

Lactose Intolerance: The Norm Among the World's Peoples

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PROLOGUE

Lactose intolerance is presented to students in the third professional year as a portion of a required four-hour course titled "Nonprescription Product Therapeutics." Taught three times yearly, the course uses the textbook *Nonprescription Product Therapeutics*. The section on lactose intolerance occupies 30-45 minutes, depending on student questions. The lecture is supplemented with an examination of lactose intolerance products purchased by the university for demonstration purposes. Products include lactase tablets and solutions, reduced-lactose milks and lactose-free milk substitutes.

While the ethnic and racial background of our university is refreshingly diverse, the majority of students remain Caucasian. Many Caucasians have one dietary factor in common: they are able to drink milk as adults. Pharmacy students are like most other students in their desire to appear normal, both socially and medically. A major goal of this lecture is to broaden the world view of average Caucasian students to allow them to come to the realization that those who can drink milk as adults are actually abnormal, being an exception to the rule among the world's peoples. In this way, the student might gain a heightened understanding of the pervasiveness of lactose intolerance.

A secondary goal of the lecture is to differentiate food allergies from food intolerances. Many lay people misunderstand the difference, but the astute pharmacist can clarify both conditions. This allows patients with a simple intolerance such as lactose intolerance to titrate their intake to the level below that which causes symptoms, helping ensure that the maximal nutritional value may be obtained from dairy products.

INTRODUCTION

You are all familiar with food allergies. In the worst form, the person who unknowingly eats peanuts, seafood, or any other allergen-containing food may develop life-threatening anaphylaxis. In these cases, the person must avoid that food at all costs.

You may not be as familiar with another broad group of medical conditions known as food intolerances. This term applies to a food one cannot tolerate for a variety of reasons not related to allergies. For instance, as many people age, they discover that onions and peppers cause gastrointestinal irritation resulting in diarrhea and rectal burning. Other food intolerances are caused by an inability to fully digest some of the components of the food. An example is the flatulence caused by legumes or vegetables. Our topic today is another type of food intolerance known as lactose intolerance (LI), hypolactasia, or lactase deficiency.

THE IMPORTANCE OF LACTASE

The enzyme lactase is a disaccharidase which acts selectively upon lactose contained in milk and dairy products, hydrolyzing it into its two component monosaccharides, glucose and galactose(1). It is located in the brush-border membrane of the small intestine, specifically toward the outer surface of the microvillus membrane. Lactase can be detected in the human fetus by the eighth week of gestation. Levels continue to rise during the remainder of gestation, peaking the second to third day postpartum and remaining high during infancy.

Lactose is unique to the milk of mammals(2). Unfortunately, humans cannot absorb lactose for use as a nutrient. Thus, lactase is critical in allowing the mammal to gain nutritional value from milk and other dairy products by allowing absorption and use of the component monosaccharides. Further, if undigested lactose reaches the small or large intestine, it produces numerous troublesome symptoms.

CAUSES OF LACTOSE INTOLERANCE

There are three types of LI. By far the most common is primary LI, although secondary LI is also seen by the pharmacist. The third, congenital alactasia, is uncommon.

Primary Lactose Intolerance

In order to understand the physiology behind primary LI, we must examine what happens to lactase activity as childhood proceeds. We mentioned before that lactase levels remain high during infancy. However, what happens after infancy is determined by one's genetic makeup. If one possesses the more common autosomal recessive gene, lactase activity begins to drop between the ages of 2 and 20 years(3,4). On the other hand (or chromosome), if one possesses the less common autosomal dominant gene, lactase activity remains high into adulthood.

What does this mean to those of us sitting in this room? How many of you can drink milk right now and be free of any problems? Raise your hands. Do those of you with your hands raised realize that you are mutants? When I told my sons they were mutants, they had visions of Ninja Turtles and X-Men, but I had to clarify that they don't get to live in the sewers or chase bad guys. Why are you mutants?

No mammal other than man has the ability to ingest milk as an adult. Even then, only a small percentage of the world's humans are actually lactase persistent, as those of you who raised your hands are known. As many as 75 percent of

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humans are not able to drink milk as adults without experiencing embarrassing and painful symptoms. Why did some population groups develop the mutation that allowed them to drink milk as adults? For one possible answer, we turn to simple Darwinian evolutionary theory.

