Is abnormal 25 g fructose breath test a predictor of symptomatic response to a low fructose diet in irritable bowel syndrome?

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IS ABNORMAL 25 G FRUCTOSE BREATH TEST A PREDICTOR OF SYMPTOMATIC RESPONSE TO A LOW FRUCTOSE DIET IN IRRITABLE BOWEL SYNDROME?

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Key words: Fructose breath test; irritable bowel syndrome; predictive factor; low fructose diet; Irritable Bowel Syndrome-Symptom Severity Score

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ABSTRACT

BACKGROUND: Fructose malabsorption may trigger gastrointestinal symptoms in irritable bowel syndrome patients and a low fructose diet seems to improve digestive symptoms.

AIM: The aim of our study was to determine whether fructose malabsorption detected by a 25g fructose breath test could be a predictor of the efficacy of a low fructose diet.

METHODS: 88 patients (73 women, median age, 45.5 years, range 18-69) with irritable bowel syndrome according to Rome III criteria were included in this prospective, controlled study. All 88 patients had a 25 g fructose breath test; 37 had a positive test result defining fructose malabsorption. All 88 patients followed a low fructose diet for 2 weeks, blinded to their test results. Patients filled self validated-questionnaires before and at the end of the dietary period. The main outcome measurement was the Irritable Bowel Syndrome-Symptom Severity Score.

RESULTS: Irritable Bowel Syndrome-Symptom Severity Score significantly decreased in fructose absorbers and fructose malabsorbers after a low fructose diet (-68.0 [-137 ; 0] vs -73.5 [-173 ; -11.5]) with no difference according to fructose breath test result (adjusted p=0.984).

CONCLUSION: A positive 25 g fructose breath test is not a predictor of the efficacy of a low fructose diet in irritable bowel syndrome.

Registered clinical trial : www.clinicaltrials.gov (NCT02188680)

INTRODUCTION

Irritable bowel syndrome (IBS) is the main functional disorder worldwide and is characterized by chronic abdominal pain associated with transit disorders. The underlying pathogenesis of IBS is considered complex and several functional alterations have been described. These include altered visceral sensitivity, bowel dysmotility and secretory dysfunctions, immune intestinal activation, gut dysbiosis, brain gut alterations, somatic and psychiatric co-morbidities. A link between food intake and the occurrence or the exacerbation of IBS symptoms has been reported (1). Recently, Gibson *et al* underlined the deleterious symptomatic role of poorly absorbable and rapidly fermentable carbohydrates (FODMAPs) (2). Among FODMAPs, fructose commonly present in fruit (mainly pears and apples), vegetables, honey and sweeteners, is of particular interest. Indeed, dietary intake of fructose has increased dramatically during the last decades (4). Fructose is absorbed from the intestinal lumen by facilitated diffusion through the glucose transporter 5 (GLUT5) in the mucosa, whereas glucose facilitates this transport (3). Consequently, excessive dietary intake of fructose, in excess of glucose, can easily exceed the absorptive capacity of the small bowel, leading to incomplete absorption of fructose and, finally, causing fructose malabsorption (FM) (2). The unabsorbed fructose may play a role in osmotic load and is therefore rapidly propelled into the colon, where its contact with anaerobic microbiomes causes fermentation and the production of a gaseous feeling, abdominal bloating, and even diarrhea (4, 5). A low fructose diet is therefore recommended. Open label studies have demonstrated the effectiveness of reducing fructose in patients with IBS, achieving adequate symptom relief in 70-80% of patients (6-8). At present, it is unclear which IBS patients will benefit from a low fructose diet. The current test for FM diagnosis is the fructose breath test (FBT) (2) performed with a 25 g load of fructose as recommended by the North American consensus on breath test

(9). However, the ability of this 25 g FBT to predict the efficacy of a low fructose diet in IBS patients is still debated (6, 10).

Our objective was to study the predictive value of a 25 g FBT on the outcome of a low fructose diet in a cohort of patients with IBS using controlled, simple-blind, parallel groups.

