FRUCTOSE MALABSORPTION IS ASSOCIATED WITH EARLY SIGNS OF MENTAL DEPRESSION

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Abstract: 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, CO₂ and H₂. Bloating, cramps, osmotic diarrhea and other symptoms of irritable bowel syndrome are the consequence and can be seen in about 50% of fructose malabsorbers. Having made the observation that persons with fructose malabsorption very often seem to present not only with signs of irritable bowel syndrome but also with signs of premenstrual syndrome and mental depression, it was of interest to establish whether such an association could be demonstrated in patients. Fifty-five adults with gastrointestinal complaints of unknown origin (12 males, 43 females) were analyzed by measuring breath hydrogen concentrations after an oral dose of 50 g fructose and were classified as normals or fructose malabsorbers according to their breath H₂ concentrations. All patients filled out a Beck’s depression inventory - questionnaire. Fructose malabsorption was detected in 36 of 55 individuals (65.5%). Subjects with fructose malabsorption (ΔH₂ concentrations >10 p.p.m. after fructose load) showed a significantly higher score in the Beck’s depression inventory than normal fructose absorbers. This was true especially for females. Fructose malabsorption may play a role in the development of depressed mood. Fructose malabsorption should be considered in patients with symptoms of major depression or pre-menstrual syndrome. Further studies are needed to clarify the background of this association.

Key words: depression; fructose malabsorption; fructose load; H₂ exhalation

INTRODUCTION

Fructose malabsorption syndrome is a disease which was first described some years ago [15,17]. Patients with fructose malabsorption are unable to absorb the ingested monosaccharide in a sufficient way so that large quantities of fructose reach the colon, where it is broken down by colon bacteria into short fatty acids, CO₂ and H₂ which can be measured in the expired air. Bloating, abdominal discomfort and sometimes osmotic diarrhea are the consequences induced by the degradation products built by the colonic bacteria. It is believed that up to 36% of the European population suffer from fructose malabsorption in a more or less severe form, and about half of them are symptomatic [3]. The composition of the bacterial flora could have a role in fructose malabsorption. In earlier studies, the activity of colonic bacteria was found as an important determinant of the symptoms in people with fructose malabsorption, e.g., in anaerobic stool cultures of subjects with symptomatic fructose malabsorption the disappearance rate of fructose was significantly elevated [4].

The diagnosis of fructose malabsorption can easily be made by measuring the H₂ concentration in the exhaled breath after an oral load of fructose. Having made the observation that some patients with fructose malabsorption also tended to clinical signs of major depression, it was of interest to establish whether a statistical correlation existed between the two.

MATERIAL AND METHODS

Patients: Fifty-five otherwise healthy adult outpatients were studied who visited the physicians office for a medical health check-up and reported occasional abdominal discomfort. All patients gave informed consent to participate in this study. The patients (12 men, 43 women) were aged from 30 to 65 years (mean 44.7 years). None of the patients showed signs of inflammatory bowel disease, any other chronic diseases or infectious diseases and were – except for oral contraceptives in some cases – under no medication. All patients filled out a Beck’s depression inventory-questionnaire [19]. Body mass index was calculated for all patients.

Breath H₂ test: Breath H₂ was measured using a Bedfont gasotralizer (Bedfont Ltd., Kent, UK). The H₂ monitor used has been validated by several authors [5,8,12]. All tests were performed between 8:00 and 8:30 a.m. and body weight and height were measured. After a 12 hours overnight fast a baseline H₂ breath test was performed. An oral dose of 50 g fructose was given in 250 ml of tap water and H₂ exhalation was monitored in 30 min. intervals for 2 hours (Fig.1). Maximum H₂ exhalation...
tion (H₂-max) after fructose load was monitored and the differences to baseline levels (ΔH₂) were calculated. Cut off point for the diagnosis of fructose malabsorption were breath H₂ concentrations greater than 10 p.p.m. over baseline [13]. Subjects with a raise of breath H₂ concentrations with equal or less than 10 p.p.m. raise over baseline were considered to be normal fructose absorbers.

A t-Test for independent samples was calculated using a standard PC statistical program (STATISTICA for windows, version 5.0) [24].

RESULTS

In 36 patients breath H₂ concentrations increased more than 10 p.p.m. over basal fasting values, (Table 1) they were classified as fructose malabsorbers. The remaining 19 subjects had maximum breath H₂ concentrations lower than 10 p.p.m. over baseline and were therefore classified as normal fructose absorbers.

Mean BMI was similar in fructose malabsorbers (mean ± S.E.M.: 24.0 ± 0.8) compared to normal absorbers (23.3 ± 0.7; n.s.). There was no significant correlation between BMI and H₂ exhalation.

