Role of irritable bowel syndrome in subjective lactose intolerance 1, 2

Tuula H Vesa, Leena M Seppo, Philippe R Marteau, Timo Sahi, and Riitta Korpela

ABSTRACT It has been suggested that the symptoms of irritable bowel syndrome (IBS) may be wrongly attributed to lactose intolerance. We examined the relations among IBS, demographic factors, living habits, and lactose intolerance. On the basis of a lactose tolerance test with ethanol, 101 of the 427 healthy subjects studied were lactose maldigesters and 326 were lactose digesters. IBS was diagnosed by means of the Bowel Disease Questionnaire, according to the Rome criteria. The use of dairy products and symptoms experienced after their consumption were recorded. IBS was found in 15% of both the lactose maldigesters and lactose digesters. One-third of the subjects reported intolerance to dairy products containing ≤20 g lactose. About half of this third were lactose maldigesters and about half were lactose digesters. As explanations for this subjective lactose intolerance, the logistic regression model estimated lactose maldigestion (odds ratio: 10.3; 95% CI: 5.2, 20.4), IBS (4.6; 2.1, 10.1), experience of symptoms other than gastrointestinal ones (2.3; 1.2, 4.5), and female sex (2.1; 1.1, 4.0). Characteristics common to both subjective lactose intolerance and IBS were female sex and the experience of abdominal pain in childhood (P < 0.01). Age, regularity of meals, and the amount of physical activity were not associated with either subjective lactose intolerance or IBS. Of the subjects with IBS, the percentage of lactose maldigesters was the same as in the whole study group (24%) but the number who reported lactose intolerance was higher (60% compared with 27%, P < 0.001). We showed a strong relation among subjective lactose intolerance, IBS, the experience of abdominal pain in childhood, and female sex. Am J Clin Nutr 1998;67:710–5.

KEY WORDS Lactose intolerance, irritable bowel syndrome, functional bowel disorder, sex, Bowel Disease Questionnaire, humans

INTRODUCTION Both irritable bowel syndrome (IBS) and lactose intolerance are common causes of gastrointestinal problems. The prevalence of IBS in a healthy Finnish population has not been studied, but in other industrialised countries it is estimated to be 12–17% (1–4). The prevalence of lactose maldigestion is 17% in Finland, 15–50% in central Europe, and 6–19% in white Northern Americans (5). The symptoms of IBS resemble those of lactose intolerance and can easily be confused. It has been shown in several controlled clinical studies that gastrointestinal symptoms attributed to lactose intolerance often occur indepen- dently of lactose maldigestion and that numerous subjects experience as many symptoms after ingestion of lactose-free milk as after several grams of lactose, even those who claim to be sensitive to lactose (6–8). Lactose digesters frequently relate their gastrointestinal symptoms to milk drinking and lactose intolerance (7, 9, 10). Some authors have suggested that underlying IBS might explain some of the symptoms associated with lactose intolerance (11, 12).

The occurrence of lactose maldigestion in patients with gastrointestinal complaints has been studied in several recent works (13–16) but we know of no study that has determined the occurrence of functional bowel disorders in patients with subjective sensitivity to lactose. The present study was undertaken to examine whether IBS can explain subjective lactose intolerance, and to what extent IBS and subjective lactose intolerance are related to demographic factors, living habits, and symptoms other than gastrointestinal ones (eg, pain, tiredness, insomnia, depression, heartburn, or tachycardia).

SUBJECTS AND METHODS Subjects

The population under study included healthy subjects who had already participated in one of three studies on lactose maldigestion at the beginning of 1970s. In these earlier studies the subjects had been invited to participate during a health examination to which all students of the University of Helsinki had been called (17; study 1), had been randomly drawn for a follow-up study of lactose intolerance (18–20; study 2), and had been selected as a representative family population consisting of 11 families for investigation of the inheritance of hypolactasia (21; study 3). In the present study, 15% of the subjects were from the first study, 41% were from the second study, and 44% were from the third study.

One hundred one of the subjects (24%) were lactose maldigesters and 326 (76%) were lactose digesters on the basis

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Received June 4, 1997.
Accepted for publication September 26, 1997.
of a lactose tolerance test with ethanol (22). The criteria for lactose maldigestion were a maximal rise in blood glucose concentration < 1.1 mmol/L (20 mg/100 mL) and a maximal rise in blood galactose concentration ≤ 0.3 mmol/L (5 mg/100 mL). The possibility of secondary hypolactasia was excluded by a glucose-galactose tolerance test with ethanol or by direct enzyme assays from a small intestinal biopsy sample. The mean age of the subjects was 52 y (range: 36–74 y) and 52% were women and 48% were men; the sex distribution was the same for lactose maldigesters as for lactose digesters. All subjects were Finnish and white and had no known organic gastrointestinal diseases. The procedures used were in accordance with the Helsinki Declaration of 1975.