MATERIALS & METHODS

Patients

All consecutive IBS patients referred to the Physiology Unit of Rouen University Hospital (France) for FBT from January 2014 to January 2018 were invited to participate in the trial. Inclusion criteria were: IBS according to Rome III criteria (11), age $\geq$18 years, normal clinical examination, standard biological tests (including C Reactive Protein) and colonoscopy (with colonic biopsies) performed in the last 6 months. Exclusion criteria were: small intestinal bacterial overgrowth (SIBO) as determined by breath testing, a history of abdominal surgery (except for appendectomy), systemic scleroderma, diabetes, metabolic syndrome, anorexia and pregnancy. Other exclusion criteria were changes to IBS medication during the trial.

The study was approved by the Haute-Normandie Ethics Committee (2013-AOO116-39) on the 23rd May 2013 and was registered at www.clinicaltrials.gov (NCT02188680). Patients gave written informed consent before participation. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki and has received IRB approval.

Study design

All 88 patients included in the study had a 25 g FBT and were distributed in two balanced groups of patients: a group with positive FBT results and a group with negative FBT results. Then, all patients had a consultation with a dietician who instructed them to follow a low

fructose diet carefully during a period of 2 weeks. Improvements in digestive symptoms were recorded at the end of the diet and compliance was evaluated at 1-week and 2-week dietary periods in the two groups. Patients had to fill their dietary notebook daily while on the diet for assessment of dietary compliance (patients only filled the type of food but not the quantity).

Breath tests

Each patient had two breath tests. First, a glucose breath test was carried out in order to rule out SIBO (2). Second, if negative, a FBT was then performed with a 25 g fructose load following a methodology previously described (12). Both dieticians and participants were blinded to FBT results during the entire study duration. In contrast, the investigators were not blinded to FBT results in order to balance the number of patients in the two groups (i.e; patients with positive or negative FBT results).

Dietary advice

All included patients were referred to our experienced dieticians (M.M. and E.G.) for a standardized dietary adaptation. The initial consultation comprised an interview during which a qualitative patient-defined typical day dietary intake was recorded. Then, individual instructions for the low fructose diet were given both verbally and through written information (supplementary files, annex 1). Patients were advised to eat a maximum dose of 100 g of fruit and 200 g of vegetables per day (containing <2% of fructose), corresponding to a fructose intake of less than 6 g/day. Patients were able to contact the dieticians during the dietary period for further information. Patients with IBS already on a diet were eligible to participate in the study as long as they agreed to abandon their diet for the study duration.

Dietary compliance was assessed by live telephone interview by the investigators, one week after initiation of the dietary change and during the last assessment visit by retrieving the

patient's dietary notebook of the 2-week diet. Dietary compliance was roughly assessed by the physician and not by the dietician. Dietary compliance categories were adapted from a previous work (8) : never/rarely (<25% of the time), sometimes (25%-50% of the time), frequently (51%-75% of the time) or always (76%-100% of the time). Compliance was considered adequate if patients confirmed they had adhered to the dietary guidelines for at least 50% of the meals consumed.

Assessments and end points

The primary endpoint was a decrease in the clinical severity of IBS symptoms, self-evaluated using the irritable bowel severity scoring system (IBS-SSS) (13) before and at the end of the 2-week dietary period.

Secondary endpoints were assessed before and at the end of the dietary intervention. They included: quality of life, severity of anxiety and/or depression, stool consistency, weight and body mass index (BMI). The quality of life was assessed using the Gastrointestinal Quality of Life Index (GIQLI) (14). Anxiety and depression levels were assessed using the hospital anxiety and depression scale (HAD) (15). In addition, patients gave a description of stool quality on a scale from 1 to 7 (Bristol stool scale) (16). Patients' opinions of the low fructose diet were also recorded using two questions: "Do you think that the diet has improved your digestive symptoms?" and "Do you think you will stay on the diet at the end of the study?". Adverse events of any kind were monitored throughout the study period.

