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Research Article

PREVALENCE OF SMALL INTESTINAL BACTERIAL OVERGROWTH IN SYSTEMIC SCLEROSIS

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A B S T R A C T

Objectives: The aims of this study were to find the prevalence of small intestinal bacterial overgrowth (SIBO) in patients with SSc as well as to assess both clinical presentation and outcome of SIBO;

Methods: 101 patients with SSc underwent glucose hydrogen and methane (H2/CH4) breath test. All SSc patients also completed a questionnaire for intestinal symptoms, and a global symptomatic score (GSS) was calculated. SSc patients with SIBO were given course of antibiotic (rifaximin) for 2 weeks; glucose H2/CH4 breath test was performed at 1 month follow-up.

Results: The prevalence of SIBO was 43.4% in our SSc patients. After logistic regression, we identified the following risk factors for SIBO: presence of diarrhoea and constipation. Interestingly, we observed a marked correlation between values of GSS of digestive symptoms (≥5) and the presence of SIBO ($P=10^{-6}$); indeed, both sensitivity and specificity of GSS ≥5 to predict SIBO were as high as 0.909 and 0.862, respectively. Finally, eradication of SIBO was obtained in 52.4% of the SSc patients with a significant improvement of intestinal symptoms.

Conclusion: Our study underscores that SIBO often occurs in SSc patients. We further suggest that GSS may be systematically performed in SSc patients; since we found a correlation between GSS of digestive symptoms >5 and SIBO, we suggest that glucose H2/CH4 breath test may be performed in the subgroup of SSc patients exhibiting GSS ≥5.

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INTRODUCTION

Systemic sclerosis (SSc) is a chronic, multisystem connective tissue disease of the autoimmune etiology characterized by the microcirculation changes, skin and internal organs fibrosis and the presence of autoantibodies. SSc particularly affects the gastrointestinal tract, where lesions may lead to impairment of motor activity [1–13]. Gastric and intestinal involvement has been reported in 44–88% of SSc patients [4, 7–9]. Gastrointestinal disorders are recognized to be associated with malabsorption and intestinal pseudo-obstruction [1-13]. Malabsorption is a poor prognostic factor with a 50% mortality rate at 8.5 years [12–14]; malabsorption is mainly caused by small intestinal bacterial overgrowth (SIBO) in SSc patients [1–13, 15–23]. In few previous studies, the prevalence of SIBO has been reported to be 30–62.5% in SSc patients exhibiting gastrointestinal symptoms; in these series, SIBO was defined as microbial concentration ($>10^5$ CFU/ml) in the jejunal aspirate culture [16, 19–21, 23]. Although, the gold standard analysis for the diagnosis of SIBO is jejunal aspirate culture, this is both a complex and invasive technique for routine use. In clinical practice, glucose H2/CH4 breath test, in fact, represents a simple, non-invasive and reproducible method to depict SIBO [14, 24–30]. Indeed, the aims of the current study were to: (i) determine the prevalence of SIBO in unselected SSc patients with SIBO, using glucose hydrogen and methane (H2/CH4) breath test; (ii) assess both clinical presentation and outcome of SIBO in SSc patients;

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PATIENTS AND METHODS

Patients from January 2018 to January 2019, 101 consecutive patients with a definite diagnosis of SSc were included in the study. The criteria for the diagnosis of SSc were based on the ACR criteria [31]. Ethical approval was obtained from the local ethical committee, and informed consent was obtained from all patients. The study cohort consisted of 20 men and 81 women with a median age of 54 (range: 23–82) years; the median duration of the disease, was 4 (range: 1–37) years. Patients were grouped according to the criteria of Leroy *et al*. [32]: 50 (49.5%) patients had dcSSc and 51 (50.4%) had lcSSc. In these 101 SSc patients, the median Scleroderma Health Assessment Questionnaire (SHAQ) score [33] was 0.2 (range: 0–2.55). No patient with SSc had other CTDs or a history of liver or digestive diseases, diabetes mellitus, gastric surgery or vagotomy. Moreover, no patient received NSAIDs. 81 SSc patients received immunosuppressive drugs, i.e. low-

