Prevalence of Lactose Intolerance in Healthy Medical Students

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Abstract

The aim of this study is to analyse the prevalence of lactose intolerance in healthy subjects of Andhra Pradesh a south eastern state in India. Hydrogen Breath tests are currently used to diagnose Lactose Intolerance. We have enrolled 100 healthy medical students in Andhra Medical College, Visakhapatnam. Fifty eight were males and Fourty two were females, age range was between 17 years to 21 years. These students were subjected to Lactose Hydrogen Breath Test (Gastrolyzer UK Bedfont Hydrogen Breath Analayser) using 25 gm lactose. The subjects are instructed to come in the fasting state and Baseline readings of three breath samples were noted and later 25 gm lactose was administered , six breath samples were recorded at 20 ,40,60,80,100 and 120 minutes. A rise of 20 ppm above baseline was taken as positive hydrogen breath test. Abdominal Symptoms like pain, discomfort, bloating and diarrhoea after lactose ingestion was also noted. Appropriate measures like overnight fasting were ensured and subjects with any ailments or antibiotics were excluded. Fourty two (42 percent) were positive, that is lactose intolerant and Fifty eight (58 percent) were negative, i.e. lactose tolerant. Twelve subjects had crampy abdominal pain and four had bloating post lactose ingestion all of them were lactose intolerant. The degree of Indo-Aryan migration and intermixing with the native population is the possible cause of this dissimilarity in prevalence.

Keywords: Lactose Intolerance, Hydrogen Breath test, Bloating, Diarrhoea.

INTRODUCTION

Lactose intolerance is very common in Indian population, however there has been a wide variation of prevalence among north Indians and south Indians ranging from 27.4 percent to 66.6 percent [6].

Lactose intolerance or mal absorption is the inability to breakdown lactose because of reduced concentration of enzyme lactase. Thus lactose intolerance is not a disease rather than a normal physiological phenomenon as the infant’s capacity to digest lactose is not retained into adult [7].

Lactose intolerance has been implicated for many common gastro intestinal ailments like indigestion, bloating, gas and diarrhoea Hydrogen Breath tests and lactose tolerance tests are currently used tests to diagnose Lactose Intolerance [11].

Foods High in Lactose

牛奶  汉堡  酸奶  酵母  牛奶粉

Beer (sweet stout)  酱汁

Prevalence of Lactose Intolerance across the World
Physiology of Lactose digestion in Gut

Lactose (β-D-galactopyranosyl-(1→4)-D-glucose) found exclusively in milk and some milk products, and is the principle carbohydrate of all mammalian milks, of which human milk contains the highest concentration (70 g/L). Cows’ milk and products immediately derived from it (such as yoghurt) are major potential sources of lactose [16].

The lactase enzyme is located in the brush border (microvilli) of the small intestine enterocyte. The enzyme splits and hydrolyzes dietary lactose into glucose and galactose for transport across the cell membrane. The enzyme activity and the transit time of lactose through the jejunum mucosa are important for proper absorption [16].

Lactose intolerance occurs as a result of a loss of the capacity of the enterocytes of the duodenum to hydrolyse lactose to its constituent monosaccharides (glucose and galactose) after weaning, as a result of programmed absence of the enzyme lactose phlorizin hydrolase (LPH) on the mucosal surface of these enterocytes. (The equivalent bacterial enzyme to LPH is sometimes called “lactase”, but is more usually known as “β-galactosidase”) [6].

LPH in normal human neonates appears very late in fetal life. At 23 weeks gestation the LPH activity in the proximal jejunum is about 10% of that of a neonate and rises to 30% between 26 and 34 weeks gestation.

In lactose intolerant human subjects (by far the majority of the World’s population), LPH activity decreases progressively after weaning, becoming very low by five years of age.

Thus most humans have negligible LPH levels by the time they reach adulthood. This loss of intestinal LPH activity is genetically programmed [27]. It is irreversible, as subsequent consumption of lactose will not re-induce LPH in the human intestine. However, there is a minority of humans (the so-called “lactase persisters” or “lactose tolerant” individuals) who maintain high levels of LPH throughout adult life [9]. Low LPH activity in the small intestine is the primary cause of lactose intolerance.