Statistical analysis

The sample size calculation was based on the primary end-point (i.e. the mean change of IBS-SSS between the beginning and the end of the low fructose diet period). The mean IBS-SSS in a cohort of 241 IBS patients was estimated at 298$\pm$85 (personal unpublished data). Based on

143 this standard deviation, 40 subjects had to be included in each group (patients with or without
144 FM) to highlight a difference of 60 in the variation of IBS-SSS between the two groups with a
145 two-sided 0.05 type I error and to obtain at least 80% power.
146 The effect of diet was assessed before and after diet using paired sample t-test. Per protocol
147 analysis was performed for the primary outcome using data from all patients completing the
148 study who did not violate the protocol. Patients who did not complete the study were replaced
149 by other patients, limited to 10% of the overall population (8 patients).
150 Otherwise, demographic and clinical characteristics, GIQLI, Bristol stool scale, anxiety and
151 depression HAD at baseline were compared between IBS patients with or without FM using a
152 Mann–Whitney test. The same test was also used for comparison of score variations (IBS-
153 SSS, GIQLI, Bristol stool scale and HAD) between groups and between the beginning and the
154 end of the diet. These comparisons were adjusted for sex and age (<40 and ≥ 40) variables
155 using a logistic regression.
156 Results are presented as median with first and third quartile (Q1-Q3). A P value below 0.05
157 was considered significant. These analyses were carried out using SAS 9.3 software (SAS
158 Institute Inc., Cary, NC, USA).
159

RESULTS

A total of 88 patients (73 women, median age 45.5 [18-69] years) were included in the study. Eleven patients (12.5%) were withdrawn from the trial and seventy-seven patients (87.5%) completed their dietary course (Figure 1). The different size of the groups was due to the limited number of possible replacements (8 patients).

The demographics and the baseline characteristics of the two groups are shown in Table 1. The sex ratio was significantly different between groups (P=0.02). Patients in the group with positive FBT were significantly older than those with negative FBT (P=0.02). As age and sex ratio were different between the two groups, further analyses were performed to adjust comparisons for age and sex. There was no other significant difference in any demographic or baseline characteristic between the two groups of patients (Table 1).

Sixty-eight patients (77%) attributed their IBS symptoms to food, with high-carbohydrate foods, dairy, beans, foods rich in fats and spices, and lentils most commonly cited. Twenty-three patients among the 88 included (26%) were on special therapeutic diets at the start of the study: a low lactose diet (10 patients); a low fructose diet (4 patients); a hypo-caloric diet (5 patients); and a gluten free diet (4 patients). There was no difference concerning the frequency of food-related disorders and alimentary restrictions between the group with positive FBT and the group with negative FBT (P=0.96 and P=0.48, respectively).

Effects of a low fructose diet

There was a significant improvement in symptoms between baseline and follow-up after dietary intervention. There was a significant decrease in IBS-SSS and HAD scores and a significant increase in GIQLI after a low fructose diet, whereas no change was observed for stool consistency (Table 2). This improvement in symptoms was concomitant with patients' feelings regarding the diet. Fifty-five of 88 patients (62.5%) reported an improvement in

symptoms following their diet. Nevertheless, among them, only 34 patients (62%) were prepared to continue the low fructose diet after the end of the study, because they considered the diet to be too restrictive. In addition, the diet was associated with significant weight loss (Table 2).

Associations between breath test results and outcome of dietary programme

Figure 2 shows the effects of a low fructose diet on IBS-SSS in the two groups. The median changes at week 2 versus baseline were -73.5 [-173; -11.5] in the group with positive FBT versus -68 0 [-137; 0] in the group with negative FBT (P=0.98).

No effects of the low fructose diet were detected on quality of life, Bristol Stool Scale, or HAD scores between the two groups (Table 3). 64.9% of patients in the group with positive FBT and 72.1% of patients in the group with negative FBT reported an improvement following the diet (P=0.32).

DISCUSSION

In this controlled simple-blind prospective study of patients with IBS, a low fructose diet reduced symptom scores independently of FBT results. Of note, even in the group with negative FBT, most patients had a significant reduction in their symptom scores.