dose steroid regimen (<10mg daily) (n=51), MTX (n=10), AZA (n=10) and mycofenolate mofetil (n=10). SSc patients had pulmonary involvement as follows: interstitial lung disease (ILD) (n=20; 19.8%) and pulmonary arterial hypertension (PAH) (n=6; 5.94%); and 61 SSc patients had digital pitting scars (60.3%). All patients had undergone gastroscopy; gastroscopy revealed the following mucosal damage: oesophagitis (n=26), Barrett's oesophagus (n=6) and watermelon stomach (n=6).

Digestive Symptoms

Before undergoing glucose H2/CH4 breath test, SSc patients were systematically interviewed, using a standardized questionnaire regarding the occurrence of small bowel symptoms, i.e. nausea, vomiting, abdominal pain/discomfort, bloating, diarrhoea, constipation, abdominal tenderness, dysuria, tenesmus, fever, general illness; each symptom carried a score from 0 (no symptoms) to 3 (severe). A global symptomatic score (GSS), calculated as the sum of all symptom scores, was assigned to each patient (maximum score: 33), as described and validated previously [34, 35]. GSS of digestive symptoms was compared between SSc patients with SIBO and patients without. SSc patients underwent biochemical tests, i.e. serum total protein (grams per decilitre), serum albumin (grams per decilitre), ferritin (micrograms per litre), plasma folic acid (nanomoles per litre) and vitamin B12 (picomoles per litre), haemoglobin level (grams per decilitre), ESR (millimetres per first hour). Laboratory findings were compared between SSc patients with SIBO and patients without.

Glucose H2/Ch4 Breath Test

None of the patients was allowed to take antibiotics, probiotics, PPI, prokinetics during 4 weeks before the test. Patients were instructed to avoid foods that likely generate hydrogen for the 3 days before the test. After a 12-h fasting, breath testing started after thorough mouth washing with 40ml of 1% chlorhexidine solution, in order to eliminate oral bacteria. SSc patients underwent an initial breath test under standard conditions. H2/CH4 excretion was measured using glucose breath test. H2/CH4 breath concentration was expressed in parts per million (p.p.m.); it was measured by gas chromatography (Quintrom Microlizeranalyzer model DPplus, Milwaukee, WI, USA) in basal conditions and every 15min for at least 3h after the administration of an oral loading dose of glucose (50g in 250ml of sterile water). Alveolar air samples were collected and connected to a bag for the collection of air coming from the respiratory dead space [24–26, 28]. For SSc patients, both baseline and peak values for H2/CH4 were recorded and their total excretion of either H2/CH4 was calculated as an area under the time–concentration curve. The test was considered positive for SIBO when, at least one of the following criteria was present, i.e. (i) H2 and/or CH4 increase >20p.p.m. above basal value; (ii) H2 and/or CH4 increase >12p.p.m. on two consecutive measurements within the first 2h; and (iii) H2 and/or CH4 increase >12 p.p.m. between minimal and maximal values after glucose ingestion [24–26, 28].

Statistical Analysis

For group comparison involving binary data, we used either the chi-square test or Fisher's exact test, depending on the cells expected to count. Comparisons involving continuous data were performed using the Mann–Whitney U-test. The results were regarded as significant when the P-value was <0.05. Moreover, we performed logistic regression to identify the predictive factors of SIBO. These results are reported as odds ratio (OR) and 95% CI; the used level of significance was P<0.05 in all performed tests.

RESULTS

Prevalence of SIBO

Of these 101 unselected patients with SSc, 44(43.4%) patients were identified who fulfilled the criteria of SIBO.