Early man lived in a hunter-gatherer society. However, milk-producing ruminant animals were domesticated about 10,000 years ago, according to archaeological evidence. Go back with me to that time. In that society, famine was common, as the prey species migrated or were hunted out of existence. Further, crop-destroying insects or unusually harsh seasons made gathering difficult. Imagine your family with six children, watching them slowly starve. Eventually, you see the ruminant animal feeding its young and decide to rob the milk to give your children. You notice that while some older children develop troublesome symptoms, other children begin to fill out and thrive on the cow's milk. As awareness of this practice spreads, more villagers begin to emulate the first brave pioneers. Children who survived these repeated famines were those with the autosomal dominant mutation. Experts hypothesize that the common nature of famine in that society allowed the mutation to become a selective advantage for survival. Over the ensuing 400 generations, those populations became lactase persistent (a condition sometimes referred to as normolactasia).

Those populations most likely to be lactase persistent in this room are those whose ancestors were the ruminant herders, specifically residents of northern and northwestern Europe, Scandinavians, those from the northwestern region of the Indian subcontinent, and those living as Bedouins in desert areas (e.g., Jordan, Saudi Arabia).

Other populations domesticated animals that could not be milked, such as the pig. Thus, they never developed the mutation. This includes the remaining 75 percent of the world's peoples(3,5). As many as 90-100 percent of Native Americans, Native Africans, Asians, and Eskimos are lactose intolerant(6). As many as 80 percent of African-Americans and Mexican-Americans experience LI.

In many of the countries whose residents are lactose intolerant, ordering milk in a restaurant would bring a hearty laugh. Oriental restaurants serve water-based sauces rather than milk-based gravies and dressings. Ice cream might be unknown as a dessert in those locales, and cheese might be unheard of.

Lactose is not an inducible enzyme, so drinking milk in an attempt to raise lactase activity is a futile exercise. Those who know they are lactose intolerant may attempt to discover what their lactose toleration actually is, trying not to exceed the daily intake that is acceptable for them.

Congenital Alactasia

A very small number of babies are born without lactase(3). As an inborn metabolic error, it is extremely rare, with most of the few dozen cases occurring in Finland(7). Patients must follow a lactose-free diet, although a few may eventually develop minimal lactase activity.

Secondary Lactose Intolerance

Secondary LI is the third category of reasons why people cannot ingest lactose. Earlier, we stressed that lactase is located on the outermost surface of the intestinal cells. For this reason, various environmental insults that damage intestinal tissues also lower the levels of lactase. Further, in some cases, there is insufficient remaining small intestine to produce lac-

tase in the quantity needed or the passage through the small intestine is accelerated, preventing sufficient lactose breakdown. Eventually, many patients with secondary LI will experience regeneration of the brush-border architecture, which may return lactase activity to the pre-insult levels.

Infections may induce secondary LI through direct damage to the intestinal tissues. Among those implicated are rotavirus, hookworm, *Giardia*. Secondary LI may also follow episodes of malnutrition, celiac disease, or sprue syndromes. Resection of the small intestine resulting in short bowel syndrome can reduce the time of contact between lactose and lactase-producing tissues. Any condition which increases GI transit time (e.g., partial gastrectomy) may also result in LI.

Various regimens and medication have induced secondary LI, including antimetabolites, colchicine, tetracyclines, cimetidine, neomycin, kanamycin, aminosalicic acid, and intestinal radiation. Alcohol abuse may also produce LI.

MANIFESTATIONS OF LACTOSE INTOLERANCE

The various sequelae of inability to digest lactose occur in several anatomic locations. In the small intestine, lactose exerts an osmotic pull which prevents reabsorption of water into the body. The patient suffers from cramping, abdominal pain, nausea, and rumbling(1). Intestinal contents are moved through more rapidly to the large intestine. Bacteria in the large intestine ferment the lactose, producing hydrogen, organic acids and carbon dioxide. Abdominal pain and bloating become more pronounced. Eventually, the patient may suffer from watery diarrhea, flatulence, involuntary leakage and staining of underclothing and/or overt incontinence, even from a competent rectal sphincter.

