Digestive Diseases and Sciences, Vol. 45, No. 7 (July 2000), pp. 1255–1259

Carbohydrate Malabsorption Syndromes and Early Signs of Mental Depression in Females

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Fructose and lactose malabsorption are characterized by impaired duodenal fructose transport or by the deficiency of mucosal lactase, respectively. As a consequence, the nonabsorbed saccharides reach the colon, where they are 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 consequence and can be seen in about 50% of carbohydrate malabsorbers. We have previously shown that fructose as well as lactose malabsorption were associated with signs of mental depression. It was therefore of interest to investigate possible interactions between fructose and lactose malabsorption and their influence on the development of signs of depression. In all, 111 otherwise healthy volunteers (81 females and 30 males) with gastrointestinal complaints were analyzed by measuring breath H_2 concentrations after an oral dose of 50 g lactose and of 50 g fructose one week apart. They were classified as normals, isolated fructose malabsorbers, isolated lactose malabsorbers, and combined fructose/lactose malabsorbers. All patients filled out a Beck's depression inventory–questionnaire. Twenty-five individuals (22.5%) were neither fructose nor lactose malabsorbers (group 1), 69 (62.2%) were only fructose malabsorbers (group 2), 4 (3.6%) were only lactose malabsorbers (group 3), and 13 (11.7%) presented with fructose and lactose malabsorption together (group 4). Isolated fructose malabsorption and combined fructose/lactose malabsorption was significantly associated with a higher Beck's depression score. Further analysis of the data show that this association was strong in females ($P < 0.01$), but there was no such association between carbohydrate malabsorption and early signs of depression in males. In conclusion, the data confirm that fructose malabsorption may play a role in the development of mental depression in females and additional lactose malabsorption seems to further increase the risk for development of mental depression.

KEY WORDS: fructose malabsorption; lactose malabsorption; hydrogen breath test; malabsorption syndrome; depression.

Carbohydrate malabsorption syndromes like fructose malabsorption or lactose malabsorption are well described gastrointestinal disorders (1). Fructose malabsorption syndrome is characterized by a defect of the fructose transporter gene GLUT5, which is responsible for the duodenal uptake of the monosaccharide fructose (2). 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 colonic bacteria. It is believed that up to 36% of the European population have fructose malabsorption in a more or less severe form, and about half of them are symptomatic (3).

Manuscript received January 29, 1999; accepted November 30, 1999.

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0163-2116/00/0700-1255$18.00/0

Lactose malabsorption syndrome is characterized by a deficiency of lactase either as a primary deficiency (genetic or familial) or as a secondary (acquired) deficiency of lactase due to other gastrointestinal disorders (1). Patients with lactose malabsorption are unable to cleave and consequently insufficiently absorb the ingested disaccharide, so that large quantities of lactose reach the colon.

When nonresorbed carbohydrates such as fructose or lactose reach the colon, they are broken down by colonic bacteria into short fatty acids, CO_2 and H_2. Usually bloating, abdominal discomfort, and sometimes osmotic diarrhea are the consequences induced by the degradation products built by the colonic bacteria. The extent of gastrointestinal discomfort depends on the kind of colonic bacterial colonialization (4).

The diagnosis of all carbohydrate malabsorption syndromes can easily be made by measuring the H_2 concentration in exhaled breath after an oral load of lactose (5). We described recently that fructose malabsorption (6) and lactose malabsorption (7) were associated with early signs of mental depression. It was the aim of this study to investigate possible interactions between the two carbohydrate malabsorption syndromes and their association with signs of mental depression.

MATERIALS AND METHODS

Patients. In all, 111 otherwise healthy outpatients 17 to 81 years old (mean 45.6 ± 13.3 SD) who visited the physician's office for a medical health check-up and who complained about meteorism were studied. There were 30 males aged 23–72 years (mean ± SD, 42.9 ± 12.8 years) and 81 female patients aged 17–81 years (46.5 ± 13.5). None of the patients showed signs of inflammatory bowel disease, any other chronic disease, or infectious diseases. No patients were under medication except for contraceptives in some females. All patients filled out a Beck's depression inventory–questionnaire at the time of examination (8–10). Body weight and height were measured at the beginning of the trials and body mass index (BMI) was calculated for all individuals.

H_2 Breath Tests. All tests were performed between 8:00 and 8:30 AM, After a 12-hr overnight fast an H_2-breath test was performed with an oral dose of 50 g fructose given in 250 ml of tap water. At least one week apart another H_2-breath test was performed with an oral dose of 50 g lactose given in 250 ml of tap water. Breath H_2 was measured using a Bedfont gastrolizer (Bedfont Ltd., Kent, UK), and the method has been validated by other authors (11–13). Breath H_2 was monitored before carbohydrate load and at 30-min intervals for at least 2 hr after fructose or lactose load. Maximum breath H_2 concentrations were registered (H_2-max) and the differences from baseline values were calculated (delta H_2).

