# Impaired tolerance of indigestible carbohydrates in adults with subjective milk intolerance

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#### Abstract

**Background:** Some Finns report a diminution of milk-related gastrointestinal symptoms when they travel or live abroad. Change in the overall diet may explain the diminution of symptoms.

*Objective:* The aim was to determine whether these symptomatic subjects are actually sensitive to indigestible carbohydrates found in a typical Finnish diet.

**Design:** Nineteen symptomatic subjects whose milk-related symptoms decreased abroad were interviewed. Symptoms and hydrogen excretion were measured after ingestion of rye bread and xylitol in six symptomatic and nine control subjects. In addition, gastrointestinal symptoms during 3 day interventions with rye and wheat bread were studied in five symptomatic subjects.

**Results:** The symptomatic subjects experienced more symptoms than the controls after rye bread and xylitol ingestion (p = 0.0003, p = 0.042). Breath hydrogen excretion was similar in both groups. The symptomatic subjects experienced more symptoms during the rye bread than the wheat bread intervention (p = 0.036). **Conclusion:** Some individuals reporting milk-related gastrointestinal symptoms may actually react to indigestible carbohydrates in the diet.

Keywords: gastrointestinal symptoms; lactose malabsorption; rye bread; xylitol

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## Introduction

Some adults claim to be intolerant to cow's milk, even though neither lactose intolerance nor cow's milk allergy can be diagnosed. Some report experiencing gastrointestinal symptoms comparable to those of lactose intolerance after consumption of Finnish milk, but abroad they are able to consume local dairy products without symptoms. Most commonly used milk in Finland is homogenized, pasteurized low-fat milk (0.1-1.5% fat) (1). To the authors' knowledge, no differences in the texture or processing of milk exist between Finland and other developed countries, that could explain the dissimilarity of symptoms. However, differences in the diet are likely to occur between Finland and other countries.

The Finnish diet contains marked amounts of indigestible carbohydrates; for example, the average

daily consumption of rye products, high in indigestible fibre, is 100 g in men and 66 g in women (1). Indigestible carbohydrates, such as sweeteners (2, 3), fructo-oligosaccharides (4, 5) and galactooligosaccharides (6), have been observed to induce symptoms similar to those of lactose intolerance in some individuals, although not in all (7, 8). According to Teuri et al. (5), pseudohypolactasic subjects mistakenly believe that they have lactose malabsorption, but are actually reacting to indigestible carbohydrates.

It was hypothesized that consumers having gastrointestinal symptoms only in Finland may actually react to the indigestible carbohydrates common in the Finnish diet. The aim was to compare the tolerance of indigestible carbohydrates between these symptomatic subjects and healthy controls. Breath hydrogen excretion after ingestion of indigestible carbohydrates was also studied.

## Subjects and methods

In the first part of the study, 19 Finnish subjects (mean age 35 years, six male), who had contacted Valio Consumer Service because of their experience of better tolerance to milk outside Finland, were interviewed about their dietary habits and symptoms.

Of the interviewed subjects, six volunteered to continue with the clinical part of the study (mean age 34 years, range 24–61 years, three male). Nine volunteers with a good tolerance of Finnish milk and foods often related to gastrointestinal symptoms, i.e. rye bread, peas and onion, served as controls (mean age 43 years, range 25–63 years, two male). Digestion of lactose was diagnosed in all the study subjects. One symptomatic subject and one control were diagnosed as having hypolactasia. Because all the symptomatic subjects were able to ingest milk without symptoms abroad, there was no possibility of cow's milk protein allergy. None of the symptomatic subjects or controls had any gastrointestinal disease.

The study protocol was approved by the Ethics Committee of the Hospital District of Helsinki and Uusimaa. Informed consent was obtained from the subjects.

