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The effectiveness of rotating versus single course antibiotics for small intestinal bacterial overgrowth

Nicolas Richard[1] | Charlotte Desprez[2,3] | Fabien Wuestenberghs[2,3,4] | Anne-Marie Leroi[2,3,5] | Guillaume Gourcerol[2,3] | Chloé Melchior[1,2,5,6]

[1]Gastroenterology Department, Rouen University Hospital, Rouen, France

[2]INSERM UMR 1073, Institute for Research and Innovation in Biomedicine, Normandy University, Rouen, France

[3]Physiology Department, Rouen University Hospital, Rouen, France

[4]Department of Gastroenterology and Hepatology, CHU UCL Namur, Godinne University Hospital, UCLouvain, Yvoir, Belgium

[5]INSERM CIC 1404, Rouen University Hospital, Rouen, France

[6]Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

Correspondence
Chloé Melchior, Gastroenterology Department, Rouen University Hospital – 1 rue de Germont, 76031 ROUEN CEDEX, France.
Email: chloe.melchior@chu-rouen.fr

Abstract

Background: Small intestinal bacterial overgrowth treatment is usually based on antibiotics with no guidelines available.

Objective: This study aimed to investigate the efficacy of different antibiotics to treat small intestinal bacterial overgrowth.

Methods: Consecutive patients referred to our tertiary center and diagnosed with intestinal bacterial overgrowth were retrospectively included. Patients were diagnosed using a 75 g glucose breath test. Patients were treated either with a single antibiotic (quinolone or azole) or rotating antibiotics (quinolone and azole, one after the other) for 10 consecutive days per month for 3 months. A negative glucose breath test after antibiotic treatment was considered as remission. Quality of life (GIQLI) and gastrointestinal severity (IBS-SSS) were assessed before and after antibiotic treatment. Symptomatic evaluation was realized in simple blind of glucose breath test result: patients were unaware of their results.

Results: Between August 2005 and February 2020, 223 patients were included in the analysis (female 79.8%, mean age 50.2 ± 15.7 years). Remission was observed in 119 patients (53.4%) after one course of antibiotics and was more frequent in patients receiving rotating antibiotics than in patients receiving a single antibiotic (70.0% vs. 50.8%, $p = 0.050$). Remission was associated with a significant improvement in quality of life ($p = 0.035$) and in bloating ($p = 0.004$).

Conclusion: In this study, the treatment of small intestinal bacterial overgrowth using rotating antibiotics was more effective than treatment using a single course of antibiotic. Remission was associated with improvement in both quality of life and bloating.

KEYWORDS
antibiotics, bacterial overgrowth, breath tests, ciprofloxacin, metronidazole, norfloxacin, quality of life, remission, rotating antibiotics, SIBO, single course, small intestinal bacterial overgrowth

Key Summary

Summarize the established knowledge on this subject

- Small intestinal bacterial overgrowth is an increase in bacterial concentration in the small bowel whose common gastrointestinal symptoms are non-specific: abdominal pain, bloating and diarrhea.
- Systemic antibiotics (e.g., azole and quinolone antibiotics) are commonly used in the treatment of small intestinal bacterial overgrowth.
- Recently, rifaximin, a non-systemic antibiotic, has been proposed to improve the treatment of small intestinal bacterial overgrowth. However, this antibiotic is unavailable in this indication in some countries.

What are the significant and/or new findings of this study?

- In this study, remission of small intestinal bacterial overgrowth was more frequent in patients receiving rotating antibiotics (azole and quinolone antibiotics) than in patients receiving a single antibiotic (azole antibiotic or quinolone antibiotic).
- SIBO remission was associated with an improvement in both quality of life and bloating.

INTRODUCTION

Small intestinal bacterial overgrowth (SIBO) is defined as an increase in bacterial concentration in the small bowel.[1] Common gastrointestinal (GI) symptoms are nonspecific, including: abdominal pain, bloating and diarrhea.[1] SIBO is most likely to occur in people with gastrointestinal surgery, motility disorders (gastroparesis, systemic sclerosis), gastrointestinal disorders (Crohn's disease, celiac disease, chronic pancreatitis, irritable bowel syndrome (IBS) and possibly functional dyspepsia (FD)), obesity, immunosuppressive diseases (diabetes mellitus, cirrhosis, renal failure), and prolonged use of proton pump inhibitors (PPIs) or antibiotics.[1–4]