METHODS AND MATERIAL
Assessment of Lactose Intolerance

Mucosal biopsy of the duodenum followed by biochemical lactase assay to directly measure lactase activity is the criterion standard for diagnosing lactase insufficiency. Although this approach also may exclude other causes of secondary lactose malabsorption, utility is limited due to the invasiveness of the procedure and the patchy expression of lactase in the duodenum [13].

Several methods are available to assess lactose tolerance and intolerance in adults. Each one of these alternatives has its advantages and drawbacks.

Direct Assessment

Direct assessment of LPH enzyme activity can be performed on tissue obtained from a small intestinal biopsy. This test is the so-called “gold standard” method for determining lactose tolerance or intolerance.

However, the process is highly invasive as it requires an upper gastrointestinal endoscopy. Moreover, the LPH activity in a particular biopsy specimen is not necessarily representative of the general activity in that region of the small intestine, influencing the reliability of the test [11].

Lactose Hydrogen Breath Test

Hydrogen breath tests are specific and sensitive diagnostic tests that can be used to either confirm or eliminate the possibility of carbohydrate malabsorption or SIBO.

After the ingestion of lactose, the unabsorbable disaccharide is hydrolysed into the monosaccharides glucose and galactose, that are absorbed.

If the lactase enzyme activity is inadequate, the unabsorbed lactose will reach the large intestine, where the gut flora ferments the sugar molecules into short-chain fatty acids, carbon dioxide (CO2), hydrogen (H2), and methane (CH4). Thus released CO2 is assed in breath.

Hydrogen breath tests are specific and sensitive diagnostic tests that can be used to either confirm or eliminate the possibility of carbohydrate malabsorption or SIBO. Glucose hydrogen breath test is
more acceptable for diagnosis of SIBO whereas lactose and fructose hydrogen breath tests are used for detection of lactose and fructose malabsorption respectively. Lactulose hydrogen breath test is also used widely to measure the orocecal transit time for GI motility. These methods are noninvasive and inexpensive.

Hydrogen Breath Test Technique

The prevalence of lactose intolerance in the general population of North coastal Andhra is not known. Therefore, sample size was calculated according to established formula,

\[
\text{Sample size, } n = \left( \frac{Z_{1-\alpha}}{d} \right)^2 \left( \frac{P(1-P)}{d^2} \right)
\]

Where a) \( Z_{1-\alpha} = Z_{0.95} = 1.96 \), b) Anticipated population proportion \( P = 50\% \) and c) \( d = (\text{absolute precision, } 40-60\%) = 10 \text{ percentage points} = 0.1 \).

For \( P = 0.50 \) and \( d = 0.10 \), a sample size of 96 would be needed.

We included 100 subjects in the study and expected that would be sufficient to find out the prevalence of lactose intolerance in our community.

Statistical analysis was done using SPSS 16 version with significance level set at \( \leq 0.05 \). The chi-squared test was utilized to analyze differences between proportions. Differences in the mean age of patients with positive and negative breath test were compared by using the unpaired Student’s ‘t’ test. Correlations between variables were quantified by calculating the Spearman rank correlation coefficients. The significance level of all statistical analyses was set at \( \alpha = 0.05 \). All sensitivity, specificity, predictive values and likelihood ratios (LR) were calculated by using the absence of the specific symptom or the absence of any symptom as reference (=test negative).

We have enrolled 100 healthy medial students in Andhra Medical College, Visakhapatnam in north coastal Andhra Pradesh in the month of June 2016.
Informed consent was taken from the participants. These students were subjected to Lactose Hydrogen Breath Test using 25 gm lactose. Gastrolyzer UK Bedfont Hydrogen Breath Analyser was used. Baseline three breath samples were noted and later 25 gm lactose was administered, six breath samples were recorded at 20, 40, 60, 80, 100, and 120 minutes.

A rise of 20 ppm above baseline was taken as positive hydrogen breath test. Abdominal Symptoms like pain, discomfort, bloating and diarrhoea after lactose ingestion was also noted. Appropriate measures like overnight fasting were ensured and subjects with any ailments or antibiotics were excluded.

RESULTS
Fifty eight were males and 42 were females, age range was between 17 years to 21 years. Forty two (42 percent) were positive, that is lactose intolerant and Fifty eight (58 percent) were negative, i.e. lactose tolerant. Sixteen subjects had crampy abdominal pain and two had bloating post lactose ingestion all of them were lactose intolerant.