## Trial I

Hydrogen excretion was detected directly from tidal air with a Micro H<sub>2</sub> Meter (Micro Medical, Kent, UK). After an overnight fast (>10 h) the subjects ingested lactose (25 g, equal to 500 ml of milk; DMV International, Veghel, The Netherlands), xylitol (25 g, equal to 170 g of xylitol sweets; Oriola, Espoo, Finland) and rye bread (270 g, containing 21 g rye fibre; Fazer Bakeries, Finland). The lactose and the xylitol were both dissolved in 300 ml of water, and hydrogen was measured twice an hour for 3 h, or until hypolactasia was diagnosed (increase in breath hydrogen  $\geq 20$  ppm). The rye bread was ingested in 90 g portions with 150 ml of tea, at time 0 and after 3 h and 5 h, and hydrogen was measured twice an hour for 8 h. The subjects were forbidden to consume anything other than water during the measurements. Subjects were advised not to consume foods often related to gastrointestinal symptoms, i.e. rye bread, peas and onions, during the day before the study and on the

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study day. The challenges were performed at least 7 days apart. On each challenge day the subjects recorded flatulence, bloating, gastrointestinal pain, stomach rumbling, nausea and headache, every 1-2 h for 14 h (graded from 0 = no symptoms to 4 = severe symptoms), and the number and consistency of stools (graded from 0 = hard to 4 = watery). The possible score was 0-36 points symptom<sup>-1</sup> day<sup>-1</sup> and for the sum of gastrointestinal symptoms (flatulence, bloating and pain) 0-144 points day<sup>-1</sup>.

## Trial 2

Five symptomatic subjects (mean age 36 years, three male) participated in the last part of the study, in which gastrointestinal symptoms were compared during the 3 day challenges with rye bread (6 slices day<sup>-1</sup>, 167 g; Fazer Bakeries, Finland) and wheat bread (6 slices day<sup>-1</sup>, 158 g; Vaasan & Vaasan, Finland) in an open, randomized, cross-over setting. A 4 day washout period preceded both bread challenges. Subjects were advised to follow their normal diet, but not to consume foods that induce gastrointestinal symptoms during the washout periods and challenges. The subjects recorded abdominal pain, flatulence, bloating and nausea (graded from 0 = no symptoms to 3 = severe symptoms), and the number and consistency of stools (graded from 0 = hard to 4 = watery) daily during the study, and kept a complete food record during the days of bread consumption. The possible score for the three challenge days was 0-9 points symptom<sup>-1</sup> and for the sum of gastrointestinal symptoms (flatulence, bloating and pain) 0-27 points. All subjects consumed rye bread as a part of their conventional diet before the study.

## Statistics

In the both parts of the study the primary variables were the sum of all gastrointestinal symptoms (flatulence+bloating+abdominal pain) and the score of each symptom. The hydrogen results in parts per million (ppm) were converted to millilitres and counted as the area under curve (AUC) of the whole 3 h or 8 h of measurement. Independent samples *t*-test and Fisher's exact test were used to estimate statistical significance. The results are expressed as mean and 95% confidence interval (95% CI) for the difference. A *p*-value of <0.05 was considered significant.

### Results

Intolerance of milk was experienced only in Finland, and good tolerance of milk was experienced in France (mentioned by eight subjects), Germany (n=6), England (n=5), 12 other European countries, the USA (n = 5), the Middle East (n = 4), the Far East (n=3), South America (n=2) and Australia (n = 2). All subjects listed several countries. In 14 cases the reason for going abroad was vacation, and in 11 employment. The duration of stay stretched from 3 days to 1.5 years (median 14 days). All subjects consumed rye bread and vegetables in Finland, and abroad most of the subjects reduced (n = 8) or interrupted (n = 8) their rye bread consumption. About half of the subjects did not change their milk consumption abroad (n = 10), and the other half increased their consumption (n = 9). All subjects were able to drink more than 300 ml of milk without symptoms abroad.