TABLE 1. PATIENT CHARACTERISTICS AND DEPRESSION SCORES*

	Mean ± SD
Group 1 (N = 25)	
Age	48.8 ± 12.9
Body mass index	24.8 ± 4.1
Depression score	7.2 ± 3.6
Group 2 (N = 69)	
Age	43.7 ± 13.0
Body mass index	23.6 ± 4.5
Depression score	9.8 ± 7.6
Group 3 (N = 4)	
Age	42.0 ± 13.7
Body mass index	22.4 ± 3.1
Depression score	6.5 ± 3.7
Group 4 (N = 13)	
Age	50.1 ± 15.2
Body mass index	25.2 ± 6.8
Depression score	12.3 ± 8.7

*Normals group 1; isolated fructose malabsorption, group 2; isolated lactose malabsorption, group 3; and combined fructose- and lactose malabsorption, group 4.

Data Analysis. Breath H_2 concentrations greater than 20 ppm over baseline after the fructose or lactose load has been defined as a cutoff for the diagnosis of fructose or malabsorption, respectively (14, 15) Subjects with a rise of breath H_2 concentrations of ≤20 ppm over baseline were considered to be normal fructose or lactose absorbers. Subjects that showed neither fructose nor lactose malabsorption were classified as normals (group 1, Table 1), subjects that showed isolated fructose malabsorption were classified as fructose malabsorbers only (group 2), subjects that showed isolated lactose malabsorption were classified as lactose malabsorbers only (group 3), and subjects that showed both fructose and lactose malabsorption were classified as fructose and lactose malabsorbers (group 4).

A Kruskal–Wallis-test was performed for group comparisons. For further statistical analysis, a t test for independent samples was employed using a standard PC statistical program (Statistica for Windows version 5.0) (16). In addition, nonparametric tests (Mann-Whitney U test and Spearman rank correlation analysis) were performed for confirmation, and the results agreed well with each other (data not shown).

RESULTS

Twenty-five subjects [22.5%; 5 males (16.7% of all males) and 20 females (24.7% of all females)] were neither fructose nor lactose malabsorbers and where therefore classified as normals (group 1, Table 1). 69 subjects [62.2%; 21 males (70.0%) and 48 females (59.3%)] were isolated fructose malabsorbers (group 2), and 4 subjects [3.6%; 1 male (3.3%) and 3 females (3.7%)] were isolated lactose malabsorbers (group 3). The remaining 13 subjects [11.7%; 3 males (10%) and 10 females (12.3%)] showed signs of fructose and lactose malabsorption (group 4).

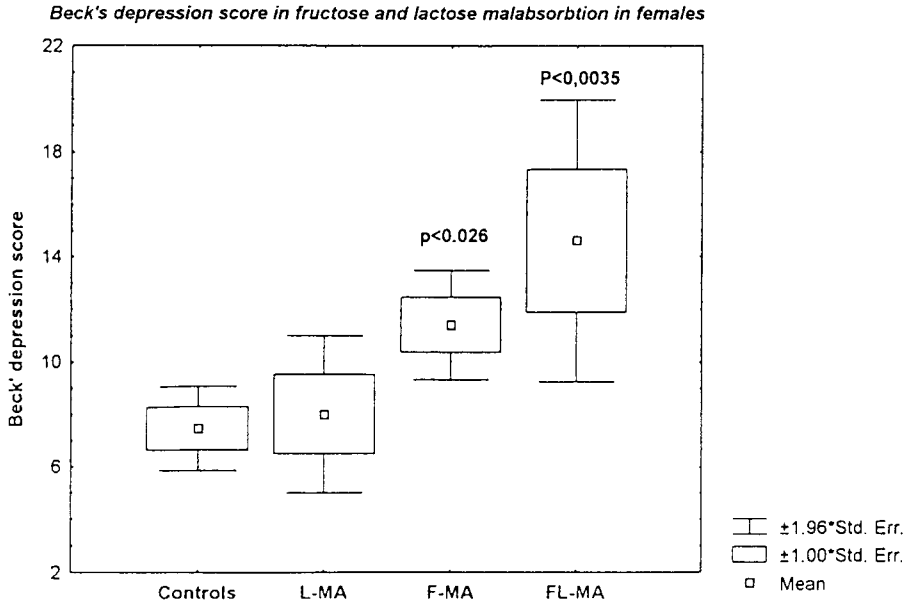

Fig 1. Association between Beck's depression score in fructose and lactose malabsorption in females compared to controls. L-MA: lactose malabsorption, F-MA: fructose malabsorption, FL-MA: combined fructose and lactose malabsorption.

Average BMI was 23.98 (SD ± 4.7), and there were no significant differences between normals and malabsorbers (Table 1); this was true in the complete data set and also when individuals were separated into two groups by sex.

