**Name of journal: World Journal of Gastroenterology**

**ESPS Manuscript NO: 14939**

**Columns: ORIGINAL ARTICLE**

***Randomized Controlled Trial***

**Self-reported dietary fructose intolerance in irritable bowel syndrome–proposal of new criteria for diagnosis**

BergLK *et al*. Fructose intolerance in IBS

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**Author contributions:** Berg LK, Florholmen J, Fagerli E and Goll R contributed equally to this work; Berg LK and Florholmen J conceived and designed the project; Berg LK, Fagerli E, Myhre AO, Florholmen J and Goll R performed the data collection; Berg LK, Fagerli E, Florholmen J and Goll R analyzed data; Berg LK, Florholmen J and Goll R wrote the paper.

**Supported** **by** Northern Norway Regional Health Authority (Helse Nord RHF); Gastro Fund, University Hospital North Norway; and Helgeland Hospitals Research Committee.

**Ethics approval:** The study was reviewed and approved by Helse Nord RHF Institutional Review Board and approved by the Regional Ethical Committee of Northern Norway.

**Clinical trial registration:** The study was registered at www.clinicaltrials.gov (NCT00555191).

**Informed consent:** All study participants provided written consent prior to study enrollment.

**Conflict-of-interest:** The authors declare no conflict of interest.

**Data sharing:** The statistical methods of this study were reviewed by Rasmus Goll from University Hospital of Northern Norway and University of Tromsø. Technical appendix, statistical code, and dataset available from corresponding author at leif.kyrre.berg@online.no

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**Received:** October 31, 2014

**Peer-review started:** October 31, 2014

**First decision:** November 26, 2014

**Revised:** December 20, 2014

**Accepted:** January 30, 2015

**Article in press:**

**Published online:**

**Abstract**

**Aim:** To study the criteria for self-reported dietary fructose intolerance (DFI) and to evaluate subjective global assessment (SGA) as outcome measure.

 **Methods:** irritable bowel syndrome (IBS) patients were randomized in an open study design with a 2 wk run-in on habitual IBS diet, followed by 12 wk w/wo additional fructose reduced diet (FRD). Daily registrations of stool frequency and consistency, symptoms on a visual-analogue scale (VAS) were performed during the first 4 wk. SGA was used for weekly registrations during the whole study period. Provocation with high-fructose diet was done at the end of the registration period. Breath tests of fructose (FBT) were performed. A total of 182 subjects performed the study according to protocol (88 FRD, 94 controls).

**Results:** We propose a new clinically feasible diagnostic standard for self-reported fructose intolerance. The instrument is based on VAS registrations of symptom relief on FRD combined with symptom aggravation upon provocation with fructose rich diet. Using these criteria 43 of 77 patients (56%) in the present cohort of IBS patients had self-reported DFI. To improve the concept for clinical evaluation, we translated the SGA scale instrument to Norwegian and validated it in context of the IBS diet regimen. The validation procedures showed a sensitivity, specificity and kappa for SGA detecting the self-reported DFI group by FRD response within the IBS patients of 0.79, 0.75, and 0.53, respectively. Addition of the provocation test yielded values of 0.84, 0.76, and 0.61, respectively. The corresponding validation results for FBT was 0.57, 0.34, and -0.13 respectively.

**Conclusion:** FRD improves symptoms in a subgroup of IBS patients. A diet trial followed by a provocation test evaluated by SGA can identify most responders to FRD.

**Key words:** Breath test;Dietary restriction; Fructose malabsorption; Functional bowel disease; Sugar intolerance

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**Core tip:** In this second report from the FINN study, new diagnostic criteria for self reported fructose intolerance, based on fructose reduced diet, have been developed. Subjective global assessment of abdominal relief seems to be a valid outcome measure, which may be used as a feasible alternative to daily visual-analogue scale registrations both in daily routine handling of these patients and in future studies of irritable bowel syndrome (IBS). More than half of IBS patients in this study seem to benefit from using fructose reduced diet in controlling their IBS symptoms.