Table 1 Intestinal symptoms in SSc patients

Clinical intestinal features of SSc patients with SIBO compared with those without			
Clinical parameters, %	SIBO, n=44	Absence of SIBO,n=57	P-value
Nausea	54.5	37.9	0.269
Vomiting	18.2	3.4	0.152
Abdominal pain	86.4	31	0.0001
Bloating	77.3	44.8	0.0246
Diarrhoea	50	10.3	0.0034
Constipation	59.1	3.4	0.00001
Abdominal tenderness	54.5	6.9	0.0027
Fever	18.2	0	0.0292
Tenesmus	13.6	0	0.074
Global symptomatic score of			
digestive symptoms, median (range)	8.5 (3–21)	3 (0–10)	10^{-6}

SSc patients complained of the following signs: nausea (45.1%), vomiting (23.8%), abdominal pain/discomfort (54.9%), bloating (58.8%), diarrhoea (27.5%), constipation (27.5%), abdominal tenderness (27.5%) and tenesmus (5.9%). In our 101 SSc patients, the median value GSS of the digestive symptoms was 4 (range: 0–21). Intestinal symptoms were further compared between SSc patients with and without SIBO (Table 1); the prevalence of the following symptoms was more common in patients with SIBO when compared with patients without: abdominal pain/discomfort (86.4 vs 31%), bloating (77.3 vs 44.8%), diarrhoea (50 vs 10.3%),constipation (59.1 vs 3.4%) and abdominal tenderness (54.5 vs 6.9%). Furthermore, the median value GSS of digestive symptoms was significantly higher in SSc patients with SIBO than in those without (8 vs 3; $P=10^{-6}$). We observed a marked correlation between value GSS of digestive symptoms ≥5 and the presence of SIBO($P=10^{-6}$) with both sensitivity and specificity of GSS of digestive symptoms ≥5 to predict SIBO were as high as 0.909 and 0.862, respectively. In our population, 38 SSc patients had GSS of digestive symptoms >5.

Predictive factors of SIBO

Table 2 General clinical data. As illustrated in Table 2,

Clinical characteristics of SSc patients with SIBO compared with those without			
	SIBO, n=44	Absence of SIBO, n=57	P-value
Clinical parameters			
Age, years	59.5 (range: 23–82)	50 (range: 34–73)	0.0292
Sex, male/female	18.2% M/81.8% F	20.7% M/79.3% F	1
SSc duration, years	8.3 (range: 1–37)	4.9 (range: 1–20)	0.0067
SSc subset	63.6% of the lcSSc	41.4% of the lcSSc	0.159
	36.4 % of the dcssc	58.6% of the dcSSc	
Digital pitting scars, %	54.5	65.5	0.564
ILD, %	31.8	44.8	0.397
PAH, %	13.6	10.3	1
SHAQ score, median (range)	0.325 (0–2.55)	0.15 (0–2.4)	0.0086

There were significant differences between patients with and without SIBO with respect to median age (59.5 vs 50 years) and median SSc duration (7.5 vs 2 years). We failed to show any statistically significant difference between subsets of scleroderma for SIBO (P=0.159). However, SIBO tended to occur earlier in dcSSc patients than in lcSSc patients; the median duration of dcSSc was shorter before SIBO onset

compared with that of lcSSc (6.5 vs 8.5 years). The prevalence of the systemic manifestations related to SSc was similar in patients with and without SIBO as follows: digital pitting scars (54.5 vs 65.5%), ILD (31.8 vs 44.8%) and PAH (13.6 vs 10.3%).Gastric and oesophageal mucosal involvement was also more common in patients with SIBO than in those without (52.4 vs 27.5%). Moreover, median value of SHAQ was significantly higher in patients with SIBO (0.325 vs 0.15). Finally, immunosuppressive therapy did not differ between SSc patients with and without SIBO for low-dose steroid regimen (18.2 vs 24.1%), MTX (4.5 vs 0%), AZA (4.5 vs 3.4%) and mycophenolate mofetil (0 vs 6.9%).

Table 3 Laboratory findings.

