

Mokslinis straipsnis

Investigation of hypolactasia in the elderly

D. Kalibatiėnė, S. Varvuolytė, V. Alekna

Vilnius University

Summary

Data on the prevalence of hypolactasia and lactose intolerance symptoms in the elderly are rather controversial, varying from the decreasing of the capacity to hydrolyse lactose with aging to the persistence of lactose activity during the lifespan. The aim of the study was to estimate the activity of intestinal lactase in the middle-aged and elderly people and the incidence of hypolactasia according to the age, sex and ethnic dependence. The classic diagnostic procedure – lactose tolerance test with measurement of blood glucose level – was performed in 143 persons 37–79 years old. Lactose malabsorption was estimated in 37.8% of the cases. The incidence of hypolactasia did not depend on the sex and age of the examined persons. The prevalence of lactose malabsorption was 41.5% in elderly people (>60 years) and 35.6% in middle-aged persons (37–59 years), but the difference was not statistically significant ($\chi^2 = 0.503$, $df = 1$, $p = 0.478$). In ethnic groups the prevalence of

hypolactasia was 37.5% in Lithuanian, 34.4% in Russian and 43.5% in Polish subgroups.

Keywords:

lactose intolerance, hypolactasia, lactose tolerance test, lactose malabsorption, geriatrics, elderly

Introduction

Lactose (milk sugar) intolerance in adults is mostly due to a genetically encoded decrease of activity of the lactase enzyme (lactase-phlorizin hydrolase, LPH) (hypolactasia) localized in membranes of intestinal epitheliocyte. The morphologic structure of the small intestine and the activity of the other enzymes remain unchanged. The prevalence of primary hypolactasia in Europe varies from 4% to 60% [1, 12, 17, 18].

Secondary hypolactasia as a consequence of intestinal mucosa damage caused by infectious and non-infectious inflammations [2, 4], some chemical substances [6], radiation [16] is far less frequent. In such cases, not only the activity of lactase and but also of other enzymes decreases, the morphology of the small intestine mucosa chan-

Address: D. Kalibatiėnė
VšĮ VMUL
Antakalnio g. 57, Vilnius
Tel.: 234 42 61; mob.: 868247545
E-mail: dank@takas.lt; danute.kalibatiene@vmul.lt

ges. The activity of the enzymes including lactase usually reverts after recovery [1, 19]. Irreversible damage of small intestine mucosa is rather rare in adults. According to Villiers [27], secondary hypolactasia can be caused by a parasitic disease – *Giardia* invasion, *Candida* colonization of small intestine, gluten-sensitive enteropathy, cystic fibrosis of small intestine, cow's milk protein enteropathy and anatomic changes such as short gut syndrome (small intestine resection, gastroenterostomy). It should be noted that in numerous researches dealing with secondary hypolactasia the belonging of the study population to certain ethnic and racial group is disregarded, therefore different prevalence of primary hypolactasia between patients and control groups might occur independently of the main disease.

An assumption that more frequent lactose intolerance in the elderly is referable to secondary hypolactasia could be done. Biologic aging process determines structural and functional changes of all organs (the digestive system included). Biologic oxidative reactions slow down, energetic resources of the cells deplete, neurohumoral changes occur. Anyway, ageing affects digestive tract relatively slightly as it has a large functional reserve. With ageing, the sense of flavour weakens, saliva production as well as the evacuatory function of the stomach decrease, resistance of gastric mucosa diminishes, so the risk of mucosa damage due to medication, particularly non-steroidal anti-inflammatory drugs, increases [20, 25, 28].

The process of ageing does not strongly affect small intestine – the architecture of the enterocyte brush-border membrane and the composition of the mesenteric plexus neurons change a little, but it has not been proven yet that these changes are clinically significant. The motory function of the intestine reverses, the transit of the intestinal content slows, the permeability and absorption of the enterocytes decrease with ageing. Although the supply of the vitamin D is sufficient, calcium absorption diminishes due to the resistance of the small intestine to the effect of 1,25-dihydroxyvitamin D, therefore the demand of calcium in the elderly's diet rises. Calcium malabsorption plays the main role in the decrease of bone mass on ageing both in female and male [13, 20].

The other authors [28] state that intestinal mucosa gets thinner on ageing, and complete mucosa extinction is observed in separate parts of the small intestine. As a consequence, there is a decrease in a number of functioning secretory glandules; the production of the intestinal enzymes and the activity of membranaceous enzymes of

the small intestine undergo changes. The absorptive function of the intestine depletes, i.e. proteins, carbohydrates, lipids are underassimilated. The microbial flora changes with ageing as follows: the number of the fermentation bacteria decreases, the number of the putrefaction bacteria increases. When the putrefaction process in the intestine becomes predominant, the levels of endotoxins increase and affect the functional state of the intestine even more. As a result of atherosclerotic changes, the mesentary circulation can diminish, so acute or usually chronic intestinal ischemia can manifest and influence the structural and functional changes in the intestine as well [13, 20].