Berg LK, Fagerli E, Myhre AO, Florholmen J, Goll R. Self-reported dietary fructose intolerance in irritable bowel syndrome–proposal of new criteria for diagnosis. *World J Gastroenterol* 2015; In press

**Introduction**

The self-reported intolerance to fructose intake has been described as fructose malabsorption (FM) due to small intestinal dysfunction. This was first reported in four patients with chronic diarrhea and colic in 1978[[1](#_ENREF_1)], in healthy subjects in 1983[[2](#_ENREF_2)] and in populations with irritable bowel syndrome (IBS) in 1986[[3](#_ENREF_3)]. Fructose is absorbed from the intestinal lumen by facilitated diffusion through the GLUT5 transporter protein in the mucosa, which is a glucose dependant transport[[4](#_ENREF_4)]. The exact mechanism(s) leading to incomplete fructose absorption is unknown, and in the literature described as ranging from a true condition to a variance of normality[[5](#_ENREF_5)]. Moreover, it is well established that factors such as dietary sorbitol[[6](#_ENREF_6),[7](#_ENREF_7)] and the dietary non-hydrolysable fructans[[8](#_ENREF_8)] aggravate IBS symptoms[[9](#_ENREF_9)]. The amount of sorbitol needed to provoke IBS symptoms appears to be 10 g or more[[10](#_ENREF_10)].

The current diagnostic test for FM, the fructose breath test (FBT), is suboptimal due to the many variations in the normal capacity of fructose absorption[5].

There are numerousfactorsthat givefalse negative and false-positive results, as reviewed by Kyaw and Mayberry[5]. These include factors such as colonization by non-hydrogen producing bacteria and gastrointestinal dysmotility[5]. In a recently published reportwe have described a discrepancy between the FBT and the effects of a fructose-reduced diet (FRD)[11].

Due to the lack of an accurate and valid test for diagnosing FM, there is an increasing interest to use self-reported responses to FRD as a diagnostic tool for FM. Goldstein *et al*[[6](#_ENREF_6)] reported that in patients with IBS or functional abdominal complaints, 56%-60% improved their symptoms when on a low-fructose diet, a finding also reported in some observational studies[12-1[4](#_ENREF_13)]. Therefore, as advocated by Fernandez *et al*[14], the use of FRD is a simple and feasible test that should be utilized more in clinical practice. So far, there is no standardized procedure for performing FRD test. This includes no standardized level for the upper load of fructose to be used per meal, as well as a lack of a clinical tool to assess the effects of FRD in IBS patients.

The aims of the present study are: 1. to define criteria for self-reported dietary fructose intolerance (DFI) in a cohort of patients with Rome II defined IBS; 2. To evaluate subjective global assessment (SGA) registration as an alternative to a diary based symptom registration (VAS scale) as an outcome measure. This is a follow-up report of the open multicentre RCT study Fructose Malabsorption in Northern Norway[11].

**MATERIALS AND METHODS**

***Enrolment and patient flow***

The study outline has been published earlier[11]. In brief, during the period July 2008 and July 2011, patients who met the Rome II criteria for diagnosis were recruited. The IBS patients were registered according to their subtypes; constipation or diarrhea. An individual diagnostic workup was performed including, but not mandatory, blood tests, stool samples, breath tests, endoscopy and histological examination and X-ray or ultrasound investigations to ensure the exclusion of organic disease or other malabsorption diseases such as lactose intolerance or celiac disease.Exclusion criteria were patients with severe chronic disease, severe chronic constipation (defined as laxative users), patients taking antibiotics or non-steroid anti-inflammatory drugs (NSAIDs), and patients whom had previously had performed a FBT or used FRD.

***Study design***

As previously described [11] the study was designed with a preregistration period of 2 wk where the patients followed their individual habitual IBS diet (HID) . The patients were then randomized without stratification to continue HID with or without additional FRD (< 2 g fructose per meal) for 12 wk.

The randomization was assisted by The Scientific Department, University Hospital of North Norway, Tromsø.

In short, individual instructions of a FRD was given both verbally and through written information which included a table in Norwegian showing the fructose content in 91 common food ingredients (a comparable table in English showing fructose content per 100 g/100 mlfood/beverage, browse nutrient list and choose fructose is referenced[15]). For a short version of the table of instructions see Appendix 1.

