ORIGINAL ARTICLE

# Fructose- and Sorbitol-reduced Diet Improves Mood and Gastrointestinal Disturbances in Fructose Malabsorbers

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**Background:** Fructose malabsorption is characterized by the inability to absorb fructose efficiently. As a consequence fructose reaches the colon where it is broken down by bacteria to short fatty acids, $CO_2$ and $H_2$. Bloating, cramps, osmotic diarrhea and other symptoms of irritable bowel syndrome are the consequences and can be seen in about 50% of fructose malabsorbers. We have previously shown that fructose malabsorption is associated with early signs of mental depression and low serum tryptophan concentrations. It was therefore of interest whether a fructose-reduced diet could not only improve gastrointestinal complaints but also depressive signs seen in fructose malabsorbers. **Methods:** Fifty-three adults (12 males, 41 females), who were identified as fructose malabsorbers according to their breath-$H_2$ concentrations, filled out a Beck's depression inventory-questionnaire, and a questionnaire with arbitrary scales for measurement of meteorism, stool frequency and quality of life for a 4-week period before dietary intervention and 4 weeks after dietary change as for fructose- and sorbitol-reduced diet. **Results:** Depression scores were reduced by 65.2% after 4 weeks of diet ($P < 0.0001$), and there was a significant reduction of meteorism ($P < 0.0001$) and stool frequency ($P < 0.01$). Improvement of signs of depression and of meteorism was more pronounced in females than in males. **Conclusion:** Fructose- and sorbitol-reduced diet in subjects with fructose malabsorption does not only reduce gastrointestinal symptoms but also improves mood and early signs of depression.

**Key words:** Depression; diet; fructose malabsorption; hydrogen ($H_2$) breath test; malabsorption syndrome; nutrition

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Fructose malabsorption is a well-described gastrointestinal disorder (1–3). Up to 36% of the European population present with fructose malabsorption in a more or less severe form, and about half of them are symptomatic (4). Fructose malabsorption is characterized by a defect of the fructose-related GLUT5 transport system, which is responsible for the duodenal uptake of the monosaccharide fructose (5). Patients are therefore unable to resorb the ingested monosaccharide sufficiently. As a result fructose reaches the colon, where it is broken down by colon bacteria into short-chain fatty acids, $CO_2$ and $H_2$ usually inducing bloating, abdominal discomfort and sometimes osmotic diarrhea. The type and extent of gastrointestinal discomfort largely depends on the kind of colonic bacterial activity (6).

Fructose malabsorption can be diagnosed by measuring the $H_2$ concentration in the exhaled breath after an oral load of fructose (2, 7, 8). We described recently that fructose malabsorption (9) and lactose malabsorption (10) were associated with early signs of mental depression and mood disturbances in some patients, especially in women. This study was designed to investigate the clinical influence of a fructose- and sorbitol-reduced diet on gastrointestinal and mood disturbances in such patients.

## Patients and Methods

### *Patients*

From 100 patients who presented at our office for a medical health check, 53 individuals with gastrointestinal complaints were consecutively chosen to participate in this follow-up study on the basis of the $H_2$-breath test results (see below). Sigmoideoscopy was previously performed in most of these patients because of chronic gastrointestinal complaints, and negative results were reasons for a further checkup in our office. For those who had not had sigmoideoscopy, this examination was prescribed to rule out inflammatory bowel diseases. The otherwise healthy outpatients, aged from 17 to 75 years (mean, $44.8 \pm 14.5$), gave informed consent to

participate in the clinical trial with fructose-reduced diet which was approved by the local ethics committee. There were 12 male (range, 23–75 years; mean 42.3 ± 14.6) and 41 female patients (range, 17–73 years; mean, 45.6 ± 14.6). Gastrointestinal infections were excluded by stool culture examination for pathogenic clostridia, yersinia, campylobacter, salmonella, shigella and candida. Routine blood examination showed no signs of systemic inflammatory or infectious diseases. Except for oral contraceptives in some females, no patient was under medication.

*Methods*

Diagnosis of fructose malabsorption was established by $H_2$-breath test after oral fructose load with 50 g fructose given in 250 ml of tap water. All $H_2$-breath tests were performed between 0800h and 0830h after a 12-h overnight fast. Breath-$H_2$ was measured using a Bedfont gastrolizer (Bedfont Ltd., Kent, UK), which had been validated by several authors (11–13). Breath-$H_2$ was monitored before fructose load and in 30 min intervals for at least 2 h after fructose load. Maximum breath-$H_2$ concentrations were registered and the differences from baseline values were calculated yielding the operating parameter $\Delta H_2$.