Questionnaires

In the autumn of 1995, two questionnaires were mailed to 580 subjects. These were all the subjects who had participated in the above-described studies and whose address was available in the Finnish Population Register at the time of the present study. The first was a Bowel Disease Questionnaire (23) and the second, sent 1 mo later, included questions about dairy product consumption, subjective sensitivity to various amounts of lactose, and diseases. Two reminders were sent if necessary. Both questionnaires, duly completed, were returned by 429 subjects (74%), two of whom were excluded because of an organic gastrointestinal disease. The final study group was 427 subjects.

The Bowel Disease Questionnaire (23) included questions on gastrointestinal symptoms and was translated into Finnish. It also included questions about psychosomatic symptoms over the previous year and gastrointestinal operations. We added questions concerning physical exercise and eating habits. IBS was determined from the questionnaire on the basis of the Rome criteria (24), which include abdominal pain experienced more than six times during the previous year in combination with two or more of the following: pain relieved frequently by defecation (on > 25% of occasions), looser or more frequent stools at the onset of pain, frequent abdominal distension, a frequent feeling of incomplete rectal evacuation, or the occurrence of mucus in feces.

The second questionnaire included questions on the quantity and frequency of milk product consumption for the following dairy products, with separate questions for low-lactose and regular products: milk, fermented milk, yogurt, ice cream, mature cheeses, and fresh cheeses. Lactose intake was calculated according to the average lactose content in these products (25).

The subjects were defined as having subjective lactose intolerance if, on the basis of their own experience, they had gastrointestinal symptoms after consuming ≤ 20 g lactose in milk or in other dairy products.

The subjects were questioned as to whether they ate regular or irregular meals and about the intensity and duration of physical activity per week, including travel to work and during their leisure time.

Statistical analysis

The chi-square test and t test for independent samples were used for group comparisons. The relation of IBS and subjective lactose intolerance with demographic factors, nongastrointestinal symptoms, and living habits was estimated by a logistic regression model by using the asymptotic covariance matrix method. All statistical analyses were performed with the STATISTICA program for Windows (StatSoft, Tulsa, OK), except for the logistic regression analyses, for which PC-90 (BMDP: Statistical Software, Los Angeles) was used.

RESULTS

As determined from the 427 completed questionnaires, 15% of the subjects met the criteria of IBS, both in the groups of lactose maldigesters and lactose digesters. Of the lactose maldigesters, 70% reported themselves intolerant to dairy products containing ≤ 20 g lactose, compared with 21% of the lactose digesters. This subjective lactose intolerance was dependent on sex. Of the maldigesters, 84% of the women reported intolerance compared with 62% of the men (P = 0.02); of the digesters, 26% of women and 15% of men reported lactose intolerance (P = 0.02). Of the subjects with subjective lactose intolerance, more had IBS (P < 0.001) and more reported having experienced

<table>
<thead>
<tr>
<th>TABLE 1</th>
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| Demographic, lifestyle, and symptom characteristics in subjects who declared themselves tolerant or intolerant of a dose of milk or other dairy products containing ≤ 20 g lactose
<table>
<thead>
<tr>
<th></th>
<th>LM</th>
<th>LD</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>50 ± 9.5</td>
<td>51 ± 8.9</td>
<td>50 ± 9.2</td>
</tr>
<tr>
<td>Women (%)</td>
<td>61</td>
<td>66</td>
<td>63</td>
</tr>
<tr>
<td>Irritable bowel syndrome (%)</td>
<td>9</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>&gt; 3 nongastrointestinal symptoms/wk (%)</td>
<td>16</td>
<td>22</td>
<td>19</td>
</tr>
<tr>
<td>Psychologic stress (%)</td>
<td>11</td>
<td>24</td>
<td>17</td>
</tr>
<tr>
<td>Reported abdominal pain as a child (%)</td>
<td>29</td>
<td>25</td>
<td>28</td>
</tr>
</tbody>
</table>

1 LM, lactose maldigester; LD, lactose digester.
2 Fifty-eight subjects were not able to report whether or not they tolerated the specified amounts of dairy products.
3 X ± SD.
4 Significant difference from all intolerant subjects, P = 0.004 (t test).
5 Significantly different from all intolerant subjects (chi-square test); 6 P < 0.001, 7 P = 0.01.
6 Back pain, headache, eye pain, insomnia, tiredness, psychologic stress, depression, feeling of weakness, heartburn, tachycardia, or physical stiffness.
7 Experienced as much as or more stress than other people in general.