In addition to daily VAS registrations of abdominal pain/discomfort, bloating, stool frequency and consistency for 4 wk, a SGA registration was completed once a week for 12 wk. Early dropouts (defined as patients whom registered less than 3 wk of the main 12 wk period) were replaced, late dropouts were not replaced. Data from patients that registered for more than 3 of the 4 wk were included in the total registration. The main reason for choosing a 4 wk VAS registration was the concern about compliancy as the subject would have to perform daily registrations throughout the whole study. After the main registration period, the patients delivered their diary books, underwent fructose breath test and were instructed in the fructose-rich provocation test for a maximum of 7 d, or for shorter time if the test provoked IBS symptoms. For the provocation test patients were told to choose sucrose rich food and to include at least 200 ml of fruit juice with only small amounts of sorbitol in each daily meal[15,16] (for example 200 ml orange juice8-9 g fructose with no sorbitol content/200 ml apple juice 15 g fructose-1 g sorbitol). Study patients were instructed to use the same information table as a guide for both reducing the fructose load and for ensuring a sufficient intake of fructose (30 g) during the provocation test[15]. The VAS score and SGA score (as compared to the last week of main registration) [11] were logged in a separate provocation diary.

***Symptom score of IBS***

The subjects filled in a symptom registration diary. Each day they marked on a VAS form (0-100 mm) the degree of pain and bloating experienced (zero mm for no symptoms, and 100 mm for maximal symptom score). In addition they counted the number of stools and gave a description of the stool quality on a scale from 1-7 (Bristol scale)[13].

***Self reported fructose intolerance: Diagnostic criteria***

Based on the experiences from our first study[11], a diagnostic test based on a self-reported (subjective) intolerance to fructose in IBS was constructed. We defined fructose-related food intolerance as a combination of symptom relief associated with dietary fructose restriction and symptom exacerbation following a fructose provocation test. In our previous study[[11](#_ENREF_12)] the Bland- Altman analysis showed that the technical detection limits (corresponding to 1.96 SD of mean bias) were 18 mm (18% on VAS scale 100 mm) for pain/discomfort and 17 mm for bloating. Based on these boundaries a response to FRD was defined as > 25 mm relief whereas a > 25 mm worsening of the VAS score during provocation was considered a positive test[11].

***SGA score of IBS***

Patients determined the SGA of abdominal relief once during every weekend of the study period by entering their assessment in their personal diary.

The assessment was completed by answering the following question: Please consider how you have felt the past week with regards to your IBS, in particular your overall wellbeing, symptoms of abdominal discomfort, pain and altered bowel habit compared to how you felt before entering the study). How do you rate your relief (or worsening) of symptoms during the past week? The scale contained 5 possible answers: (1) completely relieved; (2) considerably relieved; (3) somewhat relieved; (4) unchanged; or (5) worse[17]. Using the SGA score, patients who were somewhat relieved in week 3 and 4, or completely /considerably relieved in at least one week were considered to respond to the FRD.

***Breath tests***

Hydrogen (H2) and methane (CH4) was measured by a Microlyzer (Quintron Instr. Company Inc., Milwaukee, Wisconsin, United States) in end-expiratory breath samples according to the manufacturer’s instructions. After an overnight fast, H2 and CH4 levels were measured before drinking 15 ml solution corresponding to 50 g of fructose). Measurements were performed every half an hour until a gas peak was reached, or up to 4 h. A high load of fructose was used to minimize false negative results as indicated by Choi *et al*[12]

Incomplete absorption was defined as an increase of H2 > 20 ppm or CH4 > 12 ppm, or a sum of combined peak increase above 15 ppm. Symptoms during and after the test were recorded.

***Statistical analysis and validation***

The statistical analysis included all randomized patients (intention to treat). Patients where split into the two predefined groups according to the study protocol; either a normal IBS di*et al*one or combined with FRD.

A test-retest analysis of SGA was performed by comparing scores at preregistration with those at 1, 4 and 12 wk in the control group; delta values were run using a Wilcoxon signed rank test *vs* 0. Internal consistency was explored by ANOVA and Spearman’s correlation on delta VAS (week 0 *vs* week 4) *vs* SGA score at 4 wk in all included patients. The former analysis also yielded information regarding scale linearity and precision of the SGA measure.

Finally, the face validity denoting whether the questions made sense was performed in all of the patients and 10 healthy volunteers.