From the patient's first visit to the beginning of the therapeutic intervention 4–6 weeks passed in which extended medical and laboratory diagnostic examinations were completed. At the end of this pre-intervention period when fructose malabsorption as a diagnosis was confirmed, all patients were asked to complete the following four tests: 1) Beck's depression inventory-questionnaire (BDI) for quantifying clinical signs of mental depression (14, 15); 2) grading of meteorism on an arbitrary analogue scale ranging from 0 (no meteorism complaints) to 10 (heavy complaints); 3) monitoring stool frequency on a scale ranging from −5 (stool frequency less than once every fifth day) to +10 (stool frequency 10 and more each day); and 4) their subjective feeling of well-being on an arbitrary analogous scale ranging from 0 (no complaints) to 10 (serious complaints). Following these tests there was scheduled dietary consultation (see below). After 4 weeks of dietary change, the patients were asked again to complete the aforementioned tests on a retrospective basis.

*Diet*

The patients were instructed to maintain a diet intended to exclude or reduce the intake of fructose and sorbitol. For this purpose they were told to avoid fresh fruit (with the exception of bananas, honeydew melons, and tangerines), all kinds of dried fruits, fruit juices, soft drinks, honey and all kinds of sorbitol-containing food such as sugarless chewing gums and sugarless sweets. The patients were told that saccharose containing 50% fructose should be supplemented with 2 parts of regular sugar with 1 part of glucose, which is commonly available as Dextropur. In some cases with severe complaints patients were told to avoid stachyose- and verbascose-containing foods such as onions, beans and cauliflower. In those cases where patients did not know whether a certain vegetable was of high stachyose or verbascose content they were told to avoid this vegetable at least for the duration of the study. They were allowed to eat any other kind of carbohydrate-containing food (e.g. cereals, wheat, corn, potatoes), rich protein- (fish, meat, dairy products) and fat-containing foods.

Mean dietary fructose (as a monosaccharide) and sorbitol

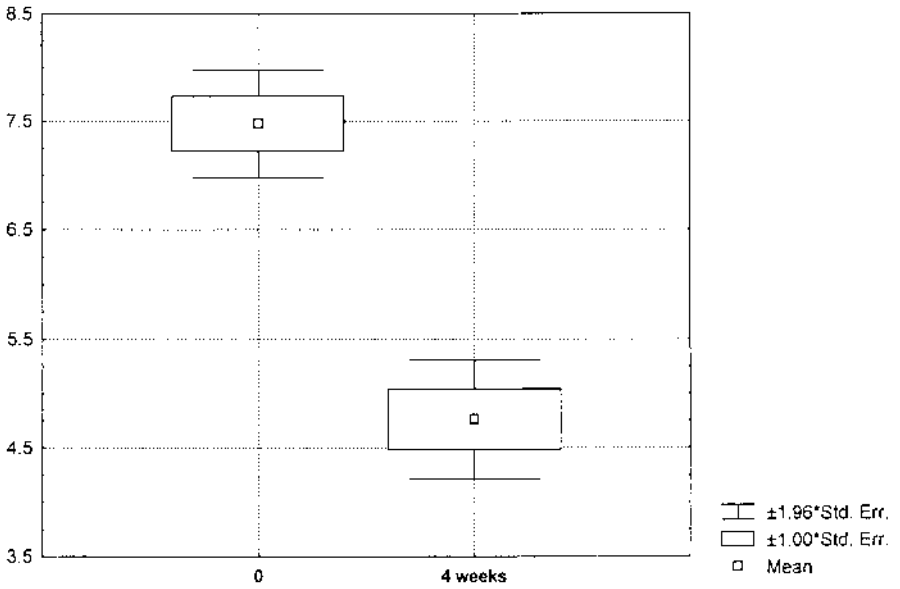


Fig. 1. Meteorism before dietary intervention (0) and 4 weeks after the beginning of dietary intervention (4 weeks) rated on an arbitrary scale from 0 (no meteorism) to 10 (severe complaints due to meteorism).

