ORIGINAL PAPERS

Management of small intestinal bacterial overgrowth by pediatric gastroenterologists in Spain

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ABSTRACT

Background: small intestinal bacterial overgrowth (SIBO) is a heterogeneous condition with nonspecific symptoms. This study aimed to report its management by pediatric gastroenterologists in Spain.

Methods: a descriptive study was performed by means of a survey sent to 184 active members of the Spanish Society of Pediatric Gastroenterology, Hepatology and Nutrition (SEGHNP).

Results: one hundred and forty-eight responses (80.4 %) were received. Forty-four patients had no predisposing condition, 31.1 % used antibiotics followed by probiotics, 33.1 % antibiotherapy concomitant with probiotics, 24.3 % only antibiotics and 10.8 % only probiotics. The diagnosis was established via clinical parameters in 73.8 % of participants and the therapeutic response was checked only by clinical data in 90 %.

Conclusions: there is high variability in the management of SIBO among pediatric population in Spain.

Keywords: Bacterial overgrowth. Pediatrics. Probiotics. Antibiotics. Hydrogen breath test.

INTRODUCTION

Small intestinal bacterial overgrowth (SIBO) is a heterogeneous condition characterized by the presence or increase of atypical bacteria in the small intestine that unbalances intestinal microbiota. SIBO is characterized by symptoms such as flatulence, distension and abdominal pain. These symptoms might be indistinguishable from those presented by patients with functional gastrointestinal disorders (FGIDs). In most cases, SIBO is associated with motility or inflammatory disorders (Table 1), but it is estimated that up to 12.5 % of patients with no predisposing intestinal condition could have SIBO (1), with a higher prevalence in cases of FGIDs, with rates of up to 90 % in a number of studies (2).

The reference standard for diagnosing SIBO is the duodenum-jejunal aspirate. In the clinical practice, a hydrogen breath test (HBT) is more frequently used. The test has adequate sensitivity and specificity (3), although they vary depending on the setting in which the test is employed. In terms of treatment, the objectives are to treat the predisposing cause of SIBO if present, as well as to provide nutri-

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Table 1. *Main entities associated with bacterial overgrowth syndrome*

Intestinal anatomical injuries
Intestinal duplication, partial atresia, stenosis and diverticula of the small intestine, enterocolic fistulas, adhesions, ileocecal valve resection (short bowel), Billroth-II gastrectomy with Roux-en-Y anastomosis
Alterations in intestinal motility
Intestinal pseudo-obstruction, Crohn's disease, celiac disease, muscular dystrophy, myotonia, myelomeningocele, diabetes mellitus, hypothyroidism, chronic renal failure, scleroderma, postsurgical blind loop syndrome, radiation enteritis
Alterations of defense mechanisms
IgA deficiency, common variable immunodeficiency syndrome, AIDS, secondary immunodeficiencies (malnutrition, lymphomas, and leukemias), hypochlorhydria (autoimmune atrophic gastritis, vagotomy, long-term use of proton pump inhibitors, total gastrectomy), exocrine pancreatic insufficiency, liver disease

Adapted from: Román E, Cilleruelo M. Síndrome de sobredesarrollo bacteriano. In: Tratamiento en Gastroenterología, Hepatología y Nutrición Pediátrica. Madrid: Ergon; 2016. pp. 343-53.

tional therapy and microbiota restoration through antibiotic and probiotic therapy. Antibiotics and probiotics are used to treat the imbalanced intestinal microbiota, but diverse antibiotic and probiotic regimens have been used with conflicting results (4). With regard to the dietary treatment, the published studies have been mainly performed with adult populations with results that are also conflicting (5).

The aim of this study was to determine the management of SIBO in our setting and report the regimens used by pediatric gastroenterologists in Spain, given the limited available scientific evidence. This study serves as a basis for preparing new studies aiming at standardizing the diagnosis and treatment of SIBO.

METHODS

A descriptive, survey research study was performed. A survey was prepared consisting of 17 questions, which could be raised to 26 depending on the answers. The survey consisted of total and partial questions with multiple-choice answers and the option of open comments (Table 4). The survey was divided into four blocks: demographic variables, diagnostic methodology, treatment (indications, antibiotic therapy, probiotic therapy, dietary therapy) and assessment of the treatment response.