A relatively small number of studies on lactose intolerance in the elderly have been published, and their results are controversial. Some authors state that the prevalence of hypolactasia does not change with ageing [9, 18, 24], the others indicate that lactose intolerance and lactose malabsorption increase in older age [12, 26]. The problem of lactose intolerance is especially relevant in geriatrics. In the elderly, calcium absorption from the intestine decreases, so there is a demand of more calcium in the nourishment. Milk and other dairy products are the main sources of calcium for human organism, whereas because of impaired digestion of these products and malabsorption of particular nutrients bone mineral density can be affected and a risk of bone fracture increases.

It was observed by Obermayer-Pietsch et al. that lactose malabsorption in the elderly was related to the reduction of calcium assimilation, a decrease of bone mineral density and osteoporotic bone fractures [22]. After investigation of 483 old persons (over the age 85 years) Enattah et al. determined that femoral and wrist bone fractures were much more frequent in persons with hypolactasia [10]. Buchowski et al. investigated lactose maldigestion and lactose intolerance correlation with calcium intake in black women at the perimenopause phase. The average calcium intake was significantly lower in women with lactose intolerance. Milk and dairy products (45%) were determined as the main calcium source for women tolerating lactose, and for those with lactose intolerance calcium was supplied from other products (46%). Body mass index was higher in women intolerating lactose, and calcium intake had a negative correlation with the body mass index [3].

According to Debongnie et al., in case of hypolactasia less proteins, calcium, magnesium, phosphorus are assimilated from the diet. Newcomer et al. have found that persons with hypolactasia can experience osteoporosis of clearly undefined etiopathogenesis, but one of its reasons

may be calcium deficiency in the organism [21]. After investigating women in New Zealand, Wheadon et al. have determined that lactose intolerance is one of risk factors for the development of type II osteoporosis in the elderly [29]. Furthermore, Griessen et al. state that individuals with high lactase activity assimilate more calcium from milk [14]. Halpern et al. [15], Wirth et al. [30] assume that calcium assimilation is not related to the lactase activity. Thus, this problem remains controversial and insufficiently explored for the moment.

The aim of the present study was to determine the activity of the intestinal enzyme lactase in middle-aged and elderly individuals, to compare hypolactasia prevalence between two study groups as well as with the results of the epidemiologic hypolactasia study formerly performed by the authors, to analyse the prevalence of hypolactasia considering the ethnic belonging, age and gender of the study population.

Study population and methods

The study was carried out in 2004–2005 at two Vilnius city primary health care institutions: Baltupiai family medicine centre and Naujamiestis subdivision of the Centras out-patient clinic. The study was approved by Lithuanian Bioethics Committee. Inclusion criteria: consent to participate in the study (carefully read and signed patient information / consent form), age over 18 years. Exclusion criteria: diabetes mellitus and other disorders of carbohydrate metabolism, perceptual disorders and disorientation, organic diseases of the digestive system.

143 persons with mild or moderate arterial hypertension without any other significant health disorders which could influence or interfere with the performance or interpretation of lactose tolerance test were investigated. The age of the individuals varied from 37 to 79 years (mean \pm standard deviation 56.38 ± 8.74). There were 99 women (69.2%) and 44 men (30.8%). All the persons were divided into two groups: the middle-aged (37–59 years) group comprised 90 individuals and the elderly (60–79 years) group consisted of 53 persons. The female and male proportion was similar in both groups. There were 61 women (67.8%) and 29 male (32.2%) in the middle-aged group, and 38 female (71.7%) and 15 male (28.3%) in the elderly group.

Hypolactasia prevalence in almost healthy individuals from Telšiai, Ukmergė, Utena, Vilnius regions [18] was investigated by the co-author of the paper D. Kalibatiėnė in 1984–1998; this cohort comprised the control group in

the present study. The random sampling method was applied. The inclusion and exclusion criteria were identical. There were 674 individuals in the prevalence study group, of them 491 belonged to the middle-aged group (37–59 years) and 183 to the elderly group (60–79 years).