Jejunal aspiration culture (with a bacterial colony count of at least 10^5 colony-forming units/mL) is considered as the gold standard for the diagnosis of SIBO but is an invasive method.[5] Recently, a threshold of 10^3 colony-forming units/mL has been considered for the diagnosis of low-grade SIBO.[6] Non-invasive breath tests, including glucose breath test (GBT) and lactulose breath test (LBT), are validated and inexpensive methods for the diagnosis of SIBO available in daily practice.[7] Treatment involves antibiotics, probiotics, diet and treatment of the predisposing conditions when possible (i.e., PPI use).[8] Historically, systemic antibiotics (e.g., ciprofloxacin, norfloxacin and metronidazole) have been used leading to higher rates of breath test normalization with an antibiotic versus placebo (51.1% vs. 9.8%).[9] More recently, rifaximin, a non-systemic antibiotic, unavailable in France in this indication, led to the eradication of SIBO in 70.8% of patients according to a meta-analysis.[10] However, no international consensus or guidelines are currently available, and no drugs have been approved in the United States or in Europe specifically for the treatment of SIBO. Thus, this study aimed to investigate the efficacy of different antibiotic treatments for SIBO remission and symptom improvement.

MATERIALS AND METHODS

A single center retrospective study was conducted in the Physiology Department of Rouen University Hospital, France.

Written information was given to patients before any procedure. Informed consent was obtained from all patients, especially regarding the use of their data for research purposes. The study was conducted in accordance with the ethical guidelines of the Declaration of Helsinki (6th revision, 2008) and was approved by a local human research committee on 4 June 2020 (E2020-38) as required by national legislation. The use of data was declared to the Commission Nationale de l'Informatique et des Libertés (CNIL) (*n*° 817.917), in compliance with French legislation. No financial support was received for this study. Authors vouch for the accuracy of reported data.

Patients

Consecutive patients, referred to our university hospital with a first positive GBT before antibiotic treatment, were included if they had at least a second GBT after antibiotic treatment during their follow-up. Patients with only one GBT available, with unknown treatment or with medication considered unusual or rare were not included (Figure 1).

Clinical data were collected by reviewing medical charts. Age, gender, weight, height, body mass index (BMI), medical history (abdominal surgery, systemic sclerosis, diabetes mellitus) as well as treatment (PPI intake) were systematically recorded.

Validated self-questionnaires were filled (since December 2013) at the time of each GBT, both before and after antibiotic treatment. IBS and FD were diagnosed according to Rome criteria. Between 2013 and 2016, IBS was diagnosed using an association of Rome III criteria and the presence of abdominal pain (to be the closest to the Rome IV definition). After 2016, IBS was diagnosed using Rome IV criteria.[11] Abdominal pain, quality of life and severity of GI symptoms were assessed using a visual analog scale (0–100 interval), the validated French version of the Gastrointestinal Quality of Life Index (GIQLI),[12] and the IBS Severity Scoring System (IBS-SSS),[13] respectively. Symptomatic evaluation was realized in single blind of GBT result; hence patients were unaware of their results.

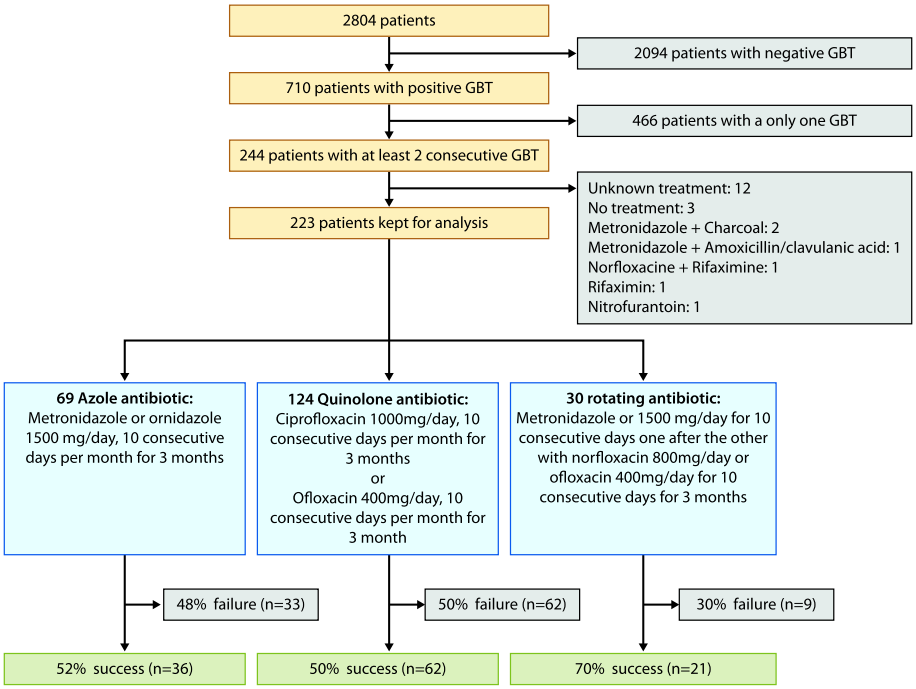

FIGURE 1 Flowchart of patients' selection and treatment. GBT: glucose breath test