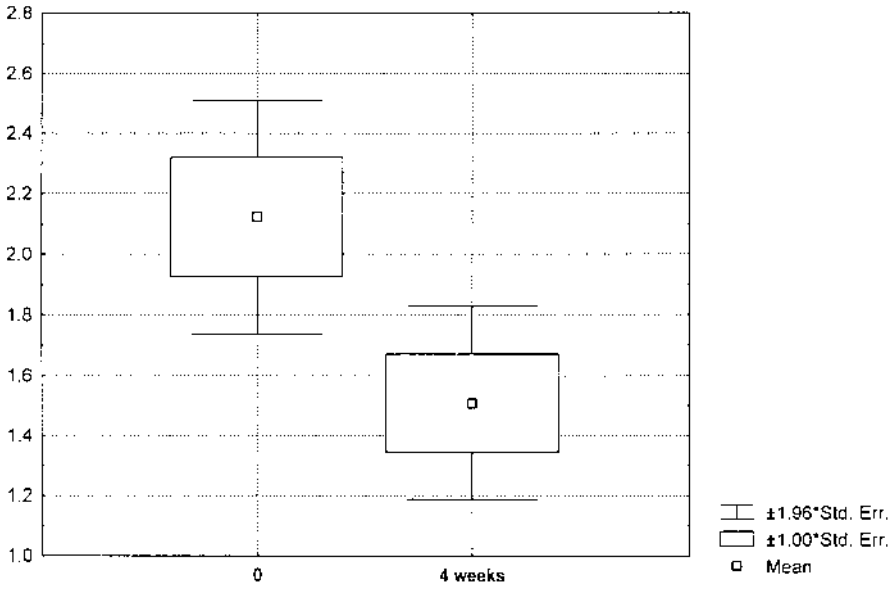


Fig. 2. Stool frequency before (0) and 4 weeks (4 weeks) after dietary change.

intake up to the dietary consultation was assessed by an additional questionnaire, and the amount of fructose and sorbitol intake after consultation during the time of study was controlled by a patient's diary.

*Data analysis*

Individuals with $\Delta H_2$ higher than 20 ppm after fructose load were classified as fructose malabsorber (2, 7, 16, 17). Subjects with $\Delta H_2$ equal or less than 20 ppm were considered as normal fructose absorbers and were therefore excluded from the study. Statistical analysis was completed using a paired *t* test with the standard statistic software STATISTICA 5.0 (18).

## Results

Mean dietary fructose intake (as a monosaccharide) was about 20 g/day during the 4 weeks prior to and about 5 g/day during the dietary observation period. On the arbitrary scale for the measurement of meteorism the mean score before intervention was $7.5 \pm 1.8$ (mean $\pm$ standard deviation) and fell to $4.8 \pm 1.9$ ($t > 1000$; $P < 0.0001$) 4 weeks after beginning the dietary intervention (Fig. 1). As for women the mean score for meteorism fell from $7.6 \pm 1.4$ to $4.8 \pm 1.7$ ($t > 1000$; $P < 0.0001$); in males the score fell from $7.0 \pm 2.6$ to $4.6 \pm 2.5$ ($t = 2.867$; $P < 0.005$).

The score for general well-being during the 4 weeks before dietary intervention was $6.4 \pm 2.3$, which fell to $4.9 \pm 2.0$ during the intervention period ($t = 4.407$; $P < 0.0001$). Women dropped from $6.6 \pm 2.3$ to $5.2 \pm 1.9$ ($t = 4.275$; $P < 0.001$) and men from $5.4 \pm 2.4$ to $3.9 \pm 2.1$ ($t = 1.480$; $P$ = not significant).

The mean stool frequency score was $2.1 \pm 1.3$ before and $1.5 \pm 1.0$ during dietary intervention ($t = 3.374$; $P < 0.01$) (Fig. 2). For women the average score was $2.2 \pm 1.3$ before and $1.6 \pm 1.1$ during intervention ($t = 2.916$; $P < 0.01$) while for men the scores were $1.8 \pm 1.1$ before and $1.2 \pm 0.3$ during dietary intervention ($t = 1.621$; $P$ = not significant).

The majority of the subjects studied showed mild to moderate mood disturbances before dietary intervention. The average BDI score was $13.8 \pm 9.3$ during the 4 weeks prior to dietary intervention. After 4 weeks of dietary change the BDI score fell by $9.1 \pm 7.7$ on average ($t = 5.290$; $P < 0.0001$) (Fig. 3), which means a reduction by 65.2% related to the whole cohort. Split by gender, the mean BDI scores for women were $15.1 \pm 10.0$ before and $9.9 \pm 8.3$ during the dietary intervention ($t = 4.880$; $P < 0.0001$), and for men the mean BDI score was $9.3 \pm 3.1$ before intervention falling to $6.5 \pm 4.2$ in the 4 weeks following dietary change ($t = 2.243$; $P < 0.05$).

## Discussion

The present study shows that fructose-reduced diet improves clinical and psychopathological symptoms of fructose malabsorption. Stool frequency and meteorism were significantly reduced. Since there was a highly significant improvement of BDI, this study further supports the notion that fructose malabsorption is involved in the development of early signs of depression in patients.

Also sorbitol intake usually leads to gastrointestinal symptoms in fructose malabsorption, therefore particularly sorbitol has to be avoided within the scope of a fructose malabsorption diet.