As far as the authors know, only one study has reported the predictive value of the FBT for a symptomatic response to a low fructose diet in IBS patients (6). Bert et al. previously demonstrated that FBT did not discriminate well between IBS patients with or without an effect of the low fructose diet (6), but they used a relatively high dose of 50 g of fructose to reduce the risk of false-negative (6). However, the ability of the human intestines to absorb fructose is limited (17). Specific intestinal fructose transporters in the intestines of humans may be easily overwhelmed by fructose >50 g (4) leading to a variety of gastrointestinal symptoms. When healthy subjects were administered 50 g fructose and had breath tests, 80% had FM (5). The higher the dose and the concentration of fructose, the greater the chance of including a false-positive and biasing the capacity of the FBT to identify the best candidates for a low fructose diet. The optimal dose for FM diagnosis is unclear (17). However, we chose a dose of 25 g because it is closer to the daily intake and has been demonstrated to be effective in FM diagnosis (4). This dose has also been recently recommended by an expert consensus [9]. We expected that lower doses of fructose would allow us to identify subjects with severely restricted fructose absorptive capacity who would benefit more from a low fructose diet. As suggested by others (6), we cannot exclude the fact that a low dose of fructose increased the risk of false-negative results in the group with negative FBT explaining the improvement in symptoms in this group.

The lack of predictive value of the 25 g FBT to identify the best candidates for a low fructose diet is hard to explain. It is possible that it is a useful test but improperly used. Indeed, the

heterogeneity of methodologies used, particularly concerning the cut-off value for breath gas concentration and the ingested dose of fructose, is obvious. A previous study (6) and our present study demonstrated that 50 g and 25 g doses of fructose were not the optimum choice to discriminate IBS patients who would benefit from a low fructose diet and those who would not. However, de Roest et al. demonstrated that a positive FBT performed with a 35 g load of fructose was strongly associated with the efficacy of a low FODMAP diet that also included a low fructose diet (10). We can hypothesize that the choice of the dose should not be determined intuitively, but from a load that best discriminates responders and non-responders to diet (2). There is a need for further large studies assessing different doses of ingested fructose and cut-off values for breath gas during FBT to determine their value to discriminate the best candidates for a low fructose diet.

Another explanation for the low predictive value of the 25 g FBT could be that FM is not the right target. The prevalence of FM in healthy populations appears to be similar to that in populations with IBS (2). The main difference between symptomatic and asymptomatic populations is the frequency of symptoms induced after fructose absorption (i.e fructose intolerance) suggesting that the sensitivity of the bowel to the change in luminal conditions induced by FM is the key difference rather than the malabsorption itself (2). However, previous studies have shown responses to a low-FODMAP diet to be similar in patients with fructose intolerance with or without malabsorption (18, 19). The beneficial effect of a low fructose diet could also be due to the dietary restriction of fermentable carbohydrates. Polymerized forms of fructose (inulins, fructans and fructo-oligosaccharides) are considered as natural prebiotic fibers with a potential beneficial effect on gut microbia that confers health benefits to the host (20). However, the beneficial effect of prebiotics in IBS remains controversial, probably related to the type and dose of prebiotics used (20). Prebiotic supplementation studies have shown some promise at low doses for modulation of the gut

bacteria and reduction of symptoms in IBS; however, larger doses may have a neutral or a negative impact on symptoms (20). In case of a beneficial effect of fructose as prebiotics, the reduced intake of fructose polymers should have a negative impact on bowel symptoms. That was not the case in our study because the low fructose diet led to a decrease in abdominal symptoms, as for the low FODMAP diet in other studies (10, 21).

Finally, it is not possible to exclude a placebo effect for the low fructose diet recordings in some patients, which could explain the poor predictive value of FBT. The improvement in anxiety and depression scale scores during the short period of low fructose diet could be an additional argument for the placebo effect.