COMPLICATIONS OF LACTOSE INTOLERANCE

Unfortunately, those who are poorly informed about possible therapeutic interventions may choose what seems to be the simplest and surest way to avoid symptoms of LI: avoid intake of milk and all dairy products. This seemingly straightforward approach can have drastic consequences, since most of the average U.S. citizens' dietary calcium comes from foods containing lactose(3). Thus, a population whose calcium intake is already quite low becomes even more prone to poor skeletal growth and osteoporosis(8).

TREATMENT OF LACTOSE INTOLERANCE

Differentiating LI from Cow's Milk Allergy

Often, the patient with LI says to the pharmacist, "I'm allergic to milk." True allergy to cow's milk (usually to the proteins) mimics LI somewhat, in that both produce diarrhea, abdominal pain and excessive flatulence(9). However, while diarrhea is the most common symptom of milk allergy, the second most common symptom is vomiting, usually within one hour of eating. Vomiting is not a common symptom of LI. Of course, if there is any question, the patient should be advised to call a physician to clarify allergy status before ingesting milk. Taking time to ascertain the difference for the patient can be rewarding. If the patient has a true allergy, total milk avoidance is mandatory. If the patient is simply lactose intolerant, on the other hand, numerous interventions can allow the patient to ingest some dairy products, obtaining calcium and other nutrients in the process.

The symptoms that do occur in LI are nonspecific and could also mimic other conditions such as irritable bowel(10).

The pharmacist may ask the patient if they seem to occur within 30 minutes to several hours after ingesting lactose. If the patient cannot be relatively sure of this connection, the patient should be referred for a more exhaustive physician examination. Physicians may confirm the presence of LI through a hydrogen breath test, lactose challenge test, lactose tolerance test, jejunal biopsy, or stool pH examination(3).

Determination of Lactose Tolerance Level: Lactose Reduction

For the patient who is lactose intolerant, it is usually too drastic to eliminate all milk from the diet. Only about 5-10 percent of U.S. citizens need do this. The remainder still have some lactase activity, but cannot exceed a given intake of lactose without overwhelming their available lactase(11). The pharmacist can help advise patients about a method to determine their symptom-free lactose intake level. The patient first eliminates all sources of lactose from the diet (e.g., milk, cheeses, cream, ice cream, whey, casein, and all the foods to which they are added or from which they are prepared). If LI is present, all symptoms should resolve. The patient remains on the lactose-free diet for three weeks. Then, lactose-containing foods are introduced one at a time gradually over a number of days. If symptoms occur with the equivalent of 1.5 cups of milk daily, the patient would reduce to the previous intake, such as 1 cup of milk daily. There are several milk products and substitutes which are lactose-reduced or lactose-free, allowing the patient to maintain a semblance of dietary normality (e.g., CalciMilk, Dairy Ease Milk, Lactaid Lowfat Milk, Vitamite).

Lactase Supplementation

Another approach to prevention of lactose intolerance is to utilize lactase in one of two different ways. In one intervention, the patient purchases lactase liquids (e.g., Lactaid Drops), adding them to milk in a ratio of 5 drops per quart to achieve 70 percent hydrolysis, or a ratio of 15 drops per quart for 99 percent hydrolysis. The milk is agitated and refrigerated for 24 hours to allow full hydrolytic action. The pharmacist should advise patients that the milk tastes somewhat more sweet than normal due to the shift in sugar composition, but it is not unpleasant.

Of course, there are several instances where this technique is impractical, as when dining out, or with solid lactose products such as cheese or ice cream. In these cases, the patient may ingest lactase in the form of tablets or capsules immediately before ingesting the lactose-containing food. Most patients notice that symptoms decrease or disappear, although it may take some experimentation with lactase adjustment to find the exact dose needed. These products include Dairy Ease, Lactaid, and Lactaid Ultra.

SUMMARY

To summarize, those of you who can now ingest milk are indeed fortunate among the world's peoples in having access to this unique nutrient source. For those who are not quite so lucky, for either genetic or environmental reasons, however, the pharmacist can suggest a combination of lactose reduction and lactase supplementation strategies to prevent patients from experiencing troubling symptoms.

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