The invitation to participate was sent to 184 active SEGHNP members, primarily dedicated to pediatric gastroenterology. To validate the results, a sample size of 128 was estimated with a 10 % precision and a 95 % confidence interval (CI). For data analysis, mean, median, standard deviation and interquartile range were used. The survey remained active for three months. The study data were collected and managed using the REDCap (ResearchElectronic Date Capture) tool (6) for the electronic capture of data stored at the SEGHNP (www.seghnp.org). Technical support was provided by the AEGREDCap Support Unit, shared with the Spanish Association of Gastroenterology (AEG).

RESULTS

One hundred and forty-eight responses were received (80.4 % of the surveys sent). The participants' median clinical experience in pediatric gastroenterology was 12 years (interquartile range, 8-17.25). Pediatric gastroenterologists from 86 different centers participated in the survey. Half of the respondents reported diagnosing SIBO in at least ten patients a year and 13.5 % diagnosed SIBO in more than 20 patients a year. The value of mandatory response items that were not answered was less than 3 % in all of them.

The results about the diagnostic system for SIBO and in terms of treatment are shown in tables 2 and 3, respectively. Ninety percent of the respondents reported checking treatment response only through clinical data, with 74 % of the respondents considering the treatment to be effective, regardless of the cause.

Table 2. *Diagnostic systematics for bacterial overgrowth syndrome*

Suspected diagnosis			Diagnostic method		
Patients with predisposing condition	Patients without predisposing condition	Both conditions	Duodenum-jejunal aspirate	Clinical data	Hydrogen breath test
23.8 % (35)	29.9 % (44)	46 % (68)	0 % (0)	73.8 % (107)	68.3 % (99) 53 % of them (53) with methane measurement

Answers obtained about systematic for diagnosis of SIBO. The total number of responses obtained are included in brackets.

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Table 3. *Treating bacterial overgrowth syndrome*

Item	Options	%	Others
Regimen for patients WITHOUT predisposing condition	Antibiotherapy followed by probiotics	31.1 (26.1-36.1 %) (46)	
	Antibiotherapy concomitant with probiotics	33.1 (28.1-38.1 %) (49)	
	Antibiotherapy	24.3 (19.3-29.3 %) (36)	
	Probiotics	10.8 (5.8-15.8 %) (16)	
Regimen for patients WITH predisposing condition	Antibiotherapy followed by probiotics	33.3 (28.3-38.3 %) (48)	
	Antibiotherapy concomitant with probiotics	34.7 (29.7-39.7 %) (50)	
	Antibiotherapy	30.6 (25.6-35.6 %) (44)	
	Probiotics	1.4 (0-6.4 %) (2)	
Antibiotherapy			
< 12 years (median duration in days; interquartile range)	Metronidazole *(10; 7-12)*	95.5 (90.5-100 %) (126)	
	Rifaximin *(10; 7-10)*	20.5 (15.5-25.5 %) (27)	
	Others	15.9 (10.9-20.9 %) (21)	Trimethoprim-sulfamethoxazole, amoxicillin-clavulanate, gentamicin, paromomycin
≥ 12 years (median duration in days; interquartile range)	Metronidazole *(10; 7-14)*	80 (75-85 %) (104)	
	Rifaximin *(10; 7-10)*	49.2 (44.2-54.2 %) (64)	
	Others	10.8 (5.8-15.8 %) (14)	Trimethoprim-sulfamethoxazole, amoxicillin-clavulanate, gentamicin, paromomycin
Number of cycles	1 month	72.7 (67.7-77.7 %) (96)	
	2 months	14.4 (9.4.-19.4 %) (19)	
	3 months	12.9 (7.9-17.9 %) (17)	
Probiotics	*Lactobacilli*	66.1 (61.1-71.1 %) (74)	Bivos®, Casenbiotic®, Reuteri®, Kaleidon®
	Bifidobacteria	4.5 (0-9.5 %) (5)	
	Yeasts	25.9 (20.9-30.9 %) (29)	Ultra Levura®, Simbiótico NM®
	Combination of strains or genera	34.8 (29.8-39.8 %) (39)	Prodefen®, Vivomixx®, Megalevure®, Produo daily care®, Symbioram®, ProFaes4 Dual Vit®, Lactoflora®, VSL3#®, Lactibiane Enfant®
Number of cycles	1 month	56.3 (51.3-61.3 %) (63)	
	2 months	20.5 (15.5-25.5 %) (23)	
	3 months	23.2 (18.2-28.2 %) (26)	
Number of days	< 7 days	0.9 (0-5.9 %) (1)	
	7-10 days	30.4 (25.4-35.4 %) (34)	
	≥ 10 days	68.8 (63.8-73.8 %) (77)	
Diet	Reduced or no lactose	48.6 (43.6-53.6 %) (71)	
	No dietary treatment	27.4 (22.4-32.4 %) (40)	
	Other regimens	24 (19-29 %) (35)	Diet low in saturated fats Diet low in rapidly absorbed carbohydrates Diet low in fructose and sorbitol Partial restriction of simple sugars Diet low in FODMAPS* Diet low in processed food
Confirmation of treatment response	Duodenum-jejunal aspirate	0 (0-5 %) (0)	
	Clinical data	89.8 (84.8-94.8 %) (132)	
	Hydrogen breath test	9.5 (4.5-14.5 %) (14)	