**RESULTS**

***Enrollment of patients***

Patient inclusionin this multicentre study is described in detail in a previous publication[11].In brief, 310 patients admitted to hospital with IBS symptoms were screened, 108 patients did not meet study inclusion criteria. The included 202 patients were randomized, of these 182 patients completed the main registration period of 12 wk. All early dropouts were replaced. All patients reported a combination of constipation and diarrhea. A total of 88 patients were randomized to FRD. Of these we experienced missing data from 11 patients, 9 due to a missing provocation diary and 2 patients that missed markings for SGA change in week four of the main diary. The remaining 77 patients reported complete VAS and SGA data both during the pre- and main registration periods, as well as a complete registration during the provocation test. We found no significant differences in age, sex ratio, abdominal pain/discomfort, bloating, stool frequency or Bristol scale stool consistency between the FRD+HID diet group and the HID group (Table 1).

***Validation analysis of SGA***

Internal consistency was tested by calculating the VAS change for each of the 182 patients by comparing status at 4 weeks with preregistration.

These delta-values were compared to SGA scores at week 4 using the Spearman Rank correlation test. The analysis yielded ρ values of 0.59 (SGA *vs* pain/discomfort; *P <* 0.0005); 0.58 (SGA *vs* bloating; *P <* 0.0005); and 0.84 (bloating *vs* pain/discomfort; *P <* 0.0005). The graph for the control group illustrated in fig 1, shows that SGA is a stable measure throughout the three month study period. A test-retest analysis was performed by analysing the control group SGA values in pairs. For each record, the differences between preregistration week 0 and weeks 1, 4 and 12 were calculated. These delta values were analyzed with a Wilcoxon signed rank test using zero as the median for the null-hypothesis. The three delta values were not significantly different from zero (*P* = 0.41, 0.13, and 0.42 for preregistration *vs* week 1, 4, and 12, respectively). Figure 1 shows the raw data distribution of VAS change registrations in the five SGA categories at four weeks for all 182 study participants.. The SGA scale is not linear, it discriminates best between the span of somewhat relieved and towards completely relieved. A two-way ANOVA analysis of this dataset (VAS by SGAxDiet group) was performed and pair wise comparison is presented in table 2. The traces for the control group in figures 2 and 3 show that the VAS measure and the SGA rating are stable over time when used in an IBS setting.

As shown in table 3, for SGA a fairly good sensitivity and specificity of 0.84 and 0.74, respectively, for identifying self-reported DFI was found. The inclusion of a provocation test in the diagnostic criteria improves the quality of the test criteria; especially it improves the negative predictive value (Table 3). The sensitivity and specificity parameters for the FBT were low (Table 3).

***Self reported dietary fructose intolerance: Agreement with breath tests***

Using our new criteria for the diagnosis of self reported DFI, we established a diagnostic tool for fructose intolerance based on the results from the agreement testing (frequency analysis) see table 3.As described in our earlier report[11], a discrepancy was found between the self-reported fructose intolerance and FBT. This was confirmed in the frequency analysis that gives a kappa value of –0.13.There was a good agreement between the diagnosis of self reported DFI and the SGA responses to FRD according to the criteria used (see methods) with a kappa value of 0.61 (table 3). When results from the provocation test were excluded from the diagnostic criteria, the kappa value was less precise (*k* = 0.53).

***Prevalence of self-reported fructose intolerance***

The prevalence of self-reported fructose intolerance, defined as a combination of response to FRD and a positive provocation test, was 56 % (43 out of 77 patients).

**DISCUSSION**

In this open labeled, unstratified, randomized multicenter study of FRD in patients with IBS, we have proposed a new diagnostic criterion for FM based on the combination of effects from FRD and a positive provocation test. This is based on symptom registration (using a VAS scale) as the outcome measure. The FBT shows poor test characteristics for identifying these patients. An alternative SGA registration, as an outcome measure for FRD, showed a good agreement with the new diagnostic criteria. Our study opens for a new approach in the management of dietary fructose intolerance in IBS patients. A fructose-restricted diet of < 2 g fructose per meal together with a standardized method for SGA registration can be used as the first step in the management of IBS patients in clinical practice. Using these new diagnostic criteria, the prevalence of self-reported fructose intolerance in the IBS cohort admitted to a gastroenterology unit was as high as 56%.

