The Practical Significance of Lactose Intolerance in Children

Lactose intolerance has been reviewed in published statements by the Protein Advisory Group of the United Nations System,1 the Food and Nutrition Board of the National Research Council,2 and the American Academy of Pediatrics, Committee on Nutrition.3 Each of these statements deals principally with the advisability of encouraging population groups with a high rate of lactose intolerance to consume nutritionally beneficial quantities of milk. All three statements conclude that it is inappropriate to discourage the use of milk on the basis of lactose intolerance. Nevertheless, controversy over the practical significance of the widespread prevalence45 of lactose intolerance has continued.

DEFINITIONS

Lactose intolerance is defined1 as a clinical syndrome of abdominal pain, diarrhea, flatulence, and bloating after the ingestion of a standard lactose tolerance test dose (2 gm of lactose per kilogram of body weight or 50 gm/sq m of body surface area, maximum 50 gm in a 20% water solution). If a maximum increase in blood glucose level of less than 26 mg/dl is observed after a lactose tolerance test dose, lactose malabsorption is diagnosed.1 Lactose intolerance is classified as primary, secondary, or congenital. Lactose intolerance is classified as primary when it is observed with no history or signs of underlying intestinal disease. If there is gastrointestinal disease, it is usually classified as secondary. Primary and secondary lactose intolerance are not uncommon; however, congenital lactose intolerance is rare. This form is present at birth, the histologic features of the gastrointestinal mucosa are normal, and brush-border lactase activity is low or completely absent.67 The three forms of lactose intolerance must be considered separately to avoid confusion.

PRIMARY LACTOSE INTOLERANCE

Major areas of concern in reviewing the practical implications of primary lactose intolerance are (1) the prevalence at specific ages in particular population groups, (2) the relationship between primary lactose intolerance and intolerance to quantities of milk usually consumed, (3) response to hydrolyzed lactose milk, and (4) the absorption of other nutrients in the presence of amounts of lactose that surpass digestive capacity but do not produce symptoms.

Studies on Lactose Intolerance

The widespread prevalence of lactose malabsorption and intolerance in children is well documented in a review by Jones and Latham.4 Prevalence at specific ages in a particular population group varies. In some groups, 90% prevalence is observed by age 4 years; in others it remains much lower throughout life. Similar information on children of American ethnic groups has been published recently.567 Paige and co-workers8 studied 116 black children 13 to 59 months old. Twenty-nine percent of these children had lactose malabsorption, and 18% had signs of intolerance. Black children 4 to 9 years old were studied by Garza and Scrimshaw.9 They reported lactose intolerance in 11% of those 4 to 5 years old, 18% of those 6 to 7 years old, and 72% of those 8 to 9 years old. Paige and co-workers10 studied another group of children 6 to 13 years old. Fifty-four percent had lactose malabsorption and 65% had symptoms of intolerance. Haverberg et al.11 and Kwon et al.12 studied black patients 14 to 19 years old and reported lactose malabsorption prevalence rates of 83% and 81%, respectively.

Studies of Mexican-American children have also been reported. Woteki et al.13 studied 282 Mexican-American children who were 2 to 14 years old. Eighteen percent of the 2- to 5-year-old children were intolerant to lactose. This prevalence increased to 56% in the 10- to 14-year-old children. Sowers and Winterfeldt14 found a similar prevalence (50%) in 9- to 21-year-old Mexican-
American children. In a study of 301 adolescents and young adults\textsuperscript{15} in rural Mexico, 222 of them were classified as having lactose malabsorption, but only 86 of these reported symptoms.

American Indians have been studied by Casky and co-workers.\textsuperscript{16} Using hydrogen breath analysis, lactose malabsorption was found in 20\% of 3- to 5-year-old children, in 10\% of those 6 to 12 years old, and in 70\% of those 13 to 19 years old. Newcomer et al.\textsuperscript{17} reported a similar study in American Indians in which 104 subjects 5 to 17 years old were studied. Lactose malabsorption was diagnosed in 63\% to 74\% of the groups stratified by age (5 to 6 years, 7 to 8 years, and so forth). Symptoms were reported in 76\% of the children with lactose malabsorption. Prevalence of lactose intolerance at specific ages was not reported.