Among 42 subjects who are Lactose intolerant 17 subjects had Constipation.

Positive Lactose Hydrogen Breath test

<table>
<thead>
<tr>
<th>Test Points (minutes)</th>
<th>ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.00 AM</td>
<td>5</td>
</tr>
<tr>
<td>7.15AM</td>
<td>6</td>
</tr>
<tr>
<td>7.30AM</td>
<td>6</td>
</tr>
<tr>
<td>7.50AM</td>
<td>2</td>
</tr>
<tr>
<td>8.10AM</td>
<td>25</td>
</tr>
<tr>
<td>8.30AM</td>
<td>36</td>
</tr>
<tr>
<td>8.50AM</td>
<td>50</td>
</tr>
<tr>
<td>9.10AM</td>
<td>46</td>
</tr>
<tr>
<td>9.30AM</td>
<td>51</td>
</tr>
</tbody>
</table>

Positive Lactose Hydrogen Breathe test:

<table>
<thead>
<tr>
<th>Recordings</th>
<th>After lactose ingestion:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base line recordings:</td>
<td></td>
</tr>
<tr>
<td>Before Lactose ingestion, in fasting.</td>
<td>7.50AM : 2 PPM</td>
</tr>
<tr>
<td>7.00 AM : 5 PPM</td>
<td>8.10AM : 25 PPM</td>
</tr>
<tr>
<td>7.15AM : 6 PPM</td>
<td>8.30AM : 36 PPM</td>
</tr>
<tr>
<td>7.30AM : 6 PPM</td>
<td>8.50AM : 50 PPM</td>
</tr>
<tr>
<td></td>
<td>9.10AM : 46 PPM</td>
</tr>
<tr>
<td></td>
<td>9.30AM : 51 PPM</td>
</tr>
</tbody>
</table>
Negative Lactose Hydrogen Breathe test

Base line recordings: Before Lactose ingestion, in fasting
- 7.00 AM : 19 PPM
- 7.15 AM : 15 PPM
- 7.30 AM : 18 PPM

After lactose ingestion:
- 7.50 AM : 13 PPM
- 8.10 AM : 17 PPM
- 8.30 AM : 14 PPM
- 8.50 AM : 18 PPM
- 9.10 AM : 14 PPM
- 9.30 AM : 15 PPM

A total of 42 (42%) subjects were found to be lactose malabsorbers (LM). Lactose intolerance was found to be equally prevalent in both sexes (male = 58, 24% and female = 42, 18%, P = 0.656). Commonest symptoms experienced by the lactose malabsorber participants of this study was diarrhea 30 (30%).

Other common symptoms were abdominal pain and flatulence experienced by 26 and 25 persons respectively. The sensitivity, specificity of individual symptoms are presented. Diarrhea has the highest sensitivity (66.0%) and a positive predictive value of 86.9%. Regression analysis showed among the symptoms, borborygmi and Diarrhea were mostly associated with LM (OR 1.957 & 1.872).

Any symptoms did not develop in 25 (14.62%) patients during the monitoring period and among these 8 (32%) had a negative lactose tolerance test. Lactose malabsorption prevalence was found to increase from subjects developing no symptom (68.0%) to subjects developing up to 3 symptoms (92.2%) following lactose load. Subjects developing 2 (16.7% vs. 41.8%, P = 0.031) or 3 {2 (6.7%) vs. 22 (15.6%)} symptoms following lactose load mostly belonged to LM group.

Demographic distribution among Lactose Malabsorbers (LM) and Non Lactose Malabsorbers (NON-LM)

<table>
<thead>
<tr>
<th></th>
<th>LM NO (%)</th>
<th>NON-LM NO (%)</th>
<th>TOTAL (%)</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volunteers</td>
<td>42(42%)</td>
<td>58(58%)</td>
<td>100(100%)</td>
<td>0.656</td>
</tr>
<tr>
<td>Male</td>
<td>24(41%)</td>
<td>34(58%)</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>18(42%)</td>
<td>24(57%)</td>
<td>42</td>
<td></td>
</tr>
</tbody>
</table>
Bar diagram showing prevalence of LM between Males and Females