Breath tests

SIBO was diagnosed using a 75 g GBT.[7] Patients were prepared according to the North American consensus.[7] Two days prior to the GBT, patients were advised to follow a diet excluding fermentable foods such as complex carbohydrates. Patients were asked to start fasting at least 8 h prior to the test. Smoking and exercise were not allowed on the day of the GBT. Both H_2 and CH_4 were measured at baseline before the glucose load. If a positive criterion (see below) was met with the instructed diet, patients were already considered as positive for SIBO. All patients ingested 75 g of glucose dissolved in 250 ml of water. End-alveolar breath samples were collected in a bag, at baseline and every 15 min, for a total duration of 2 h. H_2 and CH_4 levels in exhaled air were measured by chromatography (QuinTron Breath Trackers, QuinTron Instrument Company) and expressed in part per million (ppm). A GBT was considered positive for SIBO if any of the following criteria were met: (i) ≥10 ppm increase above the H_2 and/or CH_4 basal level for at least two consecutive measurements; (ii) ≥10 ppm increase between minimum and maximum H_2 and/or CH_4 values during the 2-h period of breath collection; and (iii) 20 ppm of H_2 and/or CH_4 at baseline if the patient had followed the preparation guidelines.[7] As the third criterion is controversial, an extra analysis excluding this criterion was performed. A negative GBT after antibiotic treatment was considered as remission. We defined relapse as a third positive breath test performed in our department after treatment.

Antibiotic treatments

Patients received a single antibiotic (an azole antibiotic or a quinolone antibiotic) or rotating antibiotics (azole and quinolone antibiotics) according to their physician's prescription.

Azole antibiotic treatment consisted in either metronidazole 500 mg three times per day for 10 consecutive days per month for 3 months or ornidazole 500 mg three times per day for 10 consecutive days per month for 3 months.

Quinolone antibiotic treatment consisted in one of the following: norfloxacine 400 mg twice per day or ciprofloxacin 500 mg twice per day for 10 consecutive days per month for 3 months or ofloxacin 200 mg twice per day for 10 consecutive days per month for 3 months.

Rotating antibiotic treatment consisted in metronidazole 500 mg three times per day for 10 consecutive days per month alternately with either norfloxacin 400 mg twice per day or ofloxacin 200 mg twice per day for 10 consecutive days per month for 3 months.

Statistical analysis

The chi-squared test was used to compare remission rates between antibiotic treatments: a single antibiotic versus rotating antibiotics. Clinical characteristics among groups were compared using Fisher's exact test used for two-class variables and Student's *t*-test for continuous variables while non-parametric values were analyzed using Mann-Whitney test. The differences assessed during first and

TABLE 1 Demographic and clinical parameters of included patients at baseline

	Single antibiotic *N* = 193	Rotating antibiotics *N* = 30	*p*-value
Female	151 (78.2)	26 (86.7)	0.342
Age (years)	50.2 ± 15.4	50.1 ± 17.5	0.966
Diabetes mellitus	9 (4.7)	0 (0.0)	0.613
Systemic sclerosis	3 (1.6)	13 (43.3)	0.0001
Cholecystectomy	2 (1.0)	3 (10.0)	0.018
Abdominal surgery history	25 (13.0)	3 (10.0)	1.000
FD	40 (20.7)	5 (16.7)	0.807
IBS	19 (9.8)	3 (10.0)	1.000
PPI use	25 (13.0)	7 (23.3)	0.159
Interval between two tests (days)	143.5 ± 84.0	191.4 ± 271.0	0.052
Baseline visual analog scale score (*n* = 55)	46.5 ± 27.7	41.0 ± 31.1	0.586
Baseline IBS-SSS score (*n* = 55)	271.2 ± 102.7	243.6 ± 141.7	0.475
Baseline GIQLI score (*n* = 57)	80.0 ± 22.2	81.4 ± 15.1	0.856
First GBT H_2 peak (ppm)	20.3 ± 19.4	11.4 ± 10.9	0.021
First GBT CH_4 peak (ppm)	20.1 ± 18.8	27.1 ± 22.9	0.067

Note: Results are expressed in number (percentage) and mean ± *SD*.

Abbreviations: FD, functional dyspepsia; GBT, glucose breath test; GIQLI, Gastrointestinal Quality of Life Index; IBS, irritable bowel syndrome; IBS-SSS, IBS-Severity Scoring System; PPI, proton pump inhibitors.

second GBT were analyzed using paired *t*-test for parametric paired values and Wilcoxon signed-rank test for non-parametric paired values. All tests were two-tailed. In all cases, $p < 0.05$ was considered as statistically different.

