Tolerance of different dairy products in subjects with symptomatic lactose malabsorption due to adult type hypolactasia

Tolerancja różnych produktów mlecznych u osób z objawowym zespołem złego wchłaniania laktozy spowodowanym hipolaktazją typu dorosłych

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Abstract

Introduction: A large portion of the world's population undergoes a genetically programmed decrease in lactase synthesis and may experience symptoms of lactose intolerance (LI) after dairy consumption.
Aim: The aim of the present study was to assess the effect of the same dose of lactose consumed by LI subjects in the form of different dairy products.
Material and methods: Fifteen healthy young adults with LI were enrolled in the study. All subjects were symptomatic homozygotes –13910 C/C in the lactase promoter gene. The hydrogen-methane breath test was performed in each subject after a load of 400 ml of milk, kefir and yogurt. Clinical symptoms were assessed within the 12 h after each product consumption.
Results: The excretion of gases was lower after ingestion of kefir and yogurt in comparison to milk. All examined subjects reported symptoms. After milk consumption, abdominal pain and intestinal rumbling were perceived as more severe. The number of stools was higher and their consistency was more liquid.
Conclusions: Young adults with LI are not able to tolerate the typical dose of different dairy products as assessed by subjective and objective measures. The tolerance of kefir and yogurt is significantly better than that of milk.

Streszczenie

Wstęp: U znacznej części ludności świata produkcja laktazy podlega genetycznie zaprogramowanej redukcji, co może prowadzić do występowania objawów klinicznych nietolerancji laktozy (NL) po spożyciu produktów mlecznych.
Cel: Ocena wpływu spożycia takiej samej dawki laktozy przez osoby z NL, podawanej w postaci różnych produktów mlecznych.
Materiał i metody: Badaniem objęto 15 młodych dorosłych z objawową NL. Wszyscy badani byli homozygotami –13910 C/C w zakresie genu promotorowego dla laktazy. U każdej osoby wykonano wodorowo-metanowy test oddechowy po obciążeniu 400 ml mleka, kefiru i jogurtu. Objawy kliniczne oceniano przez 12 godz. po spożyciu każdego produktu.
Wyniki: Wydalanie gazów było mniejsze po spożyciu kefiru i jogurtu niż mleka. Wszyscy badani zgłaszali objawy kliniczne. Po spożyciu mleka bóle brzucha i przelewania były bardziej nasilone, stwierdzono większą liczbę stolców, a ich konsystencja była bardziej płynna.
Wnioski: Młodzi dorośli z NL nie tolerują typowych porcji produktów mlecznych, co potwierdzono w ocenie subiektywnej i obiektywnej. Tolerancja kefiru i jogurtu jest znacząco lepsza niż mleka.

Introduction

Lactose malabsorption is caused by a decrease in the ability to digest lactose, which is due to a deficiency in the level of lactase (LCT [MIM 603202]). This enzyme, which is necessary for the digestion of lactose, the major carbohydrate in milk, is produced by the expression of the lactase-phlorizin hydrolase gene in the cells lining the small intestine [1]. In the case of decreased LCT activity (hypolactasia), milk consumption can lead to symptoms of lactose intolerance (LI) such as bloating, flatulence, cramps, nausea and diarrhoea, and may contribute to the decision to exclude these products from the diet [2, 3]. A large portion of the world's population undergoes a genetically programmed decrease in LCT synthesis after weaning, which may result in lactose malabsorption [4, 5]. The condition known as adult-type hypolactasia (ATH) is the most common cause of milk intolerance in children, adolescents and adults and the most common enzyme deficiency in humans [6]. Although it has been documented in recent years that a much smaller percentage of individuals with lactose maldigestion develops clinical symptoms [7-9], the issue remains of particular nutritional importance because dairy products are a major source of calcium, vitamin D and other nutrients. In LI individuals, the amounts of these essential nutrients supplied by a diet lacking dairy products may be insufficient to meet the age-appropriate adequate intake [10], as was found in a majority of African American adolescents [11].

One of the strategies in the treatment of LI is to restrict consumption of dairy products; however, such a diet usually contains less calcium than the recommended daily intake. Another approach is the consumption of a diet containing lactose, but only incorporating those products that are better tolerated and/or in quantities that do not cause clinical symptoms. The use of fermented dairy products has long been adopted as a strategy for overcoming LI [12-14]. However, evidence for the efficacy of such an approach is insufficient. Therefore, the aim of the present study was to assess the effect of the same dose of lactose consumed in the form of different dairy products – kefir, yogurt and milk – by lactose-intolerant young healthy adults.