One of the strengths of our study is its controlled single-blind design which meant that patients and dieticians could not be influenced by the results of their FBT. In addition, in this study, we chose global relief assessment as the broadest main outcome measure, as changes in specific symptoms incompletely assess the impact of treatment in IBS or changes in quality of life (19). Lastly, the single center characteristic of this study ensured the consistency of all dietary advice for all included patients.

Nevertheless, our study has several limitations. First, our two groups of patients were not identical. Patients in the group with positive FBT were older and more frequently male than patients in the group with negative FBT. In a previous paper, we already found that male gender was more frequent in patients with malabsorption (12). To our knowledge, these findings have never been reported in the literature and we do not have any clear explanation for this. However, we have taken these differences into consideration in our statistical analysis. Considering the sample size and the low number of men in the study (n=15) our results should only be applied in women with IBS. Second, we performed a diet of short

duration to limit the risk of non-compliance and withdrawals whereas a 6-week dietary period is recommended (22). Third, we did not calculate the precise amount of fructose in patients' diets before and during the study. Based on the first interview with the dietician, we were able to determine if patients were on a specific diet. Four patients who were on a low fructose diet before the study linked the ingestion of some fruit and vegetables to their abdominal symptoms. However, it has been demonstrated that people who identify themselves as severely food-intolerant (to lactose for example) may mistakenly attribute a variety of abdominal symptoms to food intolerance (23). Indeed, none of the 4 patients who attributed their abdominal symptoms to fructose and who were on a low fructose diet before the study, had a positive fructose breath test. As our main objective was to determine the usefulness of the fructose breath test and not the efficacy of the low fructose diet, we chose to include these patients. During the study, we asked patients to follow a restrictive diet with less than 6 g/day of fructose guided by dietary recommendations. However, we did not prepare the meals and patients only recorded information on the type of food and not on the exact quantity of fructose or its weight. Dietary compliance was self-reported during telephone calls and the last assessment visit.

Conclusion

We have demonstrated that a 2-week low fructose diet significantly improved the bowel symptoms and the quality of life of IBS patients whatever their fructose absorption status defined by a FBT with a 25 g load of fructose. The 25 g FBT as performed in this study cannot be used to predict the beneficial effect of a low fructose diet. Further studies are needed to identify the best predictive test for dietary changes in IBS patients with the goal of achieving better control of symptoms.

Acknowledgements

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Statement of authorship

CM and AML designed the research study

CM, CD, GG, MM, PD and AML performed the research,

CM, CD, LB, LAD, GG and AML collected the data,

EH, CM, GG, AML and PD analysed the data,

CM, GG, AML, and PD wrote the paper,

All authors approved the final version of the article**.**

Conflict of interest statement

No competing interest to declare.