All patients underwent clinical investigation. Lactose tolerance test was employed for the assessment of the activity of the intestinal enzyme lactase due to its high specificity (up to 96%) and sensitivity (up to 94%) as well as a relatively simple procedure using the facilities of out-patient clinic [1]. The patient drank 50 g lactose dissolved in 200 ml water (boiled) of room temperature. Blood glucose levels in capillary blood were assessed just before drinking and afterwards every twenty minutes for an hour (four times in total). Elevation of the glycemic curve was evaluated. If the increase of the capillary blood glucose level did not exceed 1.1 mmol/l, hypolactasia was confirmed. If the glucose level was higher than 1.1 mmol/l, it was considered that the activity of enzyme lactase was not decreased [1, 18, 19, 23].

All the patients were questioned as well. One group of questions included items concerning the detection of the tolerance of milk and other dairy products tolerance, digestion disorders, especially after meals, and other diseases that could influence digestion. Additionally, questions about family eating habits were presented. The other part of questions aimed to determine the patients' ethnic belonging by inquiring about patients' birthplace (country, district) and patients', their parents' and grandparents' mother-tongue. The form concerning lactose intolerance symptoms was also incorporated in the questionnaire.

The statistical analysis of the study data was done using "SPSS 12.0 for Windows" statistical package. Equality of the means was verified using Student's t test along with the evaluation of dispersion measure of the samples. The difference of dispersion measures and means of the samples were considered statistically significant when p was less than 0.05. The association of the prevalence rate of hypolactasia with the nationality, age and gender was assessed using the Chi square test of independence. The variables were significantly related to each other then p was less than 0.05. The Chi square test for homogeneity was used to verify the hypothesis about the equality of variable proportions.

Results

According to the questionnaire, 72 individuals out of 143 investigated persons regarded themselves as Lit-

huanians (50.3%), 32 as Russians (22.4%), 23 as Poles (16.1%) and 15 as other (11.2%) ethnic groups. There were 436 Lithuanians (64.7%), 20 Russians (3%), 102 Poles (15.1%) and 116 other or mixed nationalities persons (17.2%) in the group of prevalence study (674 persons). The other nationalities included Byelorussians, Ukrainians, Jews.

After testing lactose tolerance it was determined that in the study population of 143, 89 persons (62.2%) showed no decrease in the activity of the small intestine enzyme lactase, and hypolactasia was diagnosed in 54 individuals (37.8%). 436 persons (64.7%) out of 674 persons in the prevalence study group did not experience any decrease in lactase activity and 238 individuals (35.3%) confirmed to have hypolactasia. There was no significant difference ($p < 0.05$) in hypolactasia prevalence rate when comparing the patients' group to the prevalence study group.

After evaluating hypolactasia prevalence rate in middle-aged and elderly individuals in the sample of prevalence study, it was estimated that there was no increase of hypolactasia rate in the elderly. The prevalence rate of hypolactasia in the patients' group was higher (41.5% compared to 35.6%). However, statistical analysis showed

that age and hypolactasia rate were independent variables (Table 1). The rising tendency of lactose malabsorption can be explained doubly – either ageing influences lactase activity or the nationality of a person determining higher or lower prevalence rate of primary hypolactasia was not counted in this analysis.

Analysing hypolactasia prevalence rate with respect to gender, an increasing tendency of hypolactasia in women (3.0%) compared to men (33.0%) in the prevalence study was established, but there was no significant difference. No such tendency was observed in the patient group (Table 2).

The hypolactasia prevalence rate in particular ethnic groups was studied (Table 3). The rate of hypolactasia varied in patients; it was lowest in Russians, but there was no statistically significant difference, probably due to a small number of the study population. Hypolactasia was diagnosed significantly more often in Poles and more rarely in Russians in the prevalence study group. Comparing hypolactasia prevalence in groups of patients and in the prevalence study, it was stated that lactose malabsorption in Poles presented as frequently as in mixed nationality individuals. There was determined no significant difference

Table 1. Hypolactasia prevalence rate in middle-aged individuals and elderly

Study groups	Group of 37–59 years old			Group of 60–79 years old		
	Total number	H*	H* %	Total number	H*	H* %
Patients (n = 143)	90	27	35.9**	53	25	39.4**
Prevalence study group (n = 674)	491	172	35.0	183	66	36.1

* – individuals with diagnosed hypolactasia

** – nonsignificant difference between measures ($\chi^2 = 0.503$, $df = 1$, $p = 0.478$).

Table 2. Hypolactasia prevalence rate relation to gender

Study groups	Males			Females		
	Total number	H*	H* %	Total number	H*	H* %
Patients (n = 143)	44	18	40.9**	99	36	36.4**
Prevalence study group (n = 674)	502	168	33.5	609	222	36.5

* – individuals with diagnosed hypolactasia

** – proportions of hypolactasia prevalence rate in females and males are equal ($\chi^2 = 0.268$, $df = 1$, $p = 0.605$).