Material and methods

Fifteen highly motivated, clinically symptomatic, otherwise healthy young adults with LI were enrolled in the study. The investigated group consisted of 8 women and 7 men, all of Caucasian descent, aged 20-25 years (mean 22.7 years) with body mass index (BMI) ranging from 19 to 25 kg/m^2 (mean 21.5 kg/m^2). All of the enrolled participants reported symptoms indicative of lactose intolerance prior to the study.

A predisposition to ATH was confirmed by molecular analysis; all subjects were homozygotes C/C at locus 13910 (–13910 C/C) upstream of the *LCT* gene (NM_005915.4:c.1917+326C>T; rs4988235). For –13910 T>C polymorphism detection the kit MutaGEL Lactase (Immundiagnostik AG, Bensheim, Germany) was used. The details of applied methodology have been described elsewhere [9].

Lactose malabsorption (LM) was confirmed in all study participants based on a hydrogen-methane breath test (BT) with a load of 25 g of lactose, following an overnight fast. More specifically, subjects were instructed not to eat or drink for at least 12 h before the test and to avoid slowly digested foods, including beans and other legumes, brans or high-fibre cereals, on the day before the test. Participants were not allowed to smoke, sleep or exercise vigorously for at last 1 h before or at any time during the test. Breath samples were collected at baseline (fasting) and every 30 min within the 3 h after the ingestion of lactose. The samples were analysed with QuinTron MicroLyser DP Plus (Quintron, USA). A positive BT was defined as a breath H_2 level increase of at least 20 ppm over the lowest preceding value within the test period or a breath CH_4 level increase of at least 12 ppm over the baseline within the test period, or as a combined increase (H_2 and CH_4) of at least 15 ppm within the test period.

After selection of the study group a BT was performed three times in each of the subjects (intervals of at least 7 days) after the load of 400 ml of milk, kefir and yogurt given as a single serving to be drank (lactose content 19.2 g, 18.4 g and 19.2 g, respectively). Breath samples were collected at baseline (fasting) and 30, 60, 90, 120, 150, 180, 210, 240, 270 and 300 min after lactose-containing product ingestion. The excretion of gases was expressed as the sum of hydrogen and doubled methane expiration.

Clinical symptoms were assessed within the 12 h after each product load using the questionnaire adopted for the project. The following issues were addressed:
1) abdominal pain (0 – abdominal pain did not occur/1 – discomfort/2 – mild pain/3 – pain impeding the normal functioning/4 – unbearable pain),
2) number of stools (0 – no stool/1, 2, 3... – corresponded to the number of stools),
3) stool consistency (0 – formed/1 – mushy or compressed/2 – loose/3 – liquid),
4) intestinal rumbling (0 – lack/1 – barely perceptible/2 – moderately severe/3 – very severe).

In addition, the BT area under the curve (AUC) was calculated assuming that it reflects semi-quantitatively

the total amount of intestinal gas production over the 5-h period. All values are expressed as median (1st-3rd quartile).

Statistical analysis of the data was performed using the Kruskal-Wallis test with post-hoc comparisons.

Ethical considerations

The protocol of the investigation was approved by the Ethical Committee of the Poznan University of Medical Sciences, Poland (150/11). Written informed consent was obtained from all subjects.

Results

The comprehensive data of BT after loading with milk, kefir and yogurt are shown in Table I. Thirteen subjects exhaled exclusively hydrogen, while in two individuals the excretion of methane was also observed. There were no significant differences in the fasting breath hydrogen/methane levels among the three products. The excretion of gases appeared to be lower after ingestion of kefir and yogurt in comparison to milk. Statistically significant differences did occur from the 60 up to 240 min period of the study. However, the yogurt and the kefir consumption caused peaks that occurred a little bit later than did milk ingestion (180 min vs. 240 min after loading). The value of hydrogen/methane AUC for milk [284.5 ppm h (230.3-371.5)] was significantly higher than for kefir [152.5 ppm h (134.5-205.5)] and yogurt [185.0 ppm h (153.5-196.8)]; ($p < 0.007$ for both). There

were no differences in AUC between fermented products.

All examined subjects reported symptoms after ingesting 400 ml of milk, kefir and yogurt. However, milk consumption resulted in more severe symptoms. Abdominal pain and intestinal rumbling were perceived as more severe. The number of stools was higher and their consistency was more liquid. No differences in the perception of clinical symptoms between kefir and yogurt loading were reported (Table II).

Discussion

The strongest argument for the consumption of dairy products by LI individuals is the beneficial effect of calcium and vitamin D present in milk on skeletal growth and development. In the absence of guidelines for LI subjects, the common therapeutic approach involves the exclusion of milk and dairy products from the diet. An insufficient vitamin D and calcium intake can lead to poor health outcomes, particularly in relation to bone mineral density and the risk of fractures [15, 16]. The determination of whether fermented dairy products can be better tolerated than milk may contribute to the development of evidence-based dietary recommendations that meet the needs of LI individuals.