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abdominal pain in childhood ($P = 0.01$) compared with the lactose-tolerant subjects (Table 1). The results of the logistic regression model—which estimated that lactose maldigestion, IBS, experience of symptoms other than gastrointestinal ones, and female sex increased the risk of subjective lactose intolerance—are presented in Table 2.

Of the IBS patients, more were women ($P < 0.007$), more reported lactose intolerance ($P < 0.001$), more had three or more symptoms other than gastrointestinal ones per week ($P < 0.001$), more experienced disturbing psychologic stress ($P = 0.01$), and more experienced abdominal pain in childhood ($P < 0.001$) than did subjects without IBS (Table 3). Age, the amount of daily physical exercise, and the regularity of meals were not associated with lactose maldigestion, subjective lactose intolerance, or IBS.

The presence of IBS did not affect the mean lactose intake. On the basis of the reported use of dairy products, lactose intake was $24 \pm 38$ g/d ($\pm$ SD) for lactose maldigesters with IBS and $27 \pm 46$ g/d for lactose maldigesters without IBS. Of the digesters, lactose intake was $36 \pm 54$ g/d for subjects with IBS and $38 \pm 56$ g/d for subjects without IBS. Of the digesters, 34% of patients with IBS reported that a lactose intake < 5 g caused symptoms compared with 8% in the non-IBS group (Table 4). Lactose digesters with IBS also consumed a lactose-free diet more often than did digesters without IBS (19% and 6%, $P = 0.003$). On the other hand, there was no difference between the IBS and the non-IBS groups in the percentage of lactose maldigesters who consumed a lactose-free diet (27% and 29%, respectively).

The regular occurrence of gastrointestinal symptoms (excessive flatulence, abdominal bloating and pain, and loose stools) was not significantly different between lactose maldigesters and lactose digesters with IBS ($P > 0.34$). In the whole study group, however, significantly more lactose maldigesters than digesters reported frequent occurrence of abdominal bloating (46% compared with 30%, $P = 0.004$) and excessive flatulence (60% compared with 41%, $P = 0.004$).

The prevalence of IBS was calculated separately in a subpopulation ($n = 189$) of 11 families to determine the influence on this prevalence of hereditary- and family-related factors. The prevalence was 15% in this subpopulation compared with 14% in the remainder of the population ($n = 238$). The relation between education and IBS was determined by comparing its prevalence in tertiles according to years of education. There was no significant difference between these groups.

**Table 2**

Results of the logistic regression model explaining self-reported intolerance to \( \leq 20 \) g lactose in the study group

<table>
<thead>
<tr>
<th>Explanatory factor</th>
<th>Odds ratio</th>
<th>95% CI for odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactose maldigestion</td>
<td>10.3</td>
<td>5.2, 20.4</td>
</tr>
<tr>
<td>IBS</td>
<td>4.6</td>
<td>2.1, 10.1</td>
</tr>
<tr>
<td>&gt; 3 nongastrointestinal symptoms/wk(^2)</td>
<td>2.3</td>
<td>1.2, 4.5</td>
</tr>
<tr>
<td>Female sex</td>
<td>2.1</td>
<td>1.1, 4.0</td>
</tr>
</tbody>
</table>

\(^1\) $n = 366$. The following factors were included in the model: age, sex, lactose maldigestion, irritable bowel syndrome (IBS), presence of symptoms other than gastrointestinal ones, physical activity, psychologic stress, smoking, household size, lactose intake, coffee consumption, use of sugar alcohols, regularity of meals, and abdominal pain during childhood. Subjects who had missing data for any of these factors were excluded from the analysis.

\(^2\) Back pain, headache, eye pain, insomnia, tiredness, psychologic stress, depression, feeling of weakness, heartburn, tachycardia, or physical stiffness.

**DISCUSSION**

This study aimed to evaluate to what extent IBS, demographic factors, and living habits explain subjective lactose intolerance, which has often been shown in controlled clinical trials to not be associated with lactose maldigestion or with lactose consumption. The prevalence of IBS in Finland had not been studied previously. In this study, IBS was found in 15% of the subjects as determined by the Bowel Disease Questionnaire, which agrees with other studies conducted in the general population of industrialized countries (1–4). The prevalence was the same for lactose maldigesters and digesters.

