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Subjective, but not documented, lactose intolerance accompanies irritable bowel syndrome

Original Study

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Abstract

Introduction. Lactose intolerance, due to lactase deficiency, may overlap with the symptoms of irritable bowel syndrome (IBS) or lead to an incorrect diagnosis of IBS. Identification of lactose intolerance and lactase deficiency enables targeted treatment to be implemented.
The aim of the study was to search for a frequency of a lactose intolerance symptoms in patients with IBS, depending on the results of hydrogen breath test (HBT).
Materials and Methods. The study involved 56 patients with IBS and 23 healthy people. Both, IBS patients and healthy controls, were asked to complete a survey about IBS symptoms and tolerance of lactose-containing products. A HBT was performed on all subjects.
Results. Lactase deficiency was diagnosed in 60.7% of patients with IBS and 43.5% of control group. The differences between the study groups were not statistically significant. No statistically significant differences were observed between the incidence of lactase deficiency depending on the type of IBS.
In the group of patients with IBS and normal HBT results, as well as in patients with IBS and lactase deficiency, there were no statistically significant differences in the frequency of lactose intolerance symptoms. However, among people with normal HBT results, patients with IBS reported symptoms of intolerance after consuming lactose-containing foods significantly more often compared to the control group ($p<0.05$).
Conclusions. Frequency of lactase deficiency does not differ between IBS patients and healthy individuals. Patients with IBS are more likely to report symptoms of lactose intolerance, regardless of the HBT result, compared to healthy individuals.

Keywords

irritable bowel syndrome (IBS) • lactose intolerance • lactase deficiency • hydrogen breath test (HBT)

1. Introduction

Irritable bowel syndrome (IBS) is a troublesome disease which, although it does not cause health and life-threatening complications, significantly reduces the patients' quality of life and hinders their professional work.

The pathogenesis of IBS is complex. The influence of many factors on the development of IBS has already been proven, however, we are still far from precisely explaining the exact pathophysiological mechanisms underlying this disease. Most patients with IBS associate their symptoms with the consumption of certain meals [1, 2, 3]. And although 63% of them know what foods they should avoid, the effectiveness of elimination diets is not always satisfactory [4]. In clinical studies, therefore, more and more attention is being paid to the role of diet in the pathogenesis of IBS and its importance for the clinical course of the disease.

In patients with IBS, the aggravation of disease symptoms associated with dairy product consumption represents a significant clinical problem. Lactose intolerance and lactase deficiency are common problems in the general population, and their importance for the pathogenesis of IBS remains controversial. The reports on the incidence of lactose intolerance among IBS patients are variable and range from 27% to 72%, depending on ethnicity and diagnostic methods [5, 6].

Lactase deficiency (adult type hypolactasia) is the result of the natural decline in intestinal lactase activity in genetically predisposed people, which begins in childhood even from 4 or 5 years of age. The differences in the activity of the lactase enzyme among individuals are due to genetic polymorphism. Hypolactasia leads to the symptoms of lactose intolerance, such as nausea, vomiting, flatulence, choking, gasping, excessive gas, loose stools, or abdominal pain after eating lactose-containing foods.

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These complaints may overlap the symptoms of IBS or lead to an IBS misdiagnosis. The correct diagnosis is important because, unlike IBS, lactase deficiency impairs digestive process and nutrients absorption. In addition, targeted treatment (elimination diet or lactase enzyme supplementation) in patients with hypolactasia leads to rapid clinical improvement.

Fermentation of undigested lactose in the colon by bacteria in individuals with hypolactasia causes abdominal symptoms of lactose intolerance. On the other hand, this process contributes to the short-chain fatty acids (SCFAs) production. SCFAs, mainly acetate, propionate, and butyrate, produced by microbial fermentation of undigested food substances are believed to play a beneficial role in human gut health [7]. Short-chain fatty acids influence colonic health through various mechanisms. In vitro and ex vivo studies show that SCFAs have anti-inflammatory and anticarcinogenic effects, play an important role in maintaining metabolic homeostasis in colonocytes, and protect colonocytes from external harm. SCFAs also have trophic effects, regulate the processes of water and sodium reabsorption in the intestine, and have a beneficial effect on intestinal motility and regulation of the stool rhythm.

