subjects (HS) were included in the study after informed consent. Data on 51 of these HS have already been published [19]. Consenting patients were subjected to glucose hydrogen breath test (GHBT) according to a standard protocol [7] after detailed clinical evaluation. No patient took antibiotics, prokinetics, probiotics and proton pump inhibitors (PPI) or other acid suppressive drugs within the previous 4 weeks. These drugs were stopped for 4 weeks prior to GHBT in those already on them.

2.1. Clinical evaluation

A detailed history was obtained from each patient in a structured proforma. Diagnosis of chronic pancreatitis was based on relevant clinical history in the presence of imaging features suggestive of chronic pancreatitis. Exocrine insufficiency was diagnosed on the basis of increased fecal fat. Fecal fat was estimated either over 72-h using standard technique (Van de Kamer's) after challenge with 75 g extra fat per day for 3 days prior to and during the test or by microscopic examination of spot stool specimen stained with Sudan III stain. Steatorrhoea was assessed at baseline while the patients were not on enzyme supplementation. An average value of fecal fat excretion $\geq$ 7 g/day by the former or more than 10 droplets of fat per high power field on microscopy by the latter technique were considered abnormal. Endocrine insufficiency in the form of diabetes mellitus was diagnosed on the basis of fasting plasma glucose >126 mg/dl or history of intake of drugs to control blood sugar. Glycosylated haemoglobin (HbA1c) levels were checked in diabetic patients to assess control of blood sugar.

2.2. Glucose hydrogen breath test

GHBT was performed using a breath analyser (Bedfont gastrolyzer, Bedfont Scientific Ltd., ME13QX, England) after an overnight fast. The subjects were asked to avoid slowly absorbed carbohydrates (like bread and potato) and fibre the previous night as these would cause delayed excretion of hydrogen in their breath. Cigarette smoking and exercise were avoided 2 h before and during the test, as hyperventilation can cause changes in breath hydrogen content. The subjects were asked to brush their teeth and rinse their mouth with antiseptic mouth wash (chlorhexidine) and tap water before the test, to eliminate an early hydrogen peak due to the action of oral bacteria on test sugar. An average of three values was taken as the basal breath hydrogen level. Subjects were then asked to take 100 g glucose dissolved in 200 ml of water. Thereafter, breath hydrogen values were estimated every 15 min for the next 3 h. Persistent rise in breath hydrogen 12 ppm above basal (at least two readings) was considered diagnostic of SIBO. Patients with high basal breath hydrogen levels were re-tested on another day after ensuring repetition of all the above precautions.

2.3. Healthy subjects

A group of healthy controls comparable in age and gender with that of the patients were included. After informed consent, they were also subjected to GHBT using a similar protocol.

2.4. Statistical analysis

2.4.1. Sample size calculation

Assuming a frequency of SIBO in chronic pancreatitis to be 30% and that in healthy controls to be 4% from previous studies [1–6], sample size was calculated with a power of 80%, p value of <0.05, and ratio of case: control as 1:1; the minimum sample size needed was calculated to be 70 cases and 70 controls.

2.5. Data analysis

Statistical analysis was performed using Epi Info 7 (CDC, Atlanta, GA, USA) and SPSS 15.0 (SPSS Inc., Chicago, IL, USA) software. Chi-square test was used for categorical data and Students' t test was used for continuous data.

3. Results

68 patients (48 males; mean age 33.6 ± 13.6 y) and 74 healthy subjects (52 males; mean age 36.9 ± 11.0 y) were evaluated for SIBO using glucose hydrogen breath test (GHBT). Cases and controls were comparable with regards to age ($p = 0.1$) and gender ($p = 0.9$). Of 68 patients, 22 (32.3%) had alcoholic and 46 (67.6%) had idiopathic chronic pancreatitis. Sudan staining for stool fat was done in 60 (88.2%) patients while 72 h fecal fat was done in 8 (11.8%) patients.

Mean BMI of patients with chronic pancreatitis was 19.7 ± 3.07 (13.0–27.4) kg/m^2. Pain, opioid use, non-steroidal anti-inflammatory drug (NSAID) use, steatorrhoea, diabetes, use of pancreatic enzymes and pancreatic calcifications was reported by 91.2%, 58.8%, 32.4%, 29.4%, 35.3%, 66.2% and 66.2% of the patients, respectively; frequency of these parameters was not significantly different between alcoholic and idiopathic chronic pancreatitis (Table 1).

SIBO was diagnosed more often among patients with chronic pancreatitis than controls (10/68 [14.7%] vs. 1/74 controls [1.3%]; $p = 0.003$). SIBO was as commonly detected among patients with alcoholic as idiopathic pancreatitis (3/22 [13.6%] vs. 7/46 [15.2%]; $p = 0.86$). Age, gender, body mass index (BMI), steatorrhoea, pain, pancreatic calcifications, use of opioid analgesics, NSAIDs and pancreatic enzyme supplements had no relationship with the presence of SIBO (Table 2). Diabetes mellitus tended to be

Table 1
Characteristics of patients with chronic pancreatitis based on etiology.

Characteristic	Alcohol ($n = 22$)	Idiopathic ($n = 46$)	p-Value
Mean age (years)	38.05 ± 12.57	31.54 ± 13.79	0.06
Male: female	22:0	26:20	0.00
Mean BMI (Kg/m^2)	18.99 ± 2.77	20.04 ± 3.19	0.17
Median duration of pain (years)	3 (0.02–20)	2 (0.02–17)	0.56
Pain (n) (%)	21 (95.5)	41 (89.1)	0.39
Opioid analgesics (n) (%)	12 (54.5)	28 (60.9)	0.62
NSAIDS (n) (%)	9 (40.9)	13 (28.3)	0.30
Diabetes mellitus (n) (%)	8 (36.4)	16 (34.8)	0.89
Exocrine insufficiency (n) (%)	8 (36.4)	12 (26.1)	0.38
Pancreatic calcifications (n) (%)	16 (72.7)	29 (63)	0.43
On enzyme supplements (n) (%)	14 (63.6)	31 (67.4)	0.75
GHBT positive (n) (%)	3 (13.6)	7 (15.2)	0.86

BMI – body mass index.

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