Thirty-one percent of the study group reported intolerance to dairy products containing \( \leq 20 \) g lactose: 70% of the lactose maldigesters and 21% of the digesters. According to the logistic regression model in the whole study group, lactose maldigestion was the primary factor explaining subjective lactose intolerance. Lactose maldigestion increased the risk of subjective lactose intolerance \( \approx 10 \)-fold. IBS increased the risk almost fivefold, and both female sex as well as the experience of symptoms other than gastrointestinal ones increased the risk about twofold.

In considering possible explanations for the symptoms of digesters with subjective lactose intolerance, functional bowel disorders were the most important: IBS was diagnosed in 34% and dysmotility-type dyspepsia in 5%. Nonspecific functional bowel disorders may also have been responsible for some of the symptoms. Functional bowel disorders did not, however, seem to explain all the symptoms of lactose digesters. Among other explanations, the reliability of the diagnostic methods for lactose maldigestion and IBS deserve attention. The specificity of the lactose tolerance test with ethanol is excellent (96–100%), but its sensitivity is slightly less, 81–96%, than that with the method of reference—the direct lactase assay from jejunal biopsy (26, 27). There is thus a possibility of \( \approx 10 \)% false-negative diagnoses of lactose maldigestion. Although the diagnoses in our study group were made 15–20 y ago, they should be considered accurate because lactose maldigestion in Finland is considered to manifest itself between the ages of 5 and 20 y (18) and only subjects who were \( \geq 20 \) y at the time of the diagnosis were included in the study. Talley et al (23) estimated that the sensitivity and specificity of the Bowel Disease Questionnaire to discriminate functional bowel disorder from organic gastrointestinal disease were 70% and 68%, respectively, and 80% and 91% compared with healthy control subjects.

Intolerance to other components of milk does not seem to be a plausible explanation for the symptoms experienced by lactose digesters. No evidence exists of intolerance to milk fat, and milk protein allergy is rare in adults. However, some authors have proposed that an immunologic reaction after milk ingestion in adults with subjective adverse reaction to milk may be more common than was believed previously (28). Biologically active peptides, such as casomorphins, have been shown to affect intestinal motility in animals (29), but the relevance of these findings in humans is not clear. It is also possible that the subjects associated their digestive disturbances—due to nondigestible polysaccharides, resistant starch, etc—to milk drinking because lactose...
maldigestion is commonly recognized as a possible cause for abdominal symptoms in the general public in Finland. As for lactose maldigesters, it is not possible to estimate what portion of their symptoms was explained by factors other than lactose maldigestion. However, the fact that IBS and female sex were more common among intolerant than among tolerant maldigesters suggests that these characteristics are related. Lactose maldigestion is independent of sex, but this does not seem to apply to lactose intolerance. Our result that more women than men reported lactose intolerance agrees with that of Krause et al. (30), who found that, after a 50-g lactose dose, women with lactose maldigestion experienced stronger symptoms than men, although they had lower breath-hydrogen excretion. Krause et al concluded that this finding might be explained by a significant overlap with features of IBS, ie, visceral hyperalgesia. The positive relation of female sex and IBS was documented in several earlier works (1, 31, 32) and was confirmed by our results.

Both pathophysiologic (eg, intestinal motility disorders, visceral hyperalgesia, and allodynia) and psychophysiologic disturbances (eg, depression and anxiety) have been discussed as factors in the etiopathogenesis of IBS (33, 34). Because of altered intestinal motility or a lowered perception threshold for gastrointestinal symptoms, subjects with IBS possibly experience more symptoms after lactose ingestion than do healthy control subjects, especially when ingesting high amounts of lactose (> 20 g). Sciarretta et al (35) reported that IBS patients experienced symptoms at lower mean doses of lactose than did healthy control subjects. However, it is not known whether small quantities of lactose (2–3 g) can truly induce symptoms in the most sensitive individuals. Controlled trials that have shown similar symptoms in subjects in response to lactose-free test milk and to milks containing several grams of lactose in lactose maldigesters who claim to be sensitive to lactose, suggest that this is not the case (7, 8).

Many authors agree that IBS is a heterogeneous group of disorders with altered intestinal motility or sensation often present (36). In our study, the weekly occurrence of symptoms other than gastrointestinal ones (eg, pain, tiredness, insomnia, depression, heartburn, or tachycardia) was strongly associated with IBS. Other authors have also stated that patients with IBS suffer from a variety of symptoms that seem to originate outside the bowel (37, 38). In addition, subjects with IBS as well as those with subjective lactose intolerance often report having experienced abdominal pain in childhood. These subjects may have had a sensitive stomach since an early age or they may be more prone to remembering having experienced pain in childhood. Another possibility is that the occurrence of gastrointestinal symptoms in both childhood and adulthood is due to acquired social behavior patterns (39).