In this study, no control group could be included, because most of the studied subjects had gastrointestinal complaints,

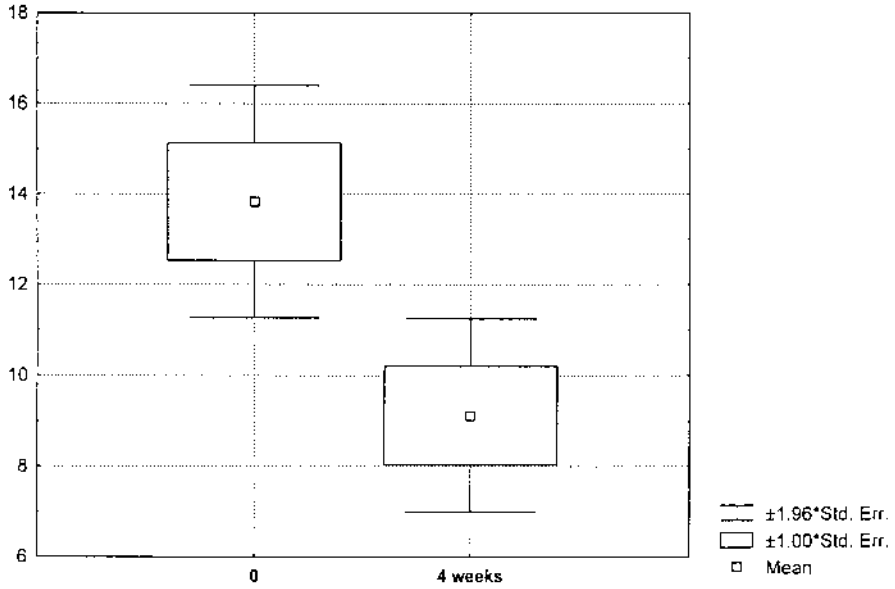


Fig. 3. Beck's depression score before (0) and 4 weeks (4 weeks) after dietary change. The normal range of symptom-free individuals is <11.

and we could not stay away from dietary interventions for ethical reasons. Thus, it cannot fully be excluded that a placebo effect could have contributed to the observed amelioration of symptoms, e.g. the improvement of BDI after dietary change. However, the first set of data was obtained at the end of the pre-intervention period, and the patients were asked to estimate the parameters of gastrointestinal symptoms using an arbitrary analogous scale retrospectively. During this period it is unlikely that the individuals changed their dietary behavior, therefore one can consider the study presented here as a preliminary follow-up investigation which outlines the consequences of a fructose-reduced diet. Furthermore, a dietary observation period of 4 weeks may compensate a potential bias owing to instantaneous amelioration of symptoms. Because all scores were measured exactly 4 weeks apart, it can be ruled out that in females the menstrual cycle would have had a major influence on the outcome of depression scores or meteorism scores.

Our own observations point to the majority of subjects with irritable bowel syndrome deriving their complaints as a result of a carbohydrate malabsorption syndrome, such as fructose malabsorption, sorbitol malabsorption, lactose maldigestion or xylitol malabsorption (unpublished data). Patients with fructose malabsorption often have a clear history of post-infective onset of their symptoms (19) as has been shown for patients with irritable bowel syndrome (20). However, during the pre-intervention period it was confirmed that all subjects were free of infectious symptoms.

We have previously shown that fructose malabsorption (9) is associated with early signs of mental depression and decreased serum tryptophan concentrations (21). Earlier studies imply that disturbances of L-tryptophan metabolism are involved in inducing depression (22–24) and pre-menstrual syndrome (25). In fructose malabsorbers the resorption of L-tryptophan seems to be disturbed. Reduction of non-absorbable intestinal fructose would probably normalize tryptophan resorption by the intestinal mucosa resulting in a higher availability of tryptophan and possibly also of other essential amino acids reducing development of signs of depression.

It is well known that carbohydrate consumption increases the transport of the amino acid L-tryptophan via the blood–brain barrier so that in turn brain 5-hydroxytryptamin (serotonin) levels increase (26–29). This seems to be the reason for the clinically well-known phenomenon of hunger for sweets in patients with depressive mood (27). Since fructose malabsorbers have a higher risk for the development of mood disturbances they are prone to develop a hunger for carbohydrates and especially for sweets. Fructose is the monosaccharide with the most intensive sweetness and its industrial production is inexpensive, too. Therefore, modern food processing involves increasingly the replacement of regular sugar in sweet foods with fructose (30). Depressive patients with fructose malabsorption and a hunger for sweets are therefore at a high risk to end up with reduced tryptophan availability. As a result a vicious circle may develop of a craving for sugar leading to a short-lived improvement of depressive symptoms but leading to a prolonged tryptophan depletion too, thus accelerating both the development of mental depression and gastrointestinal disturbances in fructose malabsorbers. At this point dietary restriction of fructose seems therefore to be the only means of suppressing this vicious cycle in these patients.

In conclusion, depressive symptoms and gastrointestinal

disturbances in patients with fructose malabsorption was significantly improved by a 4-week period of a fructose-reduced diet, which hence may represent the most effective measure to encounter this major malabsorption syndrome.

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