Results obtained from the survey in terms of treatment. Percentages obtained with a 95 % confidence interval are included and the total number of responses are shown in brackets.

Table 4. *Survey*

A. Demographic questions

How many years have you dedicated to pediatric gastroenterology?

In what hospital or center do you work? Please specify the name.

B. Diagnosis

How do you generally diagnose SIBO? You may indicate more than one answer.

A. Clinical diagnosis
B. Hydrogen breath test
C. Duodenum-jejunal aspirate

If your center has hydrogen breath tests, does your center's test incorporate the measurement of methane?

A. Yes
B. No

In approximately how many patients with suspected small intestinal bacterial overgrowth syndrome (SIBO) do you start empiric treatment?

A. < 10/year
B. 10-20/year
C. ≥ 20/year

C. Treatment

Note: Main entities associated with bacterial overgrowth syndrome (Table 1). Adapted from: Román E, Cilleruelo M. Síndrome de sobredesarrollo bacteriano. In: Tratamiento en Gastroenterología, Hepatología y Nutrición Pediátrica. Madrid: Ergon; 2016. pp. 343-53.

In what group do you most often perform bacterial overgrowth treatment?

A. Mainly in patients WITHOUT a predisposing condition with suggestive symptoms (abdominal distension, persistent diarrhea, etc.)
B. Mainly in patients WITH a predisposing condition with suggestive symptoms (abdominal distension, persistent diarrhea, etc.)
C. In both situations

What regimen do you use most often for treating SIBO in patients WITHOUT a predisposing condition?

A. Antibiotherapy regimen
B. Probiotics regimen
C. Regimen of antibiotherapy followed by probiotics
D. Regimen of antibiotherapy concomitant with probiotics
E. Other. Please indicate the regimen(s) you use

What regimen do you use most often for treating SIBO in patients WITH a predisposing condition?

A. Antibiotherapy regimen
B. Probiotics regimen
C. Regimen of antibiotherapy followed by probiotics
D. Regimen of antibiotherapy concomitant with probiotics
E. Other. Please indicate the regimen(s) you use

C.1. Antibiotic therapy

What antibiotic(s) do you use for patients younger than 12 years? You may indicate more than one answer.

A. Metronidazole. Indicate the number of days
B. Vancomycin. Indicate the number of days
C. Rifaximin. Indicate the number of days
D. Other(s). Please indicate the regimen(s) you use

What antibiotic(s) do you use for patients 12 years of age or older? You may indicate more than one answer.

A. Metronidazole. Indicate the number of days
B. Vancomycin. Indicate the number of days
C. Rifaximin. Indicate the number of days
D. Other(s). Please indicate the regimen(s) you use

Generally, for how many consecutive months do you perform antibiotherapy cycles?

A. 1 month
B. 2 months
C. 3 months or more

(Continuation in the next page)