In this study, the criteria for the diagnosis of fructose intolerance are based on self-reported symptoms of relief, whilst on FRD, and symptom aggravation following a fructose provocation test.

This was chosen due to the lack of a more precise or accurate objective test, including breath tests[5]. The international consensus of nomenclature for food related disorders from 2001[18]defines self reported fructose intoleranceas a non-allergic hypersensitive condition to fructose-rich food items. Moreover, the concept of self reporting is a descriptive term based on patient registration of symptoms[19]. In other reports of food-related disorders where objective diagnostic tests are lacking ,the patient’s symptoms are referred to as subjective[20] or perceived[21]*.*

In this study, we have used SGA as a clinical tool to assess the effects of FRD.A translated modification of a 5 degree score system of a validated questionnaire for IBS, described by Müller-Lissner *et al*[17], was performed. The validation of the Norwegian translation of SGA, used in IBS patients on a FRD, showed a good agreement with VAS measures – especially the categories completely relievedand considerably relievedindicated a substantial change in VAS recordings. The scale is not linear, and the VAS recordings do not as clearly differentiate between the category transitions somewhat relieved-unchanged and unchanged-worse.

Considering our earlier study on VAS recordings for this patient group, these transitions represent VAS differences that are lower than the technical discrimination limits of 17 and 18 mm for bloating and pain/discomfort, respectively[11]. In contrast, the categories completelyrelieved and considerably relievedboth represent a mean VAS change above the technical discrimination limit. Thus, a single SGA rating should reliably identify an improvement in symptoms when rated completely relieved or considerably relieved. The test-retest analysis showed no significant time-related bias, which was also demonstrated in the graph for the control group in figure 3. Face validity was evaluated in healthy volunteers, and revealed no problems in the interpretation of the questions. Finally, a fairly good sensitivity and specificity for identifying self-reported DFI was found for the SGA.

According to the proposed diagnostic criteria, the prevalence of self-reported fructose intolerance in a cohort of IBS patients admitted to a gastrointestinal unit was 56%. Among the few studies reporting the prevalence of fructose malabsorption, defined according to FBT, Goldstein *et al*[6] report 44% of patients with IBS or functional abdominal complaints suffer from the condition.

This was based on a consumption of 50 g fructose and 56%-60% improved on low fructose diet[[6](#_ENREF_6)], whereasBarrett *et al* found fructose malabsorption as high as 34% in healthy volunteers[22]. Finally, in the recently published FODMAP diet studies, representing a diet reduced in fructose and other carbohydrate types, some 50% of the IBS patients improve their symptoms and VAS scores[23]. Our prevalence data has to be interpreted with some caution. Including only those whom complete reported relief of their symptoms by FRD, the prevalence was reduced to some 20%. Moreover,based on the individual normal variation for the capacity offructose absorption[5], the prevalence of self-reported fructose intolerance in IBS has to be compared with the reference population, including potential factors such as genetics and the fructose content in the daily food intake.

The strength of this study is that we have performed a prospective randomized study with a validation of the SGA as a tool for assessing IBS related symptoms during a dietary treatment. The FBT was performed after the 12 wk study observation time, this to prevent potential bias during registration of symptoms.

There are some weaknesses of the study; firstly the intervention could not be blinded for obvious reasons. Secondly, a more exact diary registration of the amount of fructose, glucose, and sorbitol intake in each meal duringthe FRD[[7](#_ENREF_7)], could have given valuable information. Finally, based on our knowledge of normal variations with regards to fructose absorption capacity[5], a more detailed background registration of the fructose/sucrose content in the daily food intake of the IBS patients and in the reference population wouldhave given more comprehensive data.

A substantial increase in the prevalence of IBS has been observed in the past 20 years. During the same time period, the consumption of fructose as well as processed food and additives, has increased in the general population[[24](#_ENREF_25)]. It is tempting to speculate that the increased fructose ingestion may explain the observed increase in IBS. If so, a fructose-restricted diet could be an appropriate option both for the diagnosis and treatment of patients with IBS complaints. If this diet induces symptom relief, according to SGA registrations, a subsequent simple provocation test, 2 glasses of fruit juice with low sorbitol content to each meal in combination with an augmented intake of fructose rich food, could be performed.