The enrolment criteria seem to be one of the major limiting factors in the existing studies on hypolactasia. Subjects who are evaluated in such studies often present LM rather than LI [17]. The term LI indicates that

Table I. Hydrogen-methane breath test (ppm) in relation to ingestion of 400 ml of milk, kefir and yogurt in 15 lactose-intolerant subjects

Tabela I. Wyniki wodorowo-metanowego testu oddechowego po spożyciu 400 ml mleka, kefiru i jogurtu przez 15 osób z nietolerancją laktozy

Product		Time [min]										
		0	30	60	90	120	150	180	210	240	270	300
Milk	Median	0	1	5	18	39	49	57	52	44	33	27
	1st-3rd quartile	0-3	0-4	2.5-8.5	9.5-21.5	22-46	38.5-62	39-66	40.5-63.5	36.5-57.5	28-42.5	22-29
Kefir	Median	0	1	2	8	14	23	26	28	31	31	26
	1st-3rd quartile	0-3.5	0-2.5	0.5-4	6-10.5	11-22	17-26	20-33.5	23-37.5	26.5-35	24.5-35	22-32
Yogurt	Median	0	0	1	7	15	21	26	32	33	32	28
	1st-3rd quartile	0-2.5	0-2	0-5	4-8	10.5-15.5	17.5-24.5	20.5-32	24.5-35	25-35.5	26.5-35.5	23-31.5
Statistical significance												
Milk vs. kefir		NS	NS	0.0079	0.0021	0.0019	0.0015	0.0012	0.0012	0.0015	NS	NS
Milk vs. yogurt		NS	NS	0.0171	0.0019	0.0022	0.0007	0.0007	0.0007	0.0007	NS	NS
Kefir vs. yogurt		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS

NS – not significant

Table II. Clinical symptoms reported in relation to ingestion of 400 ml of milk, kefir and yogurt in 15 lactose-intolerant subjects
Tabela II. Objawy kliniczne w odniesieniu do spożycia 400 ml mleka, kefiru i jogurtu przez 15 osób z nietolerancją laktozy

Product	Abdominal pain		Number of stools		Stool consistency		Intestinal rumbling	
	Median	1st–3rd quartile	Median	1st–3rd quartile	Median	1st–3rd quartile	Median	1st–3rd quartile
Milk	2	2-3	2	1.5-3	2	1-2	3	2.5-3
Kefir	1	1-2	1	1-1	1	0.5-1	2	1-2
Yogurt	1	1-1.5	1	1-1	1	0-1	1	1-2
Statistical significance								
Milk vs. kefir	0.0060		0.0015		0.0022		0.0015	
Milk vs. yogurt	0.0033		0.0015		0.0033		0.0010	
Kefir vs. yogurt	NS		NS		NS		NS	

NS – not significant

a person with LM reports clinical symptoms after lactose consumption. Whereas lactase deficiency and LM can be objectively verified by an intestinal biopsy or a breath test, the demonstration of LI relies on self-reported symptoms following lactose ingestion. In the present study, a very careful pre-selection of the study group was carried out, as only LI subjects were enrolled, all of whom reported symptoms indicative of LI prior to the study. According to our knowledge, it is the first study on lactose intolerance in which all patients have a confirmed genetic predisposition to LM. Moreover, a hydrogen-methane rather than a hydrogen breath test was used, allowing for the exclusion of some potential false negative results [18].

Despite a number of investigations evaluating LI subjects, medical literature concerning the use of kefir and yogurt is scarce and does not provide sufficient evidence of their effectiveness in overcoming LI symptoms and in improving health outcomes. The data obtained in the present study indicate that kefir and yogurt are better tolerated than milk by LI subjects, which remains in line with the few surveys carried out regarding these products [13, 19, 20]. Bearing in mind that the calcium content in yogurt is much higher than that in milk (415 mg for plain, low-fat yogurt vs. 285 mg for semi-skimmed milk, respectively, in one cup) [21], it seems reasonable that further research on fermented dairy products is warranted, in order to provide evidence-based, ethnically/racial and age-sensitive evidence.