Moreover, the gut microbiota has the ability to adapt to the increased supply of dairy products. Although lactose consumption does not increase lactase expression in humans, regular consumption of dairy products appears to reduce hydrogen excretion in HBT and reduces lactose intolerance symptoms [8]. Research in vitro and in vivo demonstrates increases in *Bifidobacteria sp.* and/or *Lactobacilli sp.*, which are considered to be the beneficial components of the microbiota [9, 10]. In a study conducted in Japan, the abundance of *Bifidobacteria sp* correlated positively with dietary lactose intake [11]. Recent research indicates that the i3.1 probiotic is safe and efficacious in reducing lactose intolerance symptoms but did not change the HBT result [12].

Considering the fact that dysbiosis is postulated to play the role in the pathogenesis of IBS, it seems justified to search for methods of therapy aimed at restoring the adequate balance of the intestinal microbiota. This is all the more important as many of the drugs with proven efficacy in the treatment of IBS symptoms, such as linaclotide, plecanatide, lubiprostone or eluxadoline, are not yet widely available (they are not registered in Poland).Therefore, in accordance with the latest recommendations [3], in the treatment of IBS, it is recommended to use probiotic strains tested for efficacy in IBS, as well as rifaximin, which is a eubiotic that restores the correct composition of the intestinal microbiota in an antibacterial mechanism through its modulation. Preliminary data show also that Faecal Microbiota Transplantation (FMT) may be effective and safe in IBS treatment [1, 13, 14, 15]. A recent study showed also that increasing the dose of the transplant and/or repeating FMT led to the remission of gastrointestinal symptoms and to clinically significant improvements in fatigue and quality of life in IBS patients [16]. Nevertheless, current research is made up of short-term studies on small samples, and those data need confirmation in larger evaluations. The aim of the study was to search for a frequency of lactose intolerance symptoms in patients with IBS, depending on the results of hydrogen breath test (HBT).

2. Materials and Methods

2.1. Study design

The study included 56 patients with IBS (45 women and 11 men; mean age 41.2 ± 14.4 years) diagnosed based on the Rome III criteria. The study was conducted from 2012 to 2016. The percentage of patients with predominant diarrhea (IBS-D) was 51.8% (n = 29), with predominant constipation (IBS-C) in 28.6% (n = 16), and with mixed/unclassified type of IBS in 19.6% (n = 11). The control group consisted of 23 healthy volunteers (13 women, 10 men; mean age 38.56 ± 16.61 years). The exclusion criteria were the use of antibiotics or laxatives (including preparation for colonoscopy) within the 4 weeks prior to HBT and the coexistence of organic gastrointestinal diseases. The study was approved by the Bioethics Committee of the Medical University of Lodz on November 20, 2012 - approval No. RNN/214/12/KE.

All study participants, both IBS patients and healthy controls, were asked to complete a questionnaire on IBS symptoms and tolerance of lactose-containing products.

HBT was performed in all subjects with 50 g of lactose (dissolved in 200 ml of water) using the Gastrolyzer (Bedfont) device. The first measurement of exhaled hydrogen was made before the consumption of the lactose solution, and then after it was ingested, at 30-minute intervals, for a total of 240 minutes. An increase in the hydrogen level in the exhaled air by >20 ppm in relation to the initial value was considered a positive result of the HBT for lactase deficiency.

2.2. Statistical analysis

Statistical analyzes were performed using the Statistica 10 (Statsoft, Tulsa, USA). Two independent groups were compared in the analyzed study. Nominal variables are presented as percentages. To compare the two nominal variables, the Chi2 test with Yates's correction or the exact two-tailed Fisher test was used, depending on the size of the study groups. The level of statistical significance was $p < 0.05$.

3. Results

Lactase deficiency (positive HBT test) was diagnosed in 34 (60.7%) patients with IBS and in 10 (43.5%) subjects in the control group, which was not statistically different. There were also no statistically significant differences between the incidence of lactase deficiency in particular IBS types.