RESULTS

Between August 2005 and February 2020, 710 patients with a first positive GBT before antibiotic treatment were assessed for eligibility. Among them, 466 were not considered because a second GBT was not performed after antibiotic treatment. Twenty-one patients were not included because SIBO treatment was unknown or considered unusual or rare. Among the 223 patients kept for analysis, 69 patients received an azole antibiotic (68 metronidazole and one ornidazole), 124 patients received a quinolone antibiotic (118 norfloxacin, five ciprofloxacin and one ofloxacin) and 30 patients received rotating antibiotics (28 metronidazole and norfloxacin, two metronidazole and ofloxacin) (Figure 1). In our center, the prevalence of a positive GBT during the studied period was 28.1%.

Patients' characteristics

Among the 223 patients analyzed, 177 (79.3%) were female, with a mean age of 50.2 ± 15.7 years. In their history, 9.9% had IBS, 4.0% diabetes mellitus, 7.2% systemic sclerosis, 2.2% cholecystectomy, 12.6% abdominal surgery and 20.2% FD. PPI use was reported in 14.3% of the patients. Before antibiotic treatment, the mean scores of visual analog scale, IBS-SSS and GIQLI were 45.8 ± 27.9, 267.7 ± 107 and 80.2 ± 21.3, respectively. The mean interval between the first and the second GBT was 150 days (±126). There was no difference between the single antibiotic group and the rotating antibiotics group regarding diarrhea (6.7% vs. 3.3%, $p = 0.699$) and constipation (7.7% vs. 6.7%, $p = 1.000$). No data were available concerning medication compliance.

At baseline, socio-demographic data and the results of self-questionnaires were similar in both groups (Table 1), except for systemic sclerosis, cholecystectomy and GBT H_2 peak. Systemic sclerosis (43.3% vs. 1.6%, $p < 0.0001$) and cholecystectomy (10.0% vs. 1.0%, $p = 0.018$) were more frequent in the rotating antibiotics group compared to the single antibiotic group (Table 1). GBT H_2 peak was lower in the rotating antibiotics group ($p = 0.021$). There was no correlation between gender and other clinical parameters or between gender and clinical evolution (Supplementary Table 1).

Remission

Remission was observed in 119 patients (53.4%) after one course of antibiotics. Remission was observed in 36 patients (52.2%) receiving an azole antibiotic and in 62 patients (50.0%) receiving a quinolone antibiotic ($p = 0.88$). Remission was observed more frequently in patients receiving rotating antibiotics than in patients receiving a

single antibiotic (70.0% vs. 50.8%, $p = 0.050$) (Figure 2). Similarly, after excluding the third criterion of positivity (20 ppm of H_2 and/or CH_4 at baseline), the same result was observed: remission was observed more frequently in patients receiving rotating antibiotics (76.9% vs. 53.8%, $p = 0.027$). Patients in remission were younger compared to those not in remission (48.0 vs. 52.7 years; $p = 0.023$)

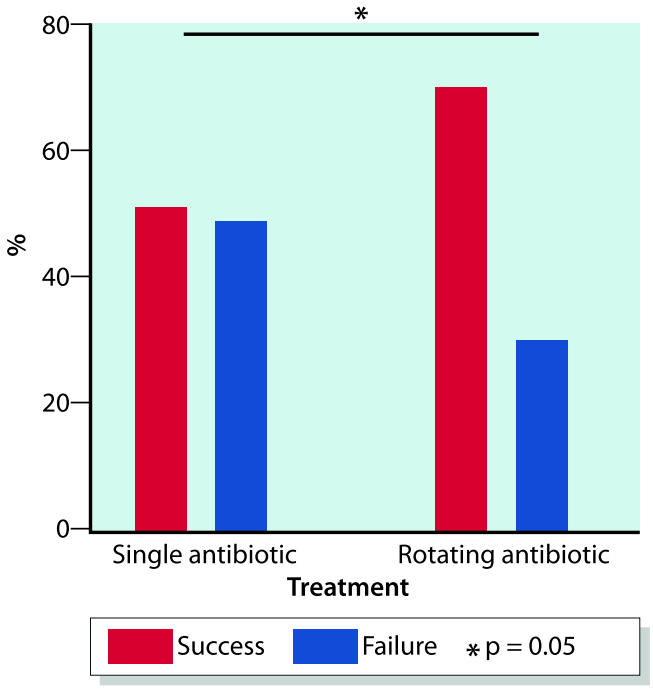

FIGURE 2 Antibiotic success rate according to the antibiotic(s) received

(Table 2). A third GBT was performed in 34 patients after failure of the first course of antibiotics. After the second course of antibiotics, 13 patients (38.2%) had GBT normalization. Among them, seven received firstly a quinolone antibiotic and secondly an azole antibiotic, one received firstly an azole antibiotic and secondly a quinolone antibiotic, one received firstly rotating antibiotics and secondly amoxicillin and clavulanic acid, one received rotating antibiotics twice, and data were missing in three patients.