Several studies have found a higher prevalence of lactose maldigestion in patients with IBS than in healthy control subjects and have shown a benefit of a lactose-free diet in lactose intolerant subjects (40–42). On the other hand, Pena and Trucolo (43) and Newcomer and McGill (44) found the same or only a slightly higher prevalence of lactose maldigestion in IBS patients than in a healthy population with a comparable ethnic background. In our study, the percentage of lactose maldigesters was the same (24%) in subjects with and without IBS, but ∼660% of the subjects with IBS said that they were lactose intolerant compared with only ∼30% of the subjects without IBS. The percentage of maldigestation was higher in our study group than in the general Finnish population (17%) because half the study group consisted of 11 families who were chosen for previous studies of the inheritance of hypolactasia (see Methods). The prevalence of IBS was the same (15%) in this group as in the rest of the study population.

### Table 3

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>IBS (n = 63)</th>
<th>No IBS (n = 364)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women (%)</td>
<td>68</td>
<td>50*</td>
</tr>
<tr>
<td>Lactose maldigestion (%)</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>Self-reported lactose intolerance (%)</td>
<td>60</td>
<td>27*</td>
</tr>
<tr>
<td>&gt; 3 nongastrointestinal symptoms/wk (%)</td>
<td>38</td>
<td>12*</td>
</tr>
<tr>
<td>Psychologic stress (%)</td>
<td>31</td>
<td>17*</td>
</tr>
<tr>
<td>Reported having abdominal pain as child (%)</td>
<td>37</td>
<td>18*</td>
</tr>
</tbody>
</table>

1 T ± SD.
2–4 Significantly different from IBS (chi-square test): 2 P = 0.007, 3 P < 0.001, 4 P = 0.01.
5 Subjects reported that they were intolerant to milk dose or other dairy product containing ≤20 g lactose.
6 Back pain, headache, eye pain, tiredness, psychologic stress, depression, feeling of weakness, heartburn, tachycardia, or physical stiffness.
7 Experienced as much stress or more than other people in general.

### Table 4

<table>
<thead>
<tr>
<th>Minimum amount of lactose that caused symptoms</th>
<th>IBS</th>
<th>No IBS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms from ≤ 5 g</td>
<td>(n = 14)</td>
<td>(n = 69)</td>
</tr>
<tr>
<td>LM (%)</td>
<td>64</td>
<td>43</td>
</tr>
<tr>
<td>LD (%)</td>
<td>35</td>
<td>8</td>
</tr>
<tr>
<td>All (%)</td>
<td>43</td>
<td>15*</td>
</tr>
<tr>
<td>Symptoms from 6–19 g</td>
<td>(n = 38)</td>
<td>(n = 248)</td>
</tr>
<tr>
<td>LM (%)</td>
<td>22</td>
<td>29</td>
</tr>
<tr>
<td>LD (%)</td>
<td>18</td>
<td>8</td>
</tr>
<tr>
<td>All (%)</td>
<td>19</td>
<td>13*</td>
</tr>
<tr>
<td>No symptoms from ≤ 20 g</td>
<td>(n = 92)</td>
<td>(n = 317)</td>
</tr>
<tr>
<td>LM (%)</td>
<td>14</td>
<td>28</td>
</tr>
<tr>
<td>LD (%)</td>
<td>47</td>
<td>84</td>
</tr>
<tr>
<td>All (%)</td>
<td>38</td>
<td>72*</td>
</tr>
</tbody>
</table>

1 Fifty-eight subjects were not able to report whether or not they tolerated the specified amounts of dairy products. LM, lactose maldigest; LD, lactose digester; IBS, irritable bowel syndrome.
2 Lactose amounts were calculated according to the average lactose content in the amount of milk or other dairy product that the subject reported as inducing gastrointestinal symptoms.
3 Significantly different from all subjects with IBS, P < 0.001 (chi-square test).
Agréus et al (3) found an association between high education and prevalence of IBS. Because 40% of our study population had a university degree compared with 14% in the general Finnish population of the same age (Finnish Statistics Center, unpublished data, 1997), the question was raised as to whether this would have affected the prevalence of IBS. The prevalence was calculated separately in tertiles according to years of education, but there were no differences between these groups. This result agrees with the findings of Jones and Lydeard (45) and those of Talley et al (32).

In conclusion, subjective lactose intolerance, IBS, and female sex seemed to be strongly associated in both lactose maldigesters and lactose digesters. Whether these associations are of psychologic or physiologic origin remains to be determined.

We thank Tuija Poussa for her skillful assistance in the statistical analyses.

REFERENCES


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