The Beck's inventory depression score was within the normal range (<19) in most patients, but 6/45 (= 13.3%) had a score higher than 19. The Beck's depression score was significantly higher (p = 0.0038) in fructose malabsorbers (11.9 ± 1.4) compared to normal fructose absorbers (5.4 ± 1.1; Table 1), and patients with fructose malabsorption were more likely to present with Beck's score >15 (X² = 4.19, p <0.05). The association between the Beck's score and the degree of H₂ production seemed to be slightly stronger in females (p <0.02) than in males (p = 0.076).

DISCUSSION

The suspicion that fructose malabsorption is associated with functional bowel disease – a typical psychosomatic disorder – was made by several authors [2,10,11,21]. However, this association could not be found by other investigators [19]. The data in the present study show that fructose malabsorption is significantly associated with a higher score in the Beck's depression questionnaire. The background of this finding is unclear. Subjects with functional gastrointestinal disorders may be susceptible for mood disorders. It is well known that mood disorders are highly prevalent in subjects with so-called functional gastrointestinal tract disorders. The increased prevalence of early signs of mental depression could result from more severe abdominal discomfort due to gut disturbances caused by fructose malabsorption and altered absorption of nutrients resulting in gut disorders. However, from the data it seems that the psychologic component alone of fructose malabsorption associated with gastrointestinal discom-

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<th>Table 1. Characteristics of individuals, H₂ concentrations and Beck’s depression score, split into two groups according to ΔH₂ concentrations after fructose load &gt;10 p.p.m.</th>
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</thead>
<tbody>
<tr>
<td><strong>Normals (12 females, 7 males):</strong></td>
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<td>Beck's depression score</td>
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<tr>
<td>5.4</td>
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<tr>
<td>Body mass index [kg/12]</td>
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<td>Age [years]</td>
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<td>ΔH₂ concentration [p.p.m.]</td>
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<td>Max. H₂ concentration [p.p.m.]</td>
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<td><strong>Malabsorbers (31 females, 5 males):</strong></td>
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<td>Beck's depression score</td>
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<tr>
<td>11.9</td>
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<td>Body mass index [kg/12]</td>
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fort cannot fully explain the observations made, rather a more complex relationship might exist.

The so-called Maillard reaction could provide an explanation how fructose malabsorption could interfere with the metabolism of L-tryptophan which is a precursor for the synthesis of serotonin (5-hydroxytryptamine). Fructose, as other reducing sugars, reacts with proteins and amino acids such as L-tryptophan [6], resulting in a decrease in protein quality due to the loss of amino acid residues and decreased protein digestibility. The formation of a fructose/ L-tryptophan complex has been well described [6]. Maillard products can also inhibit the uptake and metabolism of free amino acids such as L-tryptophan and of other nutrients such as zinc [16]. Fructose malabsorbers have high intestinal fructose concentrations and thus greater probability for forming the non-absorbable fructose-L-tryptophan complexes. As a consequence not only fructose but also L-tryptophan is absorbed to a lesser extent.

Earlier studies imply that disturbances of L-tryptophan metabolism are involved in the pathogenesis of major depression [1,9,20] and pre-menstrual syndrome [18]. Brain serotonin concentrations are controlled by the plasma concentrations of tryptophan which is transported into the brain by an active process. Serotonin is widely distributed throughout the central nervous system, and it acts as a neurotransmitter. Consequently, impaired availability of serotonin may manifest manifold consequences to the central nervous system. It is not fully clear whether impaired serotonin function is responsible for the clinical signs of major depressive disorders. However, lowering of brain serotonin function can precipitate clinical depressive symptoms in individuals who are vulnerable to major depressive disorders [23], and selective serotonin re-uptake inhibitors can be successfully applied for treatment of endogenous depression. Interestingly the association of fructose malabsorption with clinical symptoms of depression is more pronounced in females than in males. This goes along with findings of sex differences in mood responses to acute tryptophan depletion by several authors [9,18,22], and lower blood concentrations of L-tryptophan in healthy females than in males [13]. Thus, disturbed resorption of L-tryptophan may earlier cause low enough levels for clinically relevant disturbances of serotonin metabolism.

Notably, according to the Becks depression score, only a minority of patients presented with a tendency to depressive mood, the great majority of patients presented well within the range of normal. This agrees with the selection of patients, all occasionally presenting with gastrointestinal complaints of unknown origin but otherwise healthy. However, the data imply that fructose malabsorption might contribute to minor psychosomatic symptoms due to gastrointestinal discomfort and/or probably biochemical manifestations which in the long run could reach more clinical relevance.

Fructose malabsorption is significantly associated with mood disorders in females, possibly by interfering with L-tryptophan metabolism. Although the correlations found do not necessarily confirm a causal relationship, this observation suggests that fructose malabsorption may be implicated in the development of depressive syndromes, e.g. major depression and/or pre-menstrual syndrome. Further studies are needed to demonstrate the association between fructose malabsorption and disturbed tryptophan metabolism.

REFERENCES


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