Analyzing the prevalence of lactase deficiency in particular age groups of IBS patients, it was shown that there was a positive HBT result in 52% of patients under 36 years of age, 60% between 36 and 60 years of age, and in 100% of patients over 60 years of age. However, these differences between particular age groups were not statistically significant.

All study participants, both IBS patients and control groups, were asked about the occurrence of symptoms (abdominal pain, diarrhea, flatulence, or nausea) after consuming dairy and other lactose-containing food. Based on the questionnaire survey, the frequencies of gastrointestinal complaints among patients in the study group were determined. Flatulence was the most frequently reported symptom in both groups. It was found that abdominal pain and flatulence after consuming lactose were reported significantly more often in IBS patients compared to the control group ($p < 0.05$) (Fig. 1).

Abdominal pain after consuming lactose-containing food was reported significantly more often by IBS women than men (72.7% vs. 12.5%; $p < 0.05$).

There were no significant differences between particular IBS subtypes in the frequency and type of complaints reported after eating lactose-containing food (Fig. 2).

The relationship of subjective symptoms of lactose intolerance reported by the patients in the questionnaire with the results of the HBT was also analyzed (Fig. 3).

Both in the group of patients with IBS and normal HBT result and in patients with IBS and lactase deficiency confirmed by HBT, no statistically significant differences were found in the frequency of symptoms after lactose ingestion. Thus, it seems that the subjective feelings of patients in this area do not clearly indicate documented lactase deficiency.

On the other hand, when analyzing the frequency of reporting subjective symptoms of lactose intolerance among people with normal HBT results, it was found that IBS patients significantly more often reported abdominal pain, diarrhea, and flatulence after eating lactose-containing food compared to the control group ($p < 0.05$); the prevalence of nausea did not differ statistically (Fig. 4).

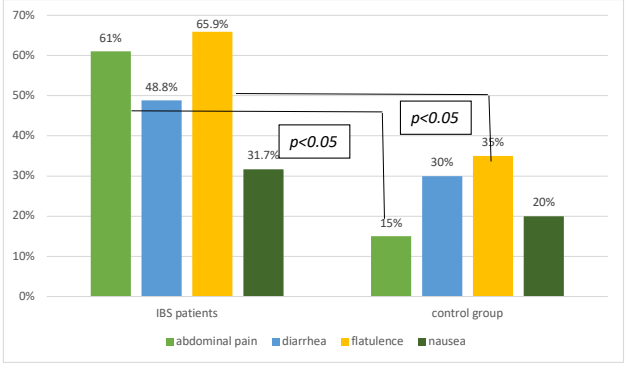


Fig. 1. Self-reported symptoms after consuming lactose in the test and control group

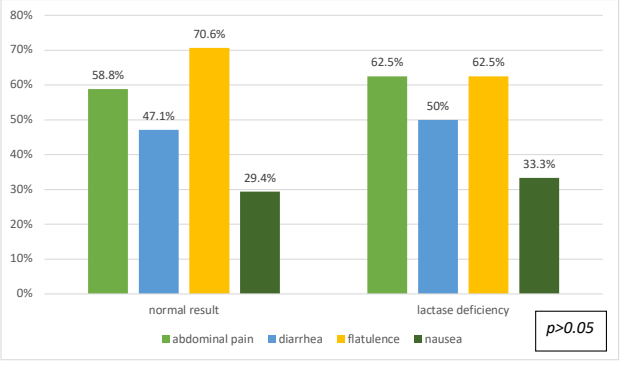


Fig. 3. Symptoms after consumption of lactose-containing products reported by patients from the study group depending on the HBT score