<table>
<thead>
<tr>
<th>SYMPTOMS</th>
<th>LM</th>
<th>NON LM</th>
<th>TOTAL (%)</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>20</td>
<td>10</td>
<td>30 (30%)</td>
<td>0.69</td>
</tr>
<tr>
<td>Flatulence</td>
<td>20</td>
<td>5</td>
<td>25 (25%)</td>
<td>0.65</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>16</td>
<td>10</td>
<td>26 (26%)</td>
<td>0.61</td>
</tr>
<tr>
<td>Bloating</td>
<td>15</td>
<td>10</td>
<td>25 (25%)</td>
<td>0.62</td>
</tr>
</tbody>
</table>

Bar diagram showing incidence of symptoms in LM and NON LM

Association of Major Symptoms with Lactose Malabsorption

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Crude Odds Ratio</th>
<th>Significance(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Pain</td>
<td>0.228</td>
<td>0.677</td>
</tr>
<tr>
<td>Borborygmi</td>
<td>0.672</td>
<td>0.118</td>
</tr>
<tr>
<td>Flatulence</td>
<td>0.310</td>
<td>0.568</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>0.627</td>
<td>0.137</td>
</tr>
</tbody>
</table>

Sensitivity and Specificity of Major Symptoms after Lactose intake

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>66%</td>
<td>53.3%</td>
</tr>
<tr>
<td>Borborygmi</td>
<td>56.7%</td>
<td>63.3%</td>
</tr>
<tr>
<td>Flatulence</td>
<td>22.7%</td>
<td>83.3%</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>22%</td>
<td>83.3%</td>
</tr>
<tr>
<td>Nausea</td>
<td>5.0%</td>
<td>93.3%</td>
</tr>
</tbody>
</table>

**Discussion**

Lactose intolerance is a genetically programmed decrease of lactase level in adult. Reports from southern part of India [3] shows that its prevalence is between 60-70%, but it is lower (20-30%) in northern part of India. There is no cure to the lactose intolerance [27]. In our study the prevalence of lactose intolerance was 42%. Degree of Indo-Aryan migration and intermixing with the native population is the possible cause of this dissimilarity in prevalence [7].

A milk allergy is related to the proteins in milk rather than the lactose. Adult patients with lactose intolerance should maintain a calcium intake of 1,200 to 1,500 mg per day. Patients should consider drinking lactose-reduced milk or taking calcium supplements. Patient education is usually highly useful in patients with lactose intolerance. Patients with mild lactose malabsorption may benefit from using lactase enzyme supplements, such as Dairy Ease and enzyme supplementation should be an adjunct. Soya milk and rice milk are also well-tolerated [19]. Patients with
secondary lactose intolerance require further investigation to identify the primary problem. Effective treatment of the underlying condition, such as administration of metronidazole for treatment of giardiasis or a gluten-free diet for management of celiac disease, may not only ameliorate symptoms but also improve lactose intolerance.

Management

The goal of treatment is to improve symptoms while maintaining an adequate intake of calcium, thus preventing secondary bone disease caused by a milk-restricted diet. The main pharmacological measures in use include lactase supplements, lactose-hydrolyzed or lactose-reduced milk, probiotics, colonic adaptation, and rifaximin. Ingestion of probiotics containing lactase may have the potential to aid lactose digestion in intolerant patients, but studies that have investigated this have published conflicting results.

Therefore, the role of probiotics in lactose intolerance management is currently uncertain. Yoghurt containing live cultures providing endogenous beta galactosidase are an alternative source of calories and calcium, and are well tolerated by many lactose-intolerant patients. Well designed, randomized, placebo-controlled trials are still required before strong clinical recommendations can be made for the management of patients who are intolerant of lactose-hydrolyzed milk and yoghurt. Patients with bacterial overgrowth may benefit from antibiotics such as tetracycline, metronidazole, or ciprofloxacin.

CONCLUSION

In our study the prevalence of lactose intolerance was 42%, the degree of Indo-Aryan migration and intermixing with the native population is the possible cause of this dissimilarity in prevalence.

The lactose breath test, although considered the best method, may be influenced by confounding factors.

Patients developing two or more symptoms following lactose load are likely to have LM. Diarrhoea and borborygmi appeared to be the most prevalent symptoms among the lactose malabsorbers.

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