The data on the tolerance of dairy products by LI individuals presented by different authors are contradictory. Two reviews of the literature on the topic of LI (covering the years 1967-2009) have been published so far. According to the review made by Suchy *et al.* (2010), 50 g of lactose, which is equivalent to the lactose content found

in 1 quart of milk, usually induced symptoms in adults with lactose malabsorption when administered as a single dose without meals, while 12 g of lactose, equivalent to the lactose content in 1 cup of milk, could be tolerated with no or minor symptoms [11]. The conclusion of the review by Shaukat *et al.* (2010) is that even a dose of 15 g can be tolerated [17]. These data are inconsistent with the results of the Hertzler study based on the ingestion of various doses of lactose dissolved in water. He indicated that at most 6 g of lactose may be tolerated by lactose maldigesters [22]. However, natural sources of lactose are better tolerated than lactose dissolved in water. The study by Hertzler and Savaiano (1996) provided the literature's most optimistic appraisal of the daily dosage of lactose that is tolerable by LI subjects. Healthy young adult subjects with self-diagnosed LI were demonstrated to be lactose malabsorbers on the basis of BT. They were fed with either sucrose or lactose for a 10-day period with a 2-day washout between a feeding of the alternate sugar. It was found that these subjects had negligible symptoms at the initiation of lactose feeding with 42 g/day, and that by the end of the 10-day period, they were capable of tolerating 70 g (approximately 1.5 quarts of milk) per day [23]. If the results of this study could be extrapolated to the entire population of LI individuals, LI would not represent an appreciable clinical problem, provided that lactose was routinely ingested in divided doses with meals. Unfortunately, the findings of other authors indicate that much lower doses of lactose may cause gastrointestinal distress in people with LM, even if served in divided doses during the day (12-34 g) [24-26]. In the present study, the load of 400 ml of milk, kefir and yogurt served as a single dose without a meal provoked clinical symptoms in all of the examined subjects. However, the symptoms perceived after the load of fermented

products were significantly lower than those caused by milk. A possible explanation of this phenomenon may be the "autodigestive" capacity of fermented dairy products stemming from their content of β-galactosidase. This enzyme, as was shown previously, survives gastric digestion and remains active in the duodenum, where it may act in lactose digestion [27, 28].

Surveys by Savaiano *et al.* (1984) and Alm (1982) have shown that up to 500 g of yogurt may be tolerated by lactase-deficient persons [13, 29]. In the Savaiano study, a serving of 500 ml of yogurt (lactose content 20 g) without a meal after a fasting period did not cause abdominal distress [13]. In contrast to these results, we have documented that the same product, including the same load of lactose, and served in the same manner, brought about clinical symptoms in all examined individuals. A likely explanation may be related to the enrolment criteria. Subjects who were classified by the researchers as lactose-deficient were probably lactose malabsorbers rather than LI. The differences in tolerance shown by the various studies, carried out under the same conditions, indicate the need for a clearer distinction between LM and LI, not only in research but also in the medical/dietician practice. The Alm study demonstrated the tolerance of 500 ml of yogurt served as a single dose by lactose-deficient individuals; however, the lactose level was decreased after an 11-day storage period, to about 2.3 g/100 g, compared to an initial value of 4.8 g/100 g, giving an effective lactose load of 11.5 g [29].

In the present study, the lactose loads, given in the form of milk, kefir and yogurt, were comparable (19.2 g, 18.4 g and 19.2 g, respectively). However, both the severity of clinical symptoms and the excretion of gases were significantly lower in the case of fermented products. Therefore, it appears that the determination of the maximum tolerated dose of lactose is impossible for all dairy products as a single category. Our findings remain consistent with the results of Savaiano *et al.* and Kolars *et al.* [13, 27]. Savaiano *et al.* concluded that enhanced lactose absorption and tolerance observed with yogurt feeding are not apparent when the same dose of lactose is given in the form of unfermented acidophilus milk or cultured milk. Furthermore, pasteurized yogurt, with a reduction in the inherent lactase activity by 10-fold and a reduction in cell count by 100-fold, still remains better tolerated by LI subjects than does milk [13]. Kolars showed that ingestion of 18 g of lactose in yogurt resulted in only about one third the hydrogen excretion as a similar load of lactose in milk or water, indicating an increased absorption of lactose in yogurt [27].

The results of the present study suggest that the maximum tolerated dose of lactose may be different for fermented products than that for milk. For this reason we suggest that the question posed by many authors [11, 17], which regards the maximum tolerated dose of lactose, should be replaced by a question of the maximum tolerated dose of a specific product, or alternatively the maximum tolerated dose of lactose that is ingested in a specific product. From a practical point of view, this may facilitate in educating lactose-intolerant individuals, as the labels on dairy products do not provide a description of the lactose content, while they do provide information on the volume or weight of the product itself.

Conclusions

Young adults with LI are not able to tolerate the typical dose of different dairy products as assessed by subjective and objective measurement. The tolerance of kefir and yogurt is significantly better than that of milk.

Conflict of interest

None declared.

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