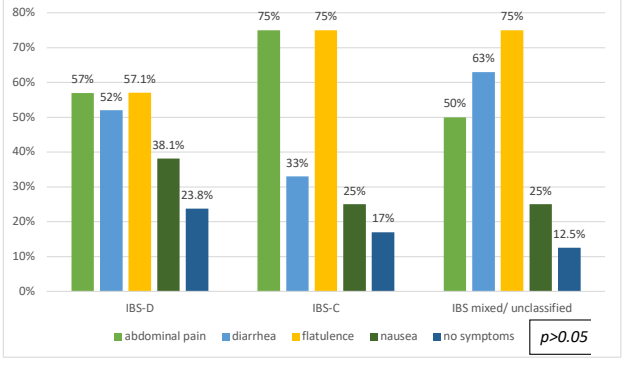


Fig. 2. Symptoms of lactose intolerance reported by patients with particular types of IBS

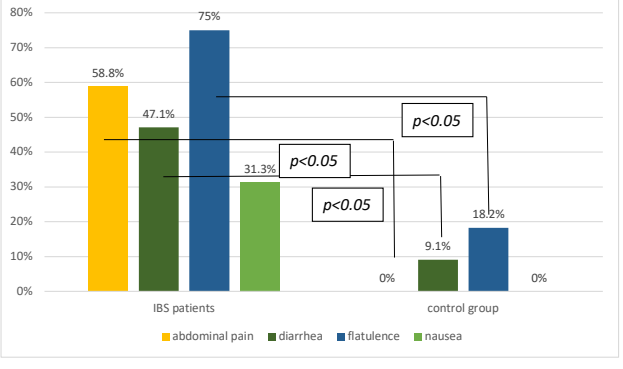


Fig. 4. The incidence of symptoms of lactose intolerance among patients with normal HBT results

The analysis of complaints reported by patients during and after HBT showed no statistically significant differences between the study and control groups.

4. Discussion

Only in about two-thirds of patients reporting symptoms of lactose intolerance, such as abdominal distension, excessive gas production, overflow sensation, vomiting, or diarrhea, is lactase deficiency confirmed by HBT [17]. In the world literature on lactose intolerance and lactase deficiency in IBS patients it has been repeatedly proven that IBS patients more often report symptoms of lactose intolerance compared to healthy people, despite the lack of significant differences in the objective HBT studies [18]. Nevertheless, most of the scientific reports concern the Asian population. So far, no such analysis has been carried out on the adult Polish population.

In the presented group of patients with IBS, lactase deficiency (based on the results of HBT) was confirmed in nearly 61% of patients and this frequency did not differ statistically from the control group. Similarly, the frequency of reporting lactose intolerance symptoms during the HBT did not differ significantly in both groups. A study by Gupta et al. in India in a group of 124 patients with IBS (diagnosis according to the Rome II Criteria) also showed no difference in the incidence of lactase deficiency and lactose intolerance between IBS patients and healthy people (72% vs. 60% and 66% vs 71%, respectively), although there, during the HBT, patients with IBS more often reported symptoms of lactose intolerance [5].

According to our analysis, no statistically significant differences were found in the incidence of lactase enzyme deficiency in individual IBS subtypes. Yang et al. evaluated lactose intolerance among patients with diarrheal IBS, depending on the dose of lactose. In their study, conducted in a group of 60 patients with IBS-D and 60 healthy people, it was shown that symptoms of lactose intolerance (after consuming 40 g of lactose) occurred in 92% of patients and 93% of healthy people [19]. However, after lower doses of lactose (10 g and 20 g), patients with IBS reported abdominal complaints more often than control subjects (18% vs 3% and 47% vs 22%, respectively); the amount of hydrogen in the exhaled air showed a positive correlation with the severity of symptoms. It is most likely caused by visceral hypersensitivity which determines the stronger perception of stimuli in patients with IBS.

The higher incidence of lactose intolerance in patients with IBS-D is noted in some ethnic groups, however, it should be considered that their symptoms may be the result of lactase deficiency, not IBS.

According to Zhu et al., visceral hypersensitivity found in these patients is responsible for the increased perception of symptoms after consuming lactose in patients with IBS [20]. A study conducted in China in a group of 277 IBS patients showed that hydrogen production and colonic distention during the HBT did not differ significantly between IBS patients and the control group. The authors showed that during the HBT, patients with IBS more often than healthy people (53.8 vs 28.1%) present symptoms of lactose intolerance, especially flatulence and a bloating, but only in 59% of them colonic distension was confirmed by objective manometry test [20]. Similar results were obtained in a study by Vesa et al. in Finland [21], where IBS patients also reported symptoms of intolerance after consuming dairy food more often than in the control group (60% vs 27%).