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Table 4 (Cont.). *Survey*

C.2. Treatment of SIBO with probiotics
If you use probiotics, what type do you use?
A. *Lactobacilli*. Please specify the brand name
B. Bifidobacteria. Please specify the brand name
C. *Saccharomyces*. Please specify the brand name
D. Combination of strains or genera. Please specify the brand name
Generally, for how many consecutive months do you perform probiotic cycles?
E. 1 month
F. 2 months
G. 3 months or more
If you use probiotics, for how long do you use them (regardless of the number of cycles you perform)?
A. < 7 days
B. 7-10 days
C. > 10 days
C.3. Dietary aspects of SIBO treatment
Do you recommend a dietary treatment for managing SIBO?
A. Yes, a diet low in lactose or lactose-free
B. Yes, other. Please specify
C. No, none
D. Assessing treatment response
In your experience, is SIBO treatment effective?
A. Yes, regardless of whether there is an underlying predisposing condition
B. No, that is why I stopped performing it
C. Yes, but only if there is an underlying predisposing condition
D. Yes, but only in cases with a diagnosis of SIBO using the hydrogen/methane
E. None of the above
If you start treatment for SIBO, how do you assess the treatment response?
A. Through clinical data (clinical signs and symptoms)
B. By performing a new hydrogen breath test
C. By performing jejunal aspiration
D. Other

DISCUSSION

The management of SIBO by pediatric gastroenterologists in Spain was heterogeneous. There are no studies with characteristics similar to ours with the objective of addressing SIBO management in children. Our study confirms the considerable variability in the medical practice when diagnosing and, especially, treating SIBO in children.

In terms of diagnosis, none of the pediatric gastroenterologists in Spain reported using invasive methods. Less than half (46 %) of the respondents admitted suspecting SIBO in patients with or without intestinal disease, despite recognizing SIBO as an added cause in healthy populations or in functional gastrointestinal disorders (7). More than half of those who used HBT did not measure methane in their patients at their centers. Methanogenic microbiota should be considered and tests implementing methane production should be used (8).

The treatment of SIBO is controversial because of the lack of studies in children. There was high variability among pediatric gastroenterologists when treating patients with SIBO, with no clear regimen to follow. They did not show differences when treating SIBO depending on the predisposing condition. However, it is important to highlight the relevance of differential diagnosis, since in the case of SIBO secondary to other entities, there may be recurrence and the need to modify the antibiotic regimen over time, until the cause originating it is solved. In terms of antibiotic therapy, Tahan et al. (9) used a regimen of trimethoprim-sulfamethoxazole (TMP-SMT) along with metronidazole, achieving an effectiveness of 95 %, observed by the HBT. In our survey, only two pediatricians report-

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ed using this combination, despite being a regimen already described in patients with intestinal failure. Published studies have also assessed the effectiveness of rifaximin in children with SIBO (10). A dosage of 600 mg/day for seven days was prescribed for patients with irritable bowel syndrome (IBS) and SIBO demonstrated by the HBT, achieving an effectiveness of 66 %. Nevertheless, this rate differed significantly from those published by other authors (11). There is more experience in adult populations. A systematic review (12) found that antibiotic therapy had efficacy rates of approximately 50 % for rifaximin, similar to those recently published by other authors (13), with efficacy rates of 70 % for rifaximin.

On the other hand, SIBO is common in patients with IBS (12), and gut microbiota appears to play an important role in both diseases. Based on this concept, dietary and probiotic therapies have been used for SIBO. In our study, there was no consensus on when to treat SIBO with probiotics. Up to 75 % of the respondents stated that they used probiotics, but up to 15 distinct preparations were used. A meta-analysis of adults found significantly greater eradication rates compared with placebo when treatment was performed with probiotics (14), although their efficacy was greater when used in combination with antibiotics. Similarly, dietary treatments have been recommended for patients with FGIDs, based on the theory of improvement after eliminating fermentable carbohydrates. Thus, diets low in lactose or low in FODMAPs (15)di- and monosaccharides and polyols (FODMAP have been used, although the evidence regarding dietary therapy is limited, due to the lack of studies. The high variability in dietary treatments in our study reflects this situation.

The most significant limitation of this study is its nature, given that it is a preliminary survey and the hypothesis needs to be confirmed in future studies with a higher methodological quality. The strengths of the study include its high survey participation rate (80 %) by pediatric gastroenterologists in Spain, which can provide a fairly close picture of the management of this syndrome in the general practice.

Based on our results, we can conclude that there is high variability among pediatric gastroenterologists in Spain when treating patients with SIBO, with no clear regimen to follow. Our results are probably similar to the management performed in other countries, given that there is no scientific evidence in the literature. The current increased incidence in SIBO means that further studies are needed to better understand the pathophysiology of the disease, to establish uniform diagnostic criteria and especially, to define the regimens to follow, the antibiotherapy to use, treatment duration and dosage. In addition, these studies will help to develop clinical practice guidelines to allow us to standardize the management of SIBO in children.

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