Peaks of CH_4 and H_2 during GBT significantly decreased after antibiotic treatment in both groups, except for H_2 in the rotating antibiotics group ($p = 0.144$) (Figure 3).

After remission, eight patients (6.7%) presented a relapse diagnosed by a new positive GBT. Three patients (10%) relapsed in the rotating antibiotics group whereas five patients (5.1%) relapsed in the single antibiotic group ($p = 0.147$). On average, patients relapsed 14.0 months after a course of rotating antibiotics and 35.8 months after a course of a single antibiotic ($p = 0.453$).

Association between symptom improvement and remission

Remission was associated with a significant increase in the GIQLI score in comparison with the treatment failure group (4.9 vs. −2.6, $p = 0.035$) (Figure 4). Analysis of GIQLI subscores regarding pain, diarrhea, bloating and constipation showed a significant improvement in bloating in case of remission ($p = 0.004$) whereas all other symptoms remained unchanged (Figure 5). The evolution in IBS-SSS score was not different between remission and treatment failure groups (+2.6 vs. −23, $p = 0.116$).

TABLE 2 Demographic and clinical parameters according to treatment response

	Success $N = 119$	Failure $N = 104$	p-value
Female	95 (79.8)	82 (78.8)	0.870
Age (years)	48.0 ± 15.8	52.7 ± 15.2	0.023
Diabetes mellitus	4 (3.4)	5 (4.8)	0.737
Systemic sclerosis	10 (8.4)	6 (5.8)	0.604
Cholecystectomy	4 (3.4)	1 (1.0)	0.375
Abdominal surgery history	13 (10.9)	15 (14.4)	0.544
FD	24 (20.1)	21 (20.2)	1.000
IBS	10 (8.4)	12 (11.5)	0.503
PPI use	19 (16.0)	13 (12.5)	0.567
Interval between two tests (days)	141.8 ± 81.6	159.3 ± 163.1	0.301
Rotating antibiotics	21 (17.6)	9 (8.7)	0.050
First GBT H_2 peak (ppm)	18.5 ± 17.4	27.3 ± 41.1	0.237
First GBT CH_4 peak (ppm)	19.7 ± 17.8	24.7 ± 23.4	0.242

Note: Results are expressed in number (percentage) and mean ± *SD*.

Abbreviations: FD, functional dyspepsia; GBT, glucose breath test; GIQLI, gastrointestinal quality of life index; IBS, irritable bowel syndrome; IBS-SSS, IBS-Severity Scoring System; PPI, proton pump inhibitors.