In the present study, patients with IBS reported abdominal pain and flatulence after consuming lactose more often than controls. However, the HBT results did not confirm a statistically significant difference in the frequency of lactase deficiency between those groups. Moreover, no significant differences were found in the frequency of reporting symptoms of intolerance after consuming 50 g of lactose during the HBT between the study group and the control group. Similarly, the results of a study by Vernia et al. in Italy indicated that both in IBS patients presenting symptoms of dairy food intolerance and in patients without those symptoms, the frequency of lactase deficiency, objectively confirmed by the HBT, did not differ statistically [22].

In our analysis, abdominal pain after consuming lactose-containing food was reported in the study group significantly more often by women than men (72.7% vs. 12.5%; $p < 0.05$). The fact that complaints related to lactase deficiency are reported more often by women has been confirmed many times [23, 24]. The gender relationship of symptom perception is multifactorial and mainly includes physiological differences in sex hormones, reactivity to stress and inflammatory responses, as well as socio-cultural differences. These factors determine differences in visceral sensitivity, gastrointestinal motility, and the balance of the autonomic nervous system as potential factors contributing to the increased perception of lactose intolerance symptoms in women. However, in a study from Brazil, carried out on a group of 75 IBS patients (diagnosed according to Rome II Criteria), where lactose intolerance was found in 37% of respondents, no relationship between age, gender or ethnic origin was found with the lactose intolerance occurrence [25]. In turn, a study from Italy showed that the incidence of lactase deficiency increases with age, significantly increasing after the age of 74 [26]. This was also confirmed by previous reports from New Zealand, where in the group of 80 healthy Caucasian women, lactase deficiency was found significantly more often in the age group 60-79 years than in the age group 40-59 (50% vs. 15%) [27]. These data, as is known from the literature, differ in different geographic areas and in different ethnic groups. In our study, we did not find any differences in the frequency of reporting lactose intolerance symptoms depending on the age of the patients, although none of the IBS patients over the age of 60 had a normal HBT result.

Interesting results were obtained from the analysis of lactose intolerance symptoms reported by patients with normal HBT results in the analyzed group—patients with IBS, compared to the control group, significantly more often reported abdominal pain, diarrhea and flatulence after consuming lactose. Two pathophysiological mechanisms are responsible for the aggravation of gastrointestinal complaints in patients with IBS after consumption of lactose-containing foods: excessive intestinal gas retention and visceral hypersensitivity, which also underlie IBS [22]. Therefore, in patients with IBS, even without lactase deficiency, there may be an increased production of fermentation gases, for example methane, and their accumulation in the lumen of the gastrointestinal tract, that intensifies pain due to accompanying visceral hypersensitivity.

5. Conclusions

Concluding, lactase deficiency is detected in over half of IBS patients. This fact is important for determining the pathogenesis of the complaints reported by IBS patients. Therefore, hydrogen tests should be performed in IBS patients in order to rationalize diet recommendations.

In addition, IBS patients are more likely to report symptoms of lactose intolerance than healthy subjects, even in the absence of detected enzyme deficiency. The awareness of this fact may be important for better understanding IBS pathogenesis as well as for elaborating the proper management of patients with this disease.

Abbreviations

HBT - hydrogen breath test, **IBS** - irritable bowel syndrome, **IBS-D** - irritable bowel syndrome with predominant diarrhea, **IBS-C** - irritable bowel syndrome with predominant constipation.

Authors' Contribution

All authors are equally responsible for design, research, and literature review. The statistical analysis and interpretation of the data as well as the preparation of the manuscript were performed by Danuta Domżał-Magrowska and Ewa Małecka-Wojciesko.

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Conflict of Interest

The authors have no potential conflicts of interest to declare.

Ethics Approval

The study was approved by the Bioethics Committee of the Medical University of Łódź on November 20, 2012 - approval No. RNN/214/12/KE.

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