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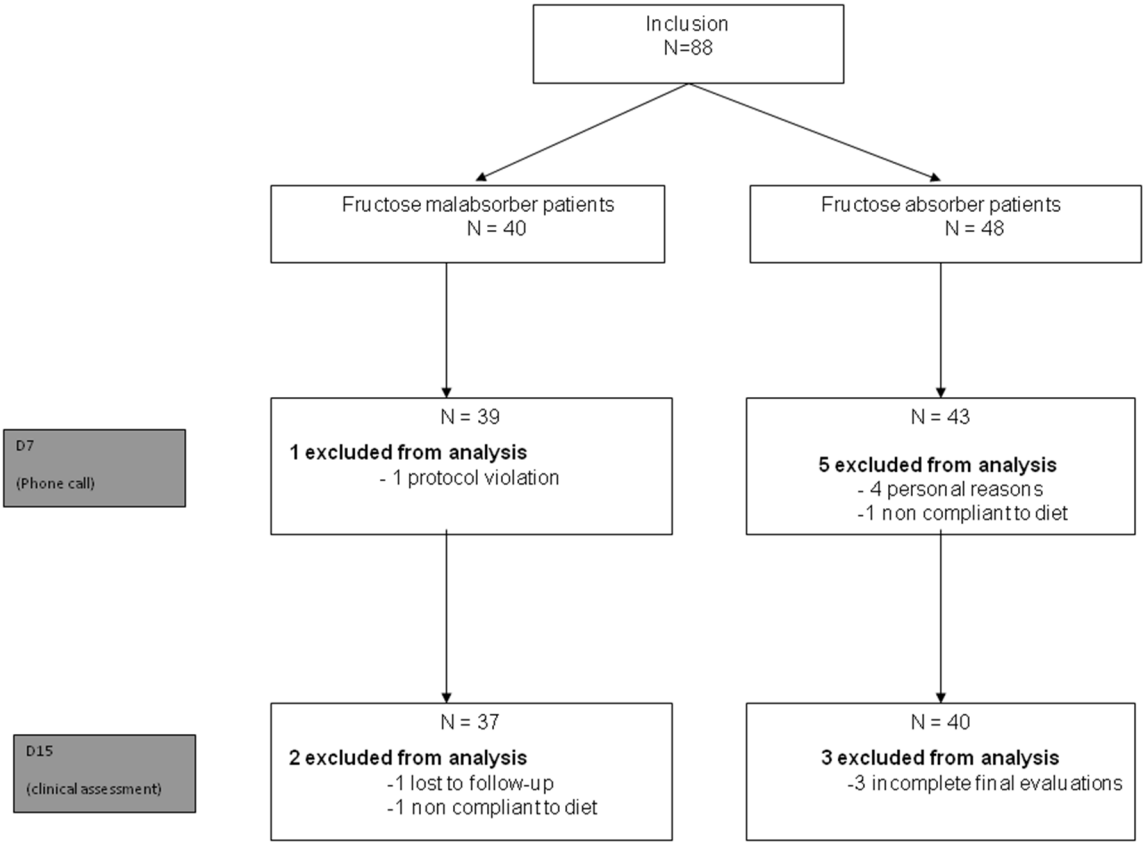
389 **Figure legends:**

390 Figure 1: Flow diagram



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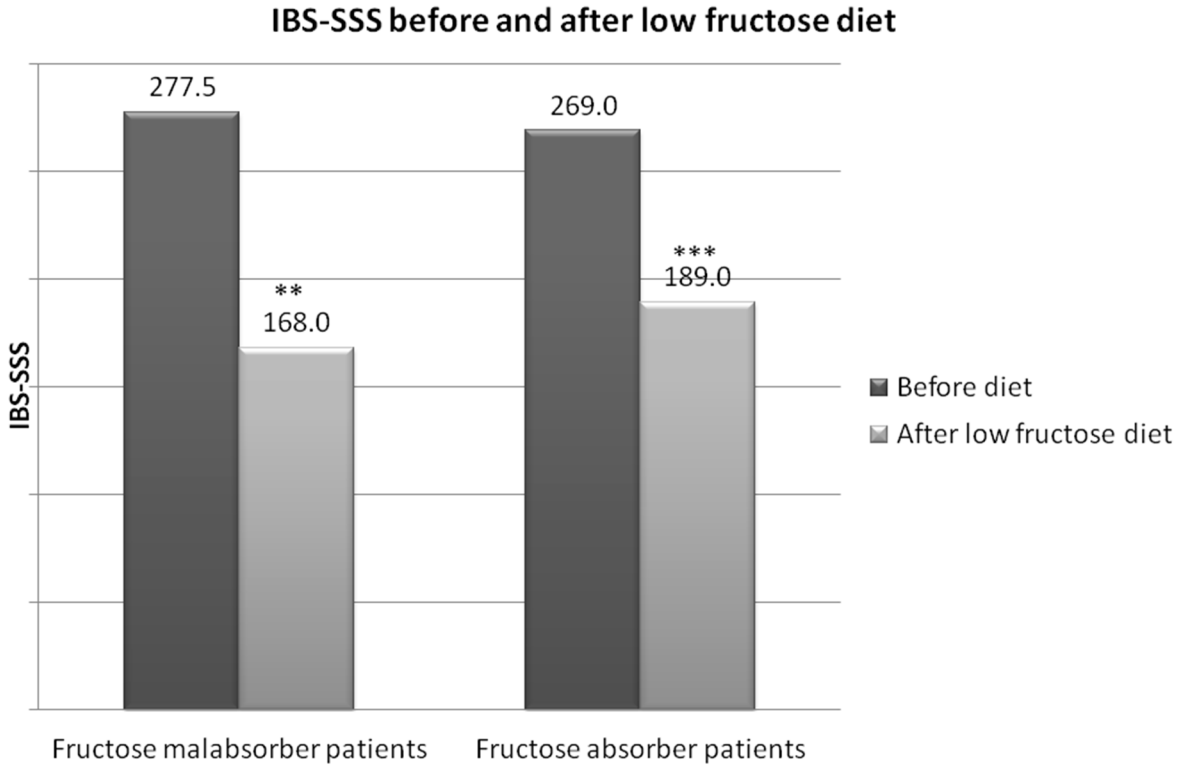
392 Figure 2: Comparison of post-diet change from baseline for IBS symptom severity score
393 between absorber and malabsorber groups.