Table 3. Ethnic reliance of hypolactasia prevalence rate

Ethnic groups	Patient group			Prevalence study group		
	Total number	H*	H* %	Total number	H*	H* %
Lithuanians	72	27	37.5**	436	142	32.6
Russians	32	11	34.4**	20	4	20.0
Poles	23	10	43.5**	102	43	42.2
Others	16	6	37.5**	116	45	38.8
Total	143	52	37.1	674	234	34.7

* – individuals with diagnosed hypolactasia

** – homogenic groups according to hypolactasia prevalence rate ($\chi^2 = 0.479$, $df = 3$, $p = 0.924$).

Table 4. Hypolactasia prevalence rate in relation to age in the ethnic group of Lithuanians

Study groups	37–59 years			60–79 years		
	Total number	H*	H* %	Total number	H*	H* %
Patients (n = 143)	39	14	35.9**	33	17	39.4**
Prevalence study group (n = 674)	314	100	31.8	122	42	34.4

* – individuals with diagnosed hypolactasia

** – nonsignificant difference between measures ($\chi^2 = 0.093, df = 1, p = 0.760$).

of hypolactasia prevalence in Lithuanian groups, and only in the Russian group hypolactasia occurred more often.

Hypolactasia was diagnosed more frequently in elderly Lithuanians (39.4%) compared to both middle aged Lithuanians (35.0%) and elderly Lithuanians in the prevalence study (34.4%) (Table 4). There was a similar prevalence of hypolactasia in middle-aged and elderly individuals in the prevalence study group (no significant difference was found). The other ethnic groups were not analysed in this regard due to a small number of participants.

Discussion

Our study showed that hypolactasia prevalence rate was 37.8% in the Vilnius population aged 37–79 years with a mild or moderate arterial hypertension and 35.3% in almost healthy population of the same age from different regions of the country. The difference was estimated not to be statistically significant, and it can be stated that the prevalence rates were equal. Thus, there is an assumption that mild arterial hypertension does not affect the activity of lactase, although to confirm this statement a larger number of study population and a thorough clinical examination as well as laboratory tests and instrumental investigations are needed. The varying hypolactasia prevalence established in our study in different ethnic groups (Fig. 2) confirms the genetic origin of primary hypolactasia, which determines the variation of hypolactasia prevalence in ethnic populations.

Hypolactasia prevalence was related neither to the gender nor to the age of the study population, and the observed increasing tendency of lactose malabsorption in the elderly over 60 years was insignificant (Fig. 1). It is stated in the conclusions of the study of lactose intolerance and malabsorption in the elderly carried out by Di Stefano et al. that the prevalence of lactose malabsorption increases with ageing. The influence of age, race and gender on lactose digestion was evaluated in the study. A significant increase of lactose malabsorption prevalence in the study po-

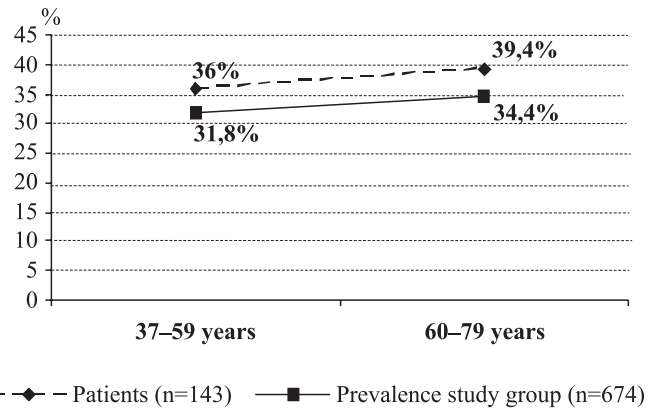


Fig 1. Hypolactasia prevalence rate in relation to age in the ethnic group of Lithuanians

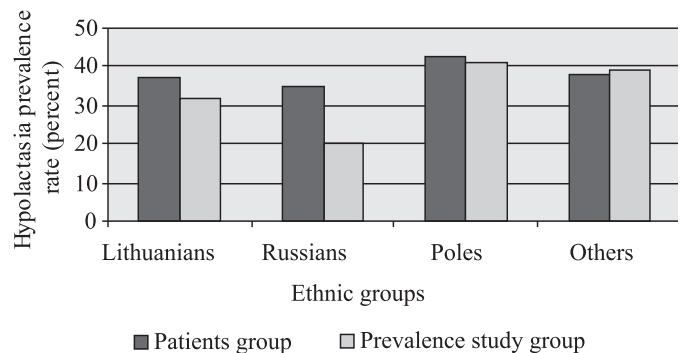


Fig. 2. Hypolactasia prevalence rate in ethnic groups

pulation older than 50 years was observed. Furthermore, the difference related to age was more often registered in representatives of the black race [9].