A new diagnostic criterion for self reported fructose intolerance, based on FRD is proposed. SGA appears to be a valid outcome measure, which is a feasible alternative to daily VAS registrations, both in daily routine management of these patients and for future studies of IBS.

**Acknowledgments**

We thank the research nurses Odd Sverre Moen Gastro lab, UNN for technical assistance, dietician Marit Marthinussen Hospital of Helgeland helped with the planning of the FRD, and our colleagues at the gastroenterology departments for help with recruiting patients.

**COMMENTS**

***Background***

A substantial increase in the prevalence of irritable bowel syndrome (IBS) has been observed in the past 20 years. The main symptoms of IBS include abdominal pain, bloating, diarrhea or constipation.During the same time period an increase in the consumption of fructose, as well as processed food and additives has been seen in the general population. Fructose intolerance is regarded as a subgroup of IBS, and it has been proposed that the increase in IBS actually represents fructose intolerance as a result of the increased intake of this sugar. In the recently published FODMAP diet studies, which consist of a diet reduced in fructose and other carbohydrate types, some 50% of the IBS patients are reported to improve their symptoms and VAS score.

***Research frontier***

The self reported intolerance to fructose intake has been described as fructose malabsorption (FM) due to small intestinal dysfunction. This was first reported in four patients with chronic diarrhea and colic in 1978. Despite later extensive studies the mechanisms behind this disease or medical condition are still unknown. One of the main unresolved problems is whether fructose intolerance is due to an overload of fructose intake and/or a defect in fructose absorption from the intestinal lumen.

***Innovation and breakthroughs***

Last year we published a report from the study Fructose malabsorption in Northern Norway (FINN study) where the fructose breath test- the only objective test of FM- was found to poorly correlate with self-reported fructose intolerance among IBS patients.In this second report from the FINN study, Subjective Global assessment of abdominal relief (subjective global assessment) is shown to be a valid end-point measure. This report also shows that a high dietary fructose load is the main explanation for this disease.

***Applications***

Validated end-point measures are necessary tools for future studies of self-reported fructose intolerance.

***Terminology***

Fructose intolerance is defined as a subjective –reported intolerance to a normal load of fructose intake. FM is a similar concept, but mainly based on the abnormal intestinal absorption of fructose measured by a fructose breath test. The two concepts are used interchangeably in the literature and most likely describe the same medical condition.

***Peer-review***

Although the findings of this study replicate commonsense practice, this is a useful addition to literature in these days of evidence-based medicine. The sequence the authors followed is historically what happened with the lactose-intolerance studies, where the focus shifted from mucosal lactase measurements to lactose tolerance curves to symptom analysis

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**P-Reviewer:** Abraham P **S-Editor:** Ma YJ **L-Editor:** **E-Editor:**

**Table 1 Demographic and baseline variables for patients included**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **All (77)** | **SRFI neg. (34)** | **SRFI pos. (43)** | ***P*-value** |
| Age (medianrange)  | 43 (18*-*73) | 46 (19*-*73) | 43 (18*-*73) | ns1 |
| Female/male ratio (%) | 61/16 | 25/9 | 36/7 | ns2 |
| Abdominal pain/discomfort (mm) | 53(3*-*89) | 58 (389) | 50 (16*-*76) | ns1 |
| Bloating (mm)  | 55 (20*-*84) | 58 (22*-*83) | 54 (20*-*84) | ns1 |
| Stool frequency (median [range]) | 1.5 (0-4) | 1.6 (1*-*4) | 1.5 (0*-*4) | ns3 |
| Boston scale stool consistency  | 4.4 (1.9 *-*6.0) | 4.6 (1.9*-*6.0) | 4.3 (2.6-5.9) | ns1 |

1independent samples *t*-test; 2The**2 test; 3Mann-Whitney *U*. SRFI: Self reported fructose intolerance. IBS:Measures are mean preregistration values [95%CI] unless otherwise stated; Treatment group differences were tested.