The symptomatic subjects had more severe gastrointestinal symptoms than the controls after a single ingestion of rye bread and xylitol: the mean symptom score after rye bread was 17.2 versus 5.0, difference 12.2 (95% CI 7.0–17.4, p = 0.0003), and after xylitol 12.7 versus 1.6, difference 11.0 (95% CI 0.6–21.5, p = 0.042; Fig. 1). All of the symptomatic subjects, but only 22% of the controls, experienced bloating after rye bread ingestion (p = 0.021). The AUC of the breath hydrogen excretion did not differ between the study groups. Ingestion of rye bread increased the breath hydrogen excretion clinically significantly (>20 ppm) in one control, and ingestion of xylitol in none of the subjects. There was no difference in stool number and consistency between the study groups.

The gastrointestinal symptoms of the symptomatic subjects were more severe during the rye bread than the wheat bread challenge, the sum of symptoms being 9.2 versus 3.2, difference 6.0 (95%) CI 0.7 - 11.3, p = 0.036; Fig. 2). There was no difference in stool number and consistency between the challenges. Mean daily ingestion of rye bread was 196 g (range 154-248 g) and mean daily ingestion of wheat bread was 177 g (156-225 g) during the respective challenges. Daily ingestion of milk remained constant over the rye and wheat bread challenges (335 and 334 g, respectively). Subjects ingested more vegetables, fruits and berries during challenge with wheat bread, compared with rye bread (290 vs 186 g day<sup>-1</sup>, p = ns). Daily intake of energy, protein, fat and carbohydrates did not significantly differ between the rye and wheat bread challenges (7.7 and 9.2 MJ, 76 and 84 g, 63 and 78 g, and 239 and 279 g, respectively). Mean intake of fibre was 27 g day<sup>-1</sup> during rye bread and 20 g  $day^{-1}$  during wheat bread challenge, the mean intake of lactose being 14 and 16 g day $^{-1}$ , respectively.

#### Discussion

The main result of the study was to show a limited tolerance of rye bread and xylitol in subjects reporting milk intolerance in Finland. The results of this study with a limited number of subjects,



*Fig. 1.* Sum of gastrointestinal symptoms during the 12 h following single challenges with rye bread and xylitol in symptomatic subjects (n = 6) and controls (n = 9) (mean  $\pm$  SD).



*Fig.* 2. Gastrointestinal symptoms during the 3 day interventions with rye and wheat bread in the symptomatic subjects (mean  $\pm$  SD, n = 5).

recruited from a small cohort, is in agreement with a study in which pseudohypolactasic milk-intolerant subjects with normal lactose absorption experienced intolerance of fructo-oligosaccharides, while healthy controls were symptom free (5).

In the present study breath hydrogen excretion did not correlate with the carefully monitored gastrointestinal symptoms. The method used is common in the diagnosis of lactose malabsorption (9), and is also reported in the measurement of absorption of indigestible carbohydrates such as dietary fibre and sweeteners (2, 10). However, hydrogen excretion does not always correspond to the symptoms (11). There was no marked difference in hydrogen excretion between the groups, but it is possible that the symptomatic subjects reacted to small increases in intestinal gas production. Gases other than hydrogen could also have caused the symptoms, but were not measured because of methodological limitations.

The consumption of liquid milk in Finland is one of the highest in the world (146 litres per capita in the year 2002; Information Centre of the Ministry of Agriculture and Forestry, Finland, 2003), and therefore the milk consumption of a Finn may decrease in countries where milk is rarely served, resulting to a diminution of milk-related symptoms. However, this was not the case among these symptomatic subjects as none of them reported decrease in milk consumption abroad. Psychological aspects may also affect the symptoms. In the present study cessation of milk-related symptoms was experienced almost as often during employment as during vacation, so relaxation during a vacation abroad cannot explain the lack of symptoms. Some subjects who experience cessation of milk-related symptoms abroad may have irritable bowel syndrome, and this should be investigated in further studies.

In conclusion, some individuals reporting milkrelated gastrointestinal symptoms may actually be reacting to indigestible carbohydrates in the diet. The cause of gastrointestinal symptoms is often difficult to identify, and therefore dietary restrictions should be conducted only after thorough dietary and symptom follow-ups.

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