Investigation of lactose tolerance in 89 adults aged 20 to 89 years (52 blacks (or African Americans), 46 whites, 48 males, 50 females) has shown that lactose malabsorption is much more frequent in individuals aged over 50 years (46%) than in younger adults (26%). There were 2.4-fold more individuals with lactose malabsorption in the blacks than in the whites group among younger adults, and this ratio was 3.6 in the groups of elderly. The differences between age and ethnic groups were extremely significant. The results of the research revealed that lactose malabsorp-

tion prevalence related to age was significantly higher in blacks [24]. Suarez et al. did not observe any difference of lactose malabsorption prevalence between two age groups (over 65 years and 20–40 years) [26]. No significant differences in lactose intolerance prevalence in an investigation of lactose malabsorption in rural Finnish areas between older and younger adults were determined [5].

Conclusions

1. A decrease of the activity of the small intestine enzyme lactase was observed in more than one third (37.8%) of middle-aged and elderly persons (37–79 years old) with a mild or moderate arterial hypertension.
2. Hypolactasia prevalence rate was related neither to age nor to gender. Hypolactasia was more frequent (41.5%) in elderly (over 60 years) with arterial hypertension compared to middle-aged (37–59 years) study population (35.6%), but the difference was insignificant.
3. There was no significant difference of hypolactasia prevalence rate in ethnic patient groups with arterial hypertension (Lithuanians 37.5%, Russians 34.4%, Poles 43.5%).

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HIPOLAKTAZIJOS TYRIMO PAGYVENUSIEMS ŽMONĖMS ĮVERTINIMAS

D. Kalibatienė, S. Varvuolytė, V. Alekna

Vilniaus universitetas

Santrauka

Hipolaktazijos ir laktozės netoleravimo pagyvenusiems asmenims tyrimai palyginti negausūs, o jų rezultatai kontraversiški: vieni autoriai teigia, kad pagyvenusiems ir seniems žmonėms hipolaktazijos dažnis nekinta, kiti pateikia įrodymų, kad vyresniame amžiuje laktozės netoleravimas ir laktozės malabsorbcija dažnėja. Mūsų tyrimo tikslas buvo ištirti plonosios žarnos fermento laktazės aktyvumą pagyvenusiems ir vidutinio amžiaus asmenims, palyginti hipolaktazijos dažnį abiejose grupėse, taip pat su autorių anksčiau atlikto epidemiologinio hipolaktazijos tyrimo rezultatais, palyginti ir išanalizuoti hipolaktazijos dažnį priklausomai nuo tiriamųjų etninės priklausomybės, amžiaus ir lyties. Hipolaktazijos diagnostikai taikėme laktozės toleran-

cijos testą, įvertinant glikeminės kreivės pakilimą, ir anketinę apklausą. Ištyrėme 143 asmenis (37–79 m.), sirgusius mažo ar vidutinio laipsnio arterine hipertenzija. Plonosios žarnos fermento laktazės aktyvumo sumažėjimas pasireiškė 37,8% vidutinio amžiaus ir pagyvenusių ligonių. Nustatytas hipolaktazijos dažnis tam tikrose etninėse ligonių grupėse – lietuvių – 37,5%, rusų – 34,4%, lenkų – 43,5%, buvo statistiškai nereikšmingas ($\chi^2 = 0,478$, $df = 2$, $p = 0,787$). Stebėta hipolaktazijos dažnėjimo tendencija vyresnio amžiaus (>60 m.) ligoniams (41,5%), palyginti su vidutinio amžiaus (37–59 m.) tiriamųjų grupe (35,6%), nors hipolaktazijos dažnio proporcijos lyginamose amžiaus grupėse buvo panašios ($\chi^2 = 0,503$, $df = 1$, $p = 0,478$), t. y. skirtumas buvo statistiškai nereikšmingas. Ištirtiems asmenims hipolaktazijos dažnis ir lytis yra nepriklausomi požymiai ($\chi^2 = 0,268$, $df = 1$, $p = 0,605$).

Raktažodžiai:

laktozės tolerancija, hipolaktazija, laktozės tolerancijos mėginys, laktozės malabsorbcija, geriatrija, pagyvenę žmonės