Table 2 **Pairwise comparisons of visual-analogue scale readings by ANOVA analysis**

|  |  |  |  |
| --- | --- | --- | --- |
| **SGA week 4****VAS bloating**  | **Model: *F =* 30.5; *P <* 0.0005****Adj *R*2 = 0.47** | **VAS difference, mean ± SE** | ***P*-value** |
|
| Unchanged *vs* | Completely relieved | 46.1 **±**6.1 | < 0.0005 |
| Considerably relieved | 23.5 **±** 3.0 | < 0.0005 |
| Somewhat relieved | 7.6 **±**2.8 | 0.066 |
| Worse | -7.4 **±** 3.3 | 0.275 |
| **SGA week 4** **VAS pain/discomfort** | **Model: *F =* 32.6; *P <* 0.0005 Adj *R*2 = 0.46** | **VAS difference, mean ± SE** | ***P*-value** |
| Unchanged *vs* | Completely relieved | 41.1 **±** 5.5 | < 0.0005 |
| Considerably relieved | 20.8 **±** 2.7 | < 0.0005 |
| Somewhat relieved | 5.9 **±** 2.5 | 0.202 |
| Worse | -9.4 **±**3.0 | 0.024 |

Results for two-way ANOVA: VAS by SGAxDiet. Mean differences in VAS change of SGA categories compared to *unchanged*, adjusted for diet type. *P* values were adjusted by Bonferroni correction. SGA: subjective global assessment.

**Table 3 Testing new diagnostic criteria of self-reported fructose intolerance in IBS (for definition, see text) against fructose breath test and response of subjective global assessment test (for definition, see text)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Predictive** | **Sensitivity**  | **Specificity** | **Positive****predictive value** | **Negative predictive value** | **Kappa** |
| FBT | 0.57 | 0.34 | 0.58 | 0.29 | -0.13 |
| SGA weeks 3-41  | 0.79 | 0.75 | 0.82 | 0.71 | 0.53 |
| SGA week 3-42 | 0.84 | 0.76 | 0.83 | 0.79 | 0.61 |

1Without result provocation;2With result provocation. FBT: Fructose breath test; SGA: Subjective global assessment test.

 **Figure 1 Scale and precision of the subjective global assessment measure.** At four weeks the change in VAS registration (compared to preregistration values) was calculated. Box and whiskers plot of VAS change in the different sub-categories of SGA at 4 wk. It is noted that the scale is not entirely linear, with best discrimination in the left part of the plot, while the right part shows smaller VAS differences between groups. SGA: Subjective global assessment; VAS: visual-analogue scale.



**Figure 2 Subjective global assessment of irritable bowel syndrome related symptoms during the whole study period.** Mean registration (95%CI) for te study groups. The control group shows stable mean value during the 2 + 12 wk registration. The mean effect of FRD is marked, showing stable improvement of symptom rating during the whole study. The SGA ratings are: 1: Completely relieved; 2: Considerably relived; 3: Somewhat relieved; 4: Unchanged; 5: Worse. FRD: fructose reduced diet; SGA: subjective global assessment; IBS: irritable bowel syndrome.



**Figure 3 visual-analogue scale registrations of irritable bowel syndrome related symptoms during the first 2 + 4 wk.** Mean registration (95%CI) for the study groups. FRD: Fructose reduced diet; IBS: Irritable bowel syndrome; VAS: visual-analogue scale.

**Appendix 1 Fructose-restricted diet (according to definition less than 2 g fructose/meal)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Food item** | **In moderation** | **Use sparingly** | **Avoid** |
| Fruit/berries | Lemon, raspberries, blueberries |  | All other types of fruit and berries |
| Vegetables | Most vegetables,avocado | Tomato purée | Carrots, legumes, boiled potatoes |
| Meat/fish/eggs | 100% ground beef and fish with no additives | Caviar, mackerel in tomato sauceAnchovies and herring |  |
| Milk products | White/brown cheeses/ cream and sour cream | Cheeses with fruit added | Fruit yoghurt, ice cream and puddings |
| Grain products |  Bread, pasta, rice and white flour |  | Sweet bakery and cereals |
| Miscellaneous | Margarine, oils, mayonnaise, nuts | Dressings, ketchup |  Sweets, chocolates |
| Drinks | Water,milk, tea, coffee, light soda and light fructose drinks | Light orange juice | Juice, nectar, sodas and fructosedrinks, milk with sugar or fructoseadded |