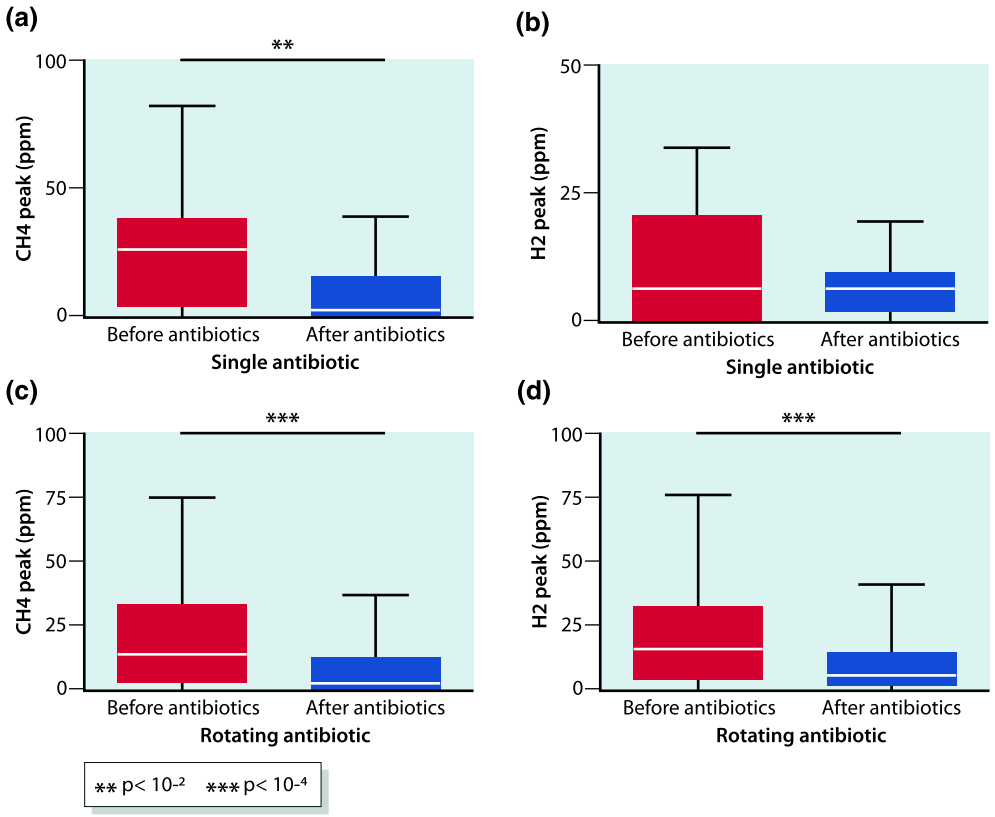

FIGURE 3 Peaks of CH_4 and H_2 during glucose breath test before and after antibiotic treatment. (a) Peak of CH_4 during glucose breath test before and after single antibiotic. (b) Peak of H_2 during glucose breath test before and after single antibiotic. (c) Peak of CH_4 during glucose breath test before and after a course of rotating antibiotics. (d) Peak of H_2 during glucose breath test before and after a course of rotating antibiotics

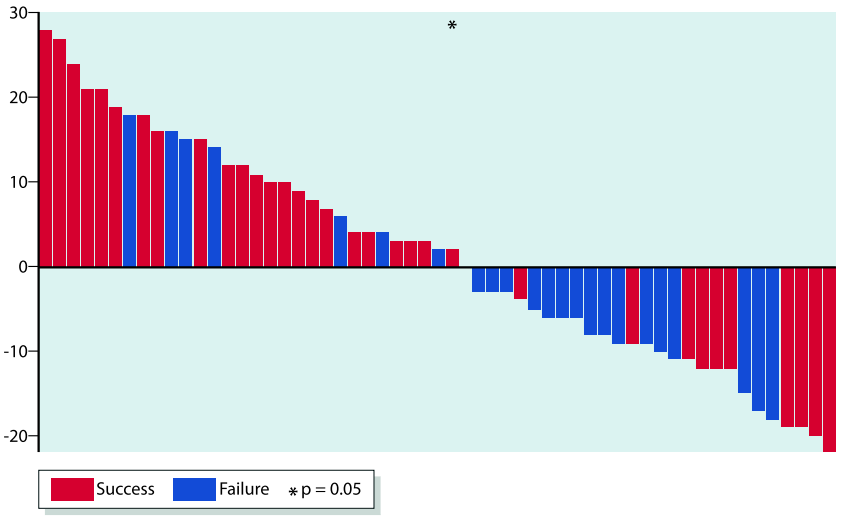

FIGURE 4 Individual evolution of each evaluable patient's gastrointestinal quality of life index (GIQLI) score before and after antibiotic treatment. Positive GIQLI score depicts an improvement in patients' symptoms after antibiotic treatment

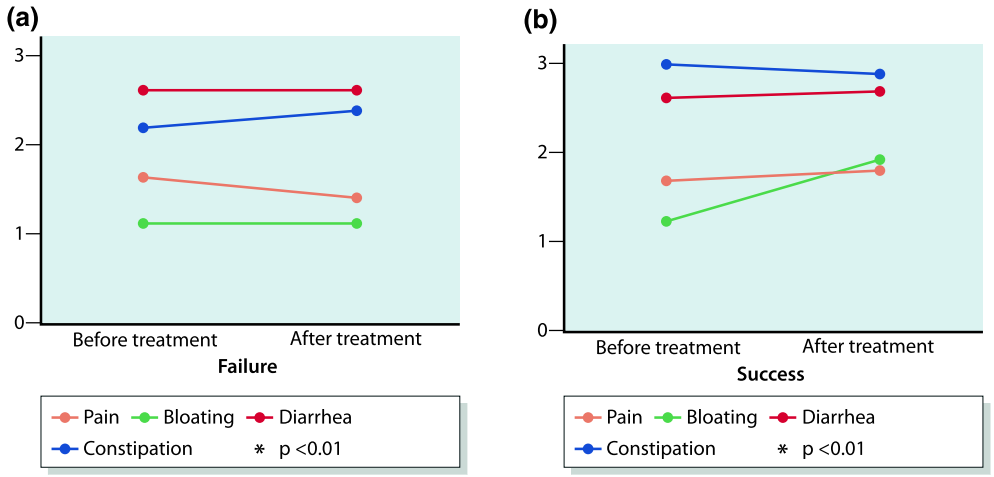

FIGURE 5 Evolution of gastrointestinal quality of life index subscores (pain, bloating, diarrhea and constipation) according to treatment efficacy. Each symptom subscore ranges from 0 to 4. 0 stands for a permanent symptom, 4 for an absence of symptoms. (a) Evolution of gastrointestinal quality of life index subscores in case of failure of treatment. (b) Evolution of gastrointestinal quality of life index subscores in case of success of treatment