Biochemical findings of SSc patients with SIBO compared with those without			
	SIBO, n=44	Absence of SIBO, n=57	P-value
Biochemical parameters, median (range)			
ESR, mm/h	24 (4–70)	8 (2–78)	0.003
Haemoglobin, g/dl	12.2 (8.9–14.5)	13.9 (10.3–15.5)	0.002
Serum total protein, g/l	65.5 (51–77)	69 (55–76)	0.066
Serum albumin, g/l	39 (32–49)	42 (30–50)	0.024
Vitamin B12, pmol/l	225 (30–748)	288 (131–587)	0.133
Folic acid, nmol/l	12 (4.6–40)	13.3 (2.5–50)	0.648
Ferritin, g/l	44.5 (5–307)	60 (2–730)	0.361
ACA, %	40.9	24.9	0.235
Anti-Scl 70 antibody, %	22.7	27.6	0.755

As seen in Table 3, high rates of ESR were significantly more numerous in the group of SSc patients with SIBO (24 vs 8mm/h). Patients with SIBO also had significantly more frequent lower median levels of serum total protein (65.5 vs 69g/dl), serum albumin (39 vs 42g/dl) and haemoglobin (12.25 vs 13.9g/dl). Autoantibody screen tests were similar in both SSc patients with and without SIBO (Table 3). After logistic regression, significant risk factors for SIBO were: diarrhoea [OR: 11.043 (95% CI: 1.933, 63.091); P=0.0009] and constipation [OR: 48.537 (95% CI: 4.885, 482.186); P=0.006]. Interestingly, we further observed a marked correlation between GSS of digestive symptoms ≥5 and the presence of SIBO ($P=10^{-6}$); as shown in ROC curve (Fig.1), both sensitivity and specificity of GSS of digestive symptoms (≥5) to predict SIBO were as high as 0.82 and 0.86, respectively; predictive positive and negative values of GSS of digestive symptoms ≥5 were 0.868 and 0.905, respectively.

Table 4 Follow-up of SSc patients with SIBO

Intestinal features of SSc patients with eradicated SIBO compared with non-eradicated SIBO			
	Eradicated SSc Patients, n=22	Non-eradicated SSc patients, n=20	P-value
Clinical parameters, %			
Nausea	9.1	30	0.31
Vomiting	0	20	0.2
Abdominal pain	27.2	90	0.008
Bloating	18.1	70	0.03
Diarrhoea	0	60	0.004
Constipation	45.5	60	0.67
Abdominal tenderness	9.1	50	0.06
GSS, median (range)	1.5 (0–9)	8 (5–23)	0.001

Antibiotic therapy (rifaximin) for SIBO were well tolerated by all SSc patients and no side effects were reported during therapy. 44 patients underwent systematic glucose H2/CH4 breath test at 1-month follow-up. Eradication of SIBO was achieved in 31.8% of the patients (n=14/44). Among the 34 remaining patients with persistent SIBO at glucose H2/CH4 breath test, rotating courses of alternative antibiotic therapy was re-instituted. Glucose H2/CH4 breath test was, once again, performed systematically after 3 months. In essence, we observed that 28.6% of these patients achieved eradication of SIBO (n=12/44). At 6-month follow-up, 23 (52.4%) of the 44 SSc patients with SIBO had eradication of SIBO; in these 23 patients, normalization of the glucose H2/CH4 breath test was associated with significant decrease of the GSS of digestive symptoms to 1.5 (range: 0–9), which corresponds to a significant decreased frequency of intestinal symptoms. As shown in Table 4, we found that eradicated SSc patients exhibited less commonly than non-eradicated SSc patients: diarrhoea (P=0.004), abdominal pain (P=0.008), bloating (P=0.03), as well as abdominal tenderness (P=0.06); in addition, median value of GSS of digestive symptoms was significantly lower in eradicated SSc patients compared with non-eradicated SSc patients (1.5 vs 8; P=0.001).