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396 **Tables:**

397 Table 1: Comparison of demographics and baseline characteristics between patients in the
398 absorber (negative fructose breath test) and malabsorber groups (positive fructose breath test.

	Absorber group (n = 48)	**Malabsorber group (n = 40)**	**P**
Female n(%)	44 (91.7)	29 (72.5)	0.02
Age (years)	41.2 [29; 51.2]	49.6 [39.9; 58.8]	0.02

	Absorber group (n = 48)	**Malabsorber group (n = 40)**	**P**
Weight (kg)	62.5 [55.5; 71]	64.5 [55; 82.5]	0.40
BMI (Kg/m²)	22.7 [21.1; 26]	23.3 [21.2; 28.1]	0.35
Types of IBS			0.084
IBS-D	24 (50)	26 (65)	
IBS-C	16 (33.3)	5 (12.5)	
IBS-M	8 (16.7)	8 (20)	
Unclassified	0	1 (2.5)	
IBS-SSS	277.5 [166.5;309.5]	269 [215; 303.5]	0.63
Bristol Stool Scale	4 [2; 6]	4 [3; 6]	0.96
GIQLI	88 [70; 97]	87 [66; 101.5]	0.62
HAD-A	11 [8; 14]	9 [6; 12.5]	0.07
HAD-D	5.5 [3; 8.5]	5 [2.5; 8]	0.51

399 BMI: Body mass index. IBS-SSS: IBS symptom severity score. GIQLI: Gastrointestinal
400 Quality of Life Index. HAD-A and B: Hospital anxiety and depression scale (HAD).

401 Results were presented as number (percentage) and median with first and third quartile [Q1-
402 Q3].
403

404 Table 2: Effect of low fructose diet on IBS severity score, Bristol Stool Scale, quality of life,
405 Hospital anxiety and depression scores, weight and body mass index for all included IBS
406 patients.

	Before diet	**End of 2-week diet**	**P**
Weight (kg)(n=80)	66.4 ± 14.4	65.3 ± 14.2	$<1.10^{-4}$
BMI (Kg/m^2)(n=80)	23.9 ± 4.3	23.6 ± 4.3	$<1.10^{-4}$
IBS-SSS (n=77)	254.5 ± 99.1	184.0 ± 98.2	$<1.10^{-4}$
Bristol Stool Scale (n=77)	4.0 ± 1.9	3.7 ± 1.6	0.17
GIQLI (n=74)	82.5 ± 20.3	96.1 ± 19.6	$<1.10^{-4}$
HAD-A (n=77)	10.5 ± 4.3	9.5 ± 4.2	0.01
HAD- D (n=76)	5.9 ± 3.9	5.0 ± 3.9	0.01

407 BMI: Body mass index. IBS-SSS: IBS symptom severity score. GIQLI: Gastrointestinal
408 Quality of Life Index. HAD-A and B: Hospital anxiety and depression scale (HAD).
409 Results are presented as mean ± standard deviation.
410

411 Table 3: Comparison of the variations of Bristol Stool Scale, quality of life, hospital anxiety
412 and depression scores, evaluated after 2-week low fructose diet between patients with and
413 without fructose malabsorption.