DISCUSSION

We conducted a study to investigate the efficacy of different antibiotics for the treatment of SIBO. Remission was observed in 53.4% of our population after one course of antibiotics. The major strength of our study is the large number of patients included. Studies comparing antibiotic protocols in SIBO treatment are scarce with small sample sizes.[14] We observed remission more frequently in patients receiving rotating antibiotics than in patients receiving a single antibiotic (70.0% vs. 50.8%) even if the study was not designed to answer this question. Despite the limited power of the statistical analysis due to the small number of patients in the rotating antibiotics group, a difference was found, suggesting a real benefit of rotating antibiotics compared to a single antibiotic. The remission rate observed in our study after treatment with a single antibiotic was consistent with previous results. In a meta-analysis, remission assessed by GBT was observed in 51% of patients treated with metronidazole.[9] The remission rate after treatment with quinolone is more difficult to evaluate. Only studies with a small number of patients are reported in the literature.[15] The observed difference may result from a broader antibacterial spectrum of the association of azole and quinolone antibiotics compared to a single antibiotic course. Norfloxacin and ciprofloxacin are known to be effective against Gram-negative and, to a lesser extent, Gram-positive infections,[16] whereas metronidazole is known to be effective against anaerobic or microaerophilic microorganisms.[17] Comparatively, qualitative culture performed on aspirates sampled from the third part of the duodenum during upper endoscopy in 62 patients with SIBO showed *Escherichia coli*, *Enterococcus* spp and *Klebsiella pneumoniae* to be the most common isolates in patients with SIBO.[18] Unfortunately, anaerobic microorganisms were not taken into account in this study, as these samples were performed under aerobic conditions.

In our study, the remission rate after treatment with rotating antibiotics was similar to that with rifaximin in the literature. In a systematic review with meta-analysis, SIBO was eradicated in 71% of patients after rifaximin treatment according to LBT or GBT results.[10] In a randomized study, GBT normalization was observed more frequently after rifaximin treatment than after metronidazole treatment (63.4% vs. 43.7%).[19] To our knowledge, no comparison is available in the literature between treatments, either with rotating antibiotics or with rifaximin. Such a comparison was not feasible in our study as rifaximin has only been available in France since 2016 and has only recently received approval for SIBO treatment. Indeed, in France, rifaximin is only available in one indication (i.e., hepatic encephalopathy) and only in hospital centers for those patients. In addition to being easily available in daily practice, a course of treatment with rotating antibiotics costs considerably less than with rifaximin. In France, the average cost of a 3-months course of treatment with metronidazole is 28.05 euros compared to 379.50 euros with rifaximin. On the contrary, rifaximin presents the advantage of a nearly absent systemic absorption (<0.4%) and thus a favorable side-effects ratio.[5] Regarding relapse in our population, too few patients relapsed to draw any firm conclusions. Furthermore, some physicians tended to treat a second time without confirming the relapse by a new GBT.

The gold standard method for SIBO diagnosis is jejunal aspiration culture. However, GBT is a recommended method for SIBO diagnosis and treatment evaluation.[1] GBT is not only a non-invasive method for SIBO diagnosis but also a much more widespread method. Thus, our results are more closely aligned with clinical practice in SIBO therapeutic management. GBT was preferred to LBT as suggested by guidelines.[7,20] GBT cut-off values are still a matter of debate. We used a delta of ≥10 ppm in our analysis in accordance with the Rome consensus[20] whereas the North American consensus recommends a delta of >20 ppm. A recent systematic review with a meta-analysis suggested that a GBT cut-off value with a delta of less than 20 ppm might be more relevant.[1] Besides, we chose to consider methane

excretion even though it has been shown to be present in healthy volunteers.[21] As recommended by the North American consensus, we measured hydrogen and methane simultaneously during breath testing in order to maximize test accuracy.[7,22] However, the clinical evaluation of gastrointestinal transit was not available for all patients with excessive methane excretion on breath test. Finally, the exclusion of the third and controversial criterion (20 ppm of H_2 and/or CH_4 at baseline) did not impact the significance of our results.