DISCUSSION

This study underlines the pathogenetic role of SIBO in the development of intestinal symptoms and the clinical effectiveness of its eradication in SSc patients.In our study, we observed a high frequency (43.4%) of SIBO. We considered a sample of 101 consecutive SSc patients without any prior selection based on clinical presentation, which tends to be representative of the entire SSc population. Our findings underscore that SIBO is prevalent in the whole population of SSc patients. Although aspiration and direct culture of jejuna contents are considered by many as the gold standards for SIBO diagnosis, those methods have several limitations such as the potential for contamination by oropharyngeal bacteria during intubation, and the fact that SIBO may be missed by a single aspiration. Overall, the reproductibility of jejunal aspiration and culture has been reported to be 38%. In addition, intubation methods may be regarded as cumbersome and invasive for patients with non-specific symptoms or for those who may require repeated testing. For this reason, a variety of non-invasive diagnostic tests have been devised for SIBO diagnosis in routine clinical practice [36, 37]. Breath tests were used, as they are sensitive, non-invasive and reproducible methods to identify patients with SIBO; the glucose breath test has, in fact, been shown to have a sensitivity of 90% [24–30]. Nevertheless, glucose breath test has some limitations in patients with SIBO, especially an inability to evaluate SIBO-related antibiotic sensitivity/resistance. Furthermore, our study underlines the pathogenic role of SIBO in the development of intestinal symptoms in SSc patients. In essence, we have found that SIBO is associated with a greater prevalence of diarrhoea, abdominal pain and gas-related symptoms (bloating and abdominal tenderness). The second main finding in the present series was that we observed a marked correlation between values of GSS of digestive symptoms ≥5 and the presence of SIBO ($P=10^{-6}$). Interestingly, we found that higher values were markedly predictive factors of SIBO, with a sensitivity of 0.90 and a specificity of 0.86; both predictive positive and negative values of global symptomatic score of digestive symptoms ≥5 were 0.868 and 0.905, respectively. Our findings therefore indicate that SIBO should be considered in SSc patients exhibiting values of GSS of digestive symptoms ≥5; we suggest that GSS of digestive symptoms ≥5 should be performed in patients to depict SIBO. Moreover, in SSc patients with SIBO, it is observed that the overgrowth of the flora competes with the hosts for nutrients, and may cause fat malabsorption [18, 38, 39]. In this instance, we have found that SSc patients with SIBO had lower levels of serum albumin and serum total protein, and both vitamin B12 and ferritin blood levels, which were probably related to underlying SIBO-associated malabsorption. We suggest that biochemical tests

(serum total protein and serum albumin, blood ferritin, vitamin B12 and folic acid) may be helpful to detect subclinical SIBO-related malabsorption in SSc patients. The pathological mechanisms of small intestinal dysmotility in SSc remain unknown. It is possible to classify intestinal motor disorders, as either myogenic (hypomotility) or neurogenic (abnormally propagated phasic contractions and failure of fed pattern response development); the myogenic abnormalities are characterized by low-amplitude intestinal contractions [7, 9, 12, 13].Our series reveals that the prevalence of SIBO tended to be higher in patients with lcSSc than in dcSSc, although not significantly so; our findings interestingly underline that the 'benign' nature of the lcSSc subset is questionable. On the other hand, our study suggests that SIBO tends to occur earlier in dcSSc compared with lcSSc (6.5 vs 8.5 years). In the present study, we found that none of the SSc systemic manifestations could be considered as predictive factors for SIBO, i.e. pitting scars, PAH and ILD. We have observed that severe oesophageal motor impairment may be considered as a factor associated with SIBO onset; our data suggest that these patients with SIBO had severe motor impairment involving both oesophagus and small intestine; in addition, oesophageal and gastric mucosal involvement was more often found in the group of SSc patients with SIBO.

CONCLUSION

Small intestinal bacterial overgrowth remains a significant clinical problem among patients suffering from systemic sclerosis. The presence of symptoms such as diarrhoea, abdominal pain, bloating, abdominal tenderness, absorption disorders and malnutrition indicates the necessity of differential diagnosis towards small intestinal bacterial overgrowth. The SIBO therapy should comprise the treatment of the symptoms and complications, a sufficient and adequate diet and cyclic antibiotic therapy. It is essential to eliminate the risk factors of SIBO, to treat the primary disease, and to neutralize the gastrointestinal motility disorders. GLUCOSE H2/CH4 breath test was used, as it was sensitive, non-invasive and reproducible method to identify patients with SIBO; and in fact, been shown to have a sensitivity of 90%.Our data suggest that SIBO should also be detected and treated in patients with low grade severity SSc, in order to improve the quality of life of these patients, who often complain of frustrating intestinal symptoms, otherwise difficult to diagnose and cure.