	Absorber group	**Malabsorber group**	**Adjusted P**
Bristol Stool Scale	n=40 0 [-1.5; 1]	n=37 0 [-2; 1]	0.86
GIQLI	n=38 16.5 [7; 26]	n=36 8 [-2; 17]	0.10
HAD-A	n=40 -1.5 [-3.5; 0.5]	n=37 0 [-1; 2]	0.05
HAD-D	n=39 -1 [-3; 1]	n=37 0 [-2; 1]	0.14

414 GIQLI: Gastrointestinal Quality of Life Index. HAD-A and B: Hospital anxiety and
415 depression scale (HAD)
416 Results are presented as number (percentage) and median with first and third quartile [Q1-
417 Q3].
418
419 **Annex:**
420 Annex 1: Low fructose diet

FOOD	**NOT RECOMMENDED**	**RECOMMENDED**
MILK AND DAIRY PRODUCTS	Sweetened milk Dairy based sweetened desserts Dairy based fruit desserts, flavoured Milk based drinks Custard desserts	Milk (powder or liquid) Yoghourt Cottage cheese } natural or without added sugar Petits suisses/fromage blanc

	Egg custard, mousse	Unsweetened desserts Cheese
MEAT **FISH** **EGGS**	Cold meats (Ham, sausage, saucisson, pâtés, white and black pudding,), quenelles, fish mousse, ready made meals	All meat, poultry Offal Fish Eggs
CARBOHYDRATES	Ready made meals, Manufactured cooked potato products Manufactured deep frozen fries Sweetened flour based products Dried vegetables and pulses Whole grains (oat, wheat, rye, barley, millet etc.) Whole-grain pasta, vegetable pasta Whole-grain rice	Potatoes, chips Rice, tapioca, pasta, semolina Wheat, buckwheat, oat, corn rice flour
BREAD	Sweetened bread, other bread crackers, toast Sweetened cereals	White bread (80 g/day), Rice crackers
GREEN VEGETABLES	Raw vegetables Dried vegetables Manufactured cooked vegetables Bean sprouts	Except cooked vegetables (200g/day): Spinach, lettuce, green beans, butter beans, carrots, celery, courgettes, tomatoes, water cress, cauliflower, avocado
FRUIT	All fresh fruit, cooked or not Fruit in syrup Stewed fruit, with or without sugar Dried fruit Candied fruit	Except (1 per day): Apricot, grapefruit, lemon, nectarine, orange, mandarin, peach, pineapple, rhubarb
FATTY PRODUCTS	Manufactured sauces Manufactured mayonnaise	Butter Oil Fresh cream Homemade mayonnaise
SWEET PRODUCTS	Sugar Honey, marmalade, jam, jelly Pastries Puff pastry, shortcrust pastry Bread pastries (brioche, croissant, pain au chocolat, pain aux raisins, etc.) Sweets biscuits, meringues, gingerbread	Unsweetened cocoa

	Whipped cream Ice cream and sorbets Confectionery, dragees, nougat, fruit jellies Chestnut mousse Chocolate and chocolate bars Sweetened chocolate powder	
DRINKS	Fermented drinks (cider, beer) Wine, aperitifs, liqueurs Fruit juices Fruit syrup Soda, lemonade Flavoured water Dairy based sweetened drinks	Still and sparkling water Flavoured water (with artificial sweeteners) Coffee, herbal infusions, tea
CONDIMENTS	Manufactured sauces Manufactured mayonnaise Tomato ketchup Mustard Manufactured tomato sauce Flavoured vinegar Garlic, onion, shallots Pickles and capers Stock cubes	Salt, pepper Gelatine Non-flavoured vinegar
MISCELLANEOUS	Some artificial sweeteners: -Sucralose	Some sugars: glucose, lactose, maltose and dextrine maltose Some artificial sweeteners: aspartame, saccharine, cyclamate, thaumatine polyols (mannitol, sorbitol)

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