Symptomatic improvement assessed by GIQLI score was associated in our study with remission. However, the measured difference in the GIQLI score cannot be considered as clinically significant. Many patients in the studied population had chronic disease which may strongly influence their quality of life unlike symptomatic questionnaires. Besides, IBS-SSS was not improved in our study after SIBO remission, but IBS-SSS is not a validated questionnaire for SIBO and was available in only one quarter of the study population. Remission has already been associated with improvement in symptoms[10,23] and even with a disappearance of IBS criteria in some patients.[24] Clinical benefit was associated, in our study, with improved symptoms of bloating but not diarrhea, constipation and pain. These results lack power as symptomatic standardized questionnaires were only proposed in December 2013, and consequently were only available in 25% of our population. Moreover, IBS subtypes were not considered. Although GBT is not the gold standard for the diagnosis of methanogenic flora,[25] the relief of bloating symptoms may result from a greater decrease in methane-producing gut flora in patients treated with rotating antibiotics. Indeed, delayed small bowel transit and colonic transit have been described in methane-producing SIBO.[26]

Female gender was overrepresented in our patients as described previously in SIBO[14] but was not associated with clinical evolution. IBS was diagnosed in one tenth of our patients while IBS criteria were assessed in only one quarter of them. SIBO is thought to play an important role in the pathogenesis of symptoms in patients with IBS. The prevalence of patients fulfilling Rome criteria for IBS among patients with SIBO is estimated to be 26%.[27] Some authors have suggested that the increase of *Prevotella* may explain the association between diarrhea-predominant IBS and SIBO.[28] Thus, the eradication of SIBO reduces GI symptoms in IBS patients with an associated diagnosis of SIBO.[24] Similarly, FD was overrepresented in our patients (1 patient out of 5) in accordance with a prospective study on the same topic.[29] Systemic sclerosis was more frequent in the rotating antibiotics group than in the single antibiotic group (43.3% vs. 1.6%). This difference between our two groups (a single antibiotic vs. rotating antibiotics) could lead to a bias. The use of rotating antibiotics in SIBO has already been studied in our center[2] and is recommended by experts in patients with systemic sclerosis[30] explaining physician prescription preferences in this case. A recent meta-analysis found only limited data regarding the eradication rate of SIBO in patients with systemic sclerosis.[31] Moreover, systemic sclerosis was not associated with remission in our study. Similarly, cholecystectomy was more frequent in the rotating antibiotics group without being associated with remission. Thus, the observed clinical differences between the rotating antibiotics group and the single antibiotic group are unlikely to explain the observed response between the two groups. Besides, H_2 peak at baseline was lower in the rotating group. However, SIBO diagnosis criteria were applied in both groups, and peak levels of H_2 and CH_4 measured during baseline GBT were not associated with remission.

Despite our large sample, our study has some limitations: it is a retrospective, single-blind, non-placebo-controlled study. A large number of patients (466) with a positive GBT were excluded from analysis because no follow-up GBT was available. Moreover, our study was conducted over a very long period of time (15 years), using different definitions of IBS, which is expected to bring heterogeneity to the data. Indeed, IBS patients defined by Rome IV criteria are known to be more severe than IBS patients defined by Rome III criteria.[32] However, we used the association of Rome III criteria with the presence of abdominal pain to be more accurate, therefore our population was more representative of an IBS population defined by Rome IV criteria. These limitations are inherent to the retrospective design of our study and must be considered when interpreting our results. However, the SIBO remission rate observed in our study is consistent with the literature as discussed before.[9,10] Moreover, it may be argued that the absence of a second GBT is an indication of symptom relief. Thus, our remission rate may well have been underestimated.

Unfortunately, data on prokinetics, probiotics and morphine use were not available for analysis in our study despite the fact that dysmotility is an underlying cause of SIBO. A single-center, cross-sectional study advocates for a preventive role of prokinetics in SIBO development on PPI.[33] Besides, in a small open-label randomized study, an alternating regimen of norfloxacin and neomycin was as effective as cisapride therapy in terms of SIBO remission in a population of patients with liver cirrhosis.[33,34] Lastly, due to the retrospective nature of the analysis, we were not able to assess the presence of adverse effects.

In this study, a course of rotating antibiotics, alternating azole and quinolone, was more effective than a single antibiotic to induce SIBO remission. Remission was associated with an improvement in quality of life and bloating.

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CONFLICT OF INTEREST

Nicolas Richard, Charlotte Desprez and Fabien Wuestenberghs declare that they have no conflict of interest. Anne-Marie Leroi is consultant at Medtronic. Guillaume Gourcerol is consultant at Allergan, Sanofi Genzyme, Kyowa Kirin and Biocodex and has received speaker fees from Kyowa Kirin, Laborie, Mayoly Spindler, Biocodex and Coloplast. Chloé Melchior is consultant or advisory board member at Kyowa Kirin, Norgine, Biocodex, Mayoly spindler, Tillots, Ipsen.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Nicolas Richard https://orcid.org/0000-0003-1294-5039
Fabien Wuestenberghs https://orcid.org/0000-0001-6100-6017
Chloé Melchior https://orcid.org/0000-0002-8146-1540

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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