References

1. Abu-Shakra M, Guillemin F, Lee P. Gastrointestinal manifestations of systemic sclerosis.Semin Arthritis Rheum 1994;24:29–39.
2. Cohen S, Laufer I, Snape WJ, Shiau YF, Levine GM, Jimenez S. The gastrointestinal manifestations of scleroderma: pathogenesis and management. Gastroenterology 1980;79:155–66.
3. Greydanus MP, Camilleri M. Abnormal postcibalantral and small-bowel motility due to neuropathy or myopathy in systemic sclerosis. Gastroenterology 1989;96: 110–5.
4. Marie I, Ducrotte P, Antonietti M, Herve S, Levesque H. Watermelon stomach in systemic sclerosis: its incidence and management. Aliment PharmacolTher 2008; 28:412–21.
5. Marie I, Dominique S, Levesque H *et al*. Esophageal involvement and pulmonary manifestations in systemic sclerosis. Arthritis Rheum 2001;45:346–54.
6. Marie I, Ducrotte ´ P, Denis P, Hellot MF, Levesque H. Oesophageal mucosal involvement in patients with systemic sclerosis receiving proton pump inhibitor therapy. Aliment PharmacolTher 2006;24:1593–601.
7. Marie I, Ducrotte ´ P, Hellot MF, Denis P, Levesque H. Outcome of small bowel motor impairment in systemic sclerosis: a prospective manometric 5-year follow-up. Rheumatology 2007;46:150–3.
8. Marie I, Levesque H, Ducrotte ´ P *et al*. Gastric involvement in systemic sclerosis: a prospective study. Am J Gastroenterol 2001;41:1874–83.
9. Marie I, Levesque H, Ducrotte ´ P *et al*. Manometry of the upper intestinal tract in patients with systemic sclerosis: a prospective study. Arthritis Rheum 1998;96: 77–83.
10. Poirier TJ, Rankin GB. Gastrointestinal manifestations of progressive systemic scleroderma based on a review of 364 cases. Am J Gastroenterol 1972;58:30–44.
11. Sallam H, McNearney TA, Chen JDZ. Systematic review: pathophysiology and management of gastrointestinal dysmotility in systemic sclerosis (scleroderma). Aliment PharmacolTher 2006;23:691–712.
12. Sjo ¨gren RW. Gastrointestinal motility disorders in scleroderma. Arthritis Rheum 1994;37:1265–82.
13. Sjo ¨gren RW. Gastrointestinal features of scleroderma. CurrOpinRheumatol 1996;8: 569–75.
14. Jaovisidha K, Csuka ME, Almagro UA, Soergel KH. Severe gastrointestinal involvement in systemic sclerosis: report of five cases and review of the literature. Semin Arthritis Rheum 2008;34:689–702.
15. Di Ciaula A, Covelli M, Berardino M *et al*. Gastrointestinal symptoms and motility disorders in patients with systemic scleroderma. BMC Gastroenterology 2008;8:7.
16. 16 Cobden I, Axon AT, Ghoneim AT, McGoldrick J, Rowell NR. Small intestinal bacterial growth in systemic sclerosis.ClinExpDermatol 1980;5:37–42.
17. Domsic R, Fasanella K, Bielefeldt K. Gastrointestinal manifestations of systemic sclerosis. Dig Dis Sci 2008;53:1163–74.
18. Ebert EC.Gastric and enteric involvement in progressive systemic sclerosis. J ClinGastroenterol 2008;42:5–12.
19. Gough A, Andrews D, Bacon PA, Emery P. Evidence of omeprazole-induced small bowel bacterial overgrowth in patients with scleroderma. Br J Rheumatol 1995;34: 976–7.
20. Kahn IJ, Jeffries GH, Sleisenger MH. Malabsorption in intestinal scleroderma.Correction by antibiotics. N Engl J Med 1966;274:1339–44.
21. Kaye SA, Lim SG, Taylor M, Patel S, Gillespie S, Black CM. Small bowel bacterial overgrowth in systemic sclerosis: detection using direct and indirect methods and treatment outcome. Br J Rheumatol 1995;34:265–9. s
22. Owens SR, Greenson JK. The pathology of malabsorption: current concepts. Histopathology 2007;50:64–82.