No significant differences were found among the four groups regarding the Beck's score when the whole set of data was analyzed. However, when individuals were separated by sex, the differences in females in Beck's inventory depression scores were significant ($P < 0.003$ Kruskal–Wallis test); there was no such difference in males ($P = 0.16$), so they were excluded from further statistical analysis. In females the Beck's inventory depression score was significantly higher ($P < 0.026$) in fructose malabsorbers (group 2), with a score of (mean ± SD) 11.4 ± 7.3, than in normals with a score of 7.5 ± 3.7, and depression score was also significantly higher ($P < 0.004$) in fructose/lactose malabsorbers (group 4) (score of 14.6 ± 8.7) (Figure 1). There was no significant difference between normals and isolated lactose malabsorbers (group 3).

DISCUSSION

The data in the present study show that isolated fructose malabsorption and combined fructose/lactose malabsorption is associated with a significantly higher score for mental depression as compared to subjects with no signs of carbohydrate malabsorption. Our earlier analysis showed that fructose malabsorption (6) and lactose malabsorption (7) each was associated with early signs of mental depression. This extended study confirms that isolated fructose malabsorbers show significantly higher depression scores than normals. This association is apparently amplified by the concomitant presence of lactose malabsorption, whereas isolated lactose malabsorbers do not show an increased Beck's score. In the majority of the study population, lactose malabsorption coexisted with fructose malabsorption, as fructose malabsorption is a very common finding in the central European population. In fact, only 4/17 individuals with lactose malabsorption suffered from isolated lactose malabsorption (three females and one male among 111 tested subjects), so the previously found association between lactose malabsorption and Beck's score most probably resulted from influence of coexisting fructose malabsorption (7). Indeed, a reexamination of the earlier investigated population with fructose malabsorption also showed that a large proportion had lactose malabsorption in addition. Thus, the earlier conclusion has to be modified, that lactose malabsorption itself has only little if any association with a higher Beck's score. However, the limited number of cases with isolated lactose malabsorption available so far does not allow a defi-

nite conclusion, although all of them had Beck's depression score ≤10.

As suggested earlier, abnormal tryptophan metabolism could be involved in the development of depression (17–19) and in the premenstrual syndrome (20). Since the development of signs of mental depression found in our patients may be related with impaired 5-hydroxytryptamine (serotonin) metabolism (21), the data suggest that fructose malabsorption interferes with the L-tryptophan availability (6). Indeed, preliminary data show significantly lower serum tryptophan concentrations in fructose malabsorbers compared to healthy controls (22). Further studies are still necessary to explore and confirm a role of altered tryptophan metabolism in contributing to the association between carbohydrate malabsorption and the development of signs of mental depression in females. Another explanation for the development of depressive signs could be the formation of toxic bacterial degradation products that may be formed when amino acid–carbohydrate compounds reach the colon possibly interfering with neurotransmitter metabolism.

Interestingly the association of fructose malabsorption with mental depression is only significant in females ($P < 0.002$). We did not find such a relationship in men. This goes along with findings of sex differences in mood responses to acute tryptophan depletion by several authors (23–25) and may serve as a further argument that fructose malabsorption interferes with L-tryptophan metabolism. In females the normal range of serum L-tryptophan concentrations was found lower than in males (26). This is probably due to a higher activity of the hepatic tryptophan-2,3-dioxygenase (= tryptophan pyrrolase), which is upregulated by estrogen. If baseline tryptophan concentrations are lower, additional influence of fructose malabsorption may more rapidly contribute to a pathologically low tryptophan level, leading to the development of depression.

Carbohydrate consumption increases the availability of the amino acid L-tryptophan, which in turn increases brain 5-hydroxytryptamin (serotonin) levels (27). As modern food processing involves replacement of regular sugar in sweet foods with fructose and/or lactose, the hunger for (sweet) carbohydrates may lead to a vicious circle of worsened fructose/lactose malabsorption and accelerate L-tryptophan depletion.

From this study it seems that lactose malabsorption does not have an effect on its own; however, it amplifies the effect of fructose malabsorption on the development of signs of depression. This amplifying effect of additional lactose malabsorption might be due to a reduced orocecal transit time in these subjects, thus decreasing the mucosal contact time of tryptophan and also of other nutrients. Consequently tryptophan availability further diminishes. In addition, micronutrient deficiencies may further aggravate the signs of mental depression.

The associations found between fructose malabsorption, lactose malabsorption, and depression do not necessarily reflect a cause–effect relationship, and both conditions may result from another yet unknown cause. However, the data suggest fructose may possibly interfere with L-tryptophan metabolism and lactose intolerance may worsen this effect. Carbohydrate malabsorption should be considered in patients with mental depression, premenstrual syndrome, and other serotonin-deficiency syndromes.

ACKNOWLEDGMENTS

We are indebted to Mr. H. Neuwirth for secretarial help.

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