23. Soudah HC, Hasler WL, Owyang C. Effect of octreotide on intestinal motility and bacterial overgrowth in scleroderma. N Engl J Med 1991;325:1461–7.
24. Corazza G, Sorge M, Strocchi A, Gasbarrini G. Glucose-H2 breath test for small intestine bacterial overgrowth. Gastroenterology 1990;98:253–4.
25. Eposito I, de Leone A, Di Gregorio G *et al*. Breath test for differential diagnosis between small intestinal bacterial overgrowth and irritable bowel disease: an observation on non-absorbable antibiotics. World J Gastroenterol 2007;13:6016–21.
26. Goshal UC, Goshal U, Das K, Misra A. Utility of hydrogen breath tests in diagnosis of small intestinal bacterial overgrowth in malabsorption syndrome, and its relationship with oro-cecal transit time. Ind J Gastroenterol 2006;25:6–10.
27. Kerlin P, Wong L. Breath hydrogen testing in bacterial overgrowth of the small intestine. Gastroenterology 1988;95:982–8.
28. Koshini R, Dai SC, Lezcano S, Pimentel M. A systematic review of diagnostic tests for small intestinal bacterial overgrowth. Dig Dis Sci 2008;53:1443–54.
29. Lin HC. Small intestinal bacterial overgrowth: a frame-work for understanding irritable bowel syndrome. JAMA 2004;292:852–8.
30. Lupascu A, Gabrielli M, Lauritano EC *et al*. Hydrogen glucose breath test to detect small intestinal bacterial overgrowth: a prevalence case-control study in irritable bowel syndrome. Aliment PharmacolTher 2005;22:1157–60.
31. Subcommittee for Scleroderma Criteria of the American Rheumatism Association Diagnostic, & Therapeutic Criteria Committee.Preliminary criteria for the classification of systemic sclerosis (scleroderma). Arthritis Rheum 1980;23:581–90.
32. Leroy EC, Black C, Fleischmajer R *et al*. Scleroderma (systemic sclerosis): classification, subsets and pathogenesis. J Rheumatol 1988;15:202–5.
33. Johnson SR, Hawker GA, Davis AM. The health assessment questionnaire disability index and scleroderma health assessment questionnaire in scleroderma trials: an evaluation of their measurement properties. Arthritis Rheum 2005;53:256–62.
34. Di Mario F, Stefani N, Bo ND *et al*. Natural course of functional dyspepsia after Helicobacter pylori eradication: a seven-year survey. Dig Dis Sci 2005;50: 2286–95.
35. Parodi A, Sessarego M, Greco A *et al*. Small intestinal bacterial overgrowth in patients suffering from scleroderma: clinical effectiveness of its eradication. Am J Gastroenterol 2008;103:1257–62.
36. Quigley EM. Bacteria: a new player in gastrointestinal motility disorders—infections, bacterial overgrowth, and probiotics. GastroenterolClin North Am 2007;36:735–48.
37. Quigley EM, Quera R. Small intestinal bacterial overgrowth: roles of antibiotics, prebiotics, and probiotics. Gastroenterology 2006;130(Suppl. 1):S78–90.
38. Shindo K, Machida M, Koide K, Fukumara M, Yamazaki R. Deconjugation ability of bacteria isolated from the jejunal fluid of patients with progressive systemic sclerosis and its gastric pH.Hepatogastroenterology 1998;45:1643–50.

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