Prevalence of lactose malabsorption in white children tends to be much lower than in these other groups. Persons classified as white in this country tend to be heterogeneous; therefore, data are difficult to compare with studies published in countries with more homogeneous populations. Data presented by Woteki et al.\textsuperscript{18} and Garza and Scrimshaw\textsuperscript{9} are representative. Lactose intolerance is rarely observed in 2- to 6-year-old children, and increases to about 30\% among adolescents. Lebenthal et al.\textsuperscript{18} have reported lactase levels from 172 of 1,077 biopsy specimens. The groups studied were white and were healthy siblings and parents of patients with cystic fibrosis, children with failure to thrive without diarrhea, and patients with “irritable colon syndrome.” No low lactase activity was encountered in children less than 5 years old.

Comparable data on the prevalence of lactose intolerance in American children from other ethnic backgrounds who were expected to have a high prevalence of lactose intolerance (e.g., Chinese, Japanese, and Greek) are not available.

Assessing the relationship between lactose and milk consumption is also important in determining the practical significance of lactose intolerance in children. Comparison of the standard lactose tolerance test dose with quantities of milk normally consumed shows that the test dose is representative of the amount of milk consumed by young infants but not of that consumed by weaned children. The 200 to 250 ml of milk usually consumed at one sitting by the latter children contains 12 gm of lactose. This is substantially less than the 2 gm/kg usually provided in the lactose tolerance test.

Paige et al.\textsuperscript{2} reported that lactose intolerance in elementary school children adversely influenced their acceptance of moderate amounts of milk. Milk’s significant role in publicly sponsored, supplemental feeding programs led Paige and other investigators to study lactose intolerance further. Paige et al.\textsuperscript{4} found no differences in milk consumption between lactose-tolerant and lactose-intolerant black children 13 to 59 months old. Garza and Scrimshaw\textsuperscript{9} found no differences in milk consumption between lactose-tolerant and lactose-intolerant black children 6 to 7 and 8 to 9 years old, although the 8- to 9-year-old black children consumed less milk regardless of lactose tolerance status than a comparable group of white children. Woteki et al.\textsuperscript{13} reported no difference in milk consumption by the lactose-tolerant and lactose-intolerant Mexican-American children they studied. In a study in rural Mexico,\textsuperscript{15} conflicting results were obtained and do not help to determine whether lactose malabsorption interferes with milk consumption.

Stephenson and Latham\textsuperscript{16} studied slightly older children with lactose malabsorption; no difference in milk consumption was observed between the lactose-tolerant and lactose-intolerant subjects in this study. In Newcomer and co-workers’ study\textsuperscript{17} of American Indians, two thirds of the 156 subjects studied were less than 18 years old, and those with lactose malabsorption had mean daily lactose intakes of 19 gm compared to 25 gm in those with lactose absorption. Woteki et al.\textsuperscript{13} reported no differences in milk intakes between those with lactose absorption and malabsorption, but children classified as Anglo-American drank more milk than the Mexican-American children. In contrast, Paige et al.\textsuperscript{21} reported that 50\% of 6- to 12-year-old children with lactose malabsorption consumed less than one-half pint of milk offered in school feeding programs. They found that children with lactose malabsorption who were classified as milk-drinkers had higher increases in blood glucose level than those classified as non-milk-drinkers. Lebenthal et al.\textsuperscript{18} have also reported greater milk consumption (> 960 ml/day) in individuals with high intestinal lactase levels and their families than in patients and families with low lactase levels (< 250 ml/day).

The question of tolerance to various lactose intake levels in intolerant subjects and those with lactose malabsorption has also been examined. Garza and Scrimshaw\textsuperscript{9} report that, despite the significant prevalence of lactose intolerance they observed in 4- to 9-year-old black children, no child was intolerant to 240 ml of milk. In contrast, Mitchell et al.,\textsuperscript{22} who studied 11- to 18-year-old black adolescents, found that 21\% had symptoms after consuming 240 ml of milk. In double-blind studies, Haverberg et al.\textsuperscript{11} and Kwon et al.\textsuperscript{12} report, respectively, that 28\% and 9\% of adoles-

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[The text continues with further details about lactose intolerance in various populations and its implications.]
cents with lactose malabsorption had symptoms after drinking 240 ml of milk, as did 16% and 19% of those with lactose absorption. In a slightly older age group studied by Stephenson and Latham, all those with lactose malabsorption could tolerate 240 ml of whole milk without any or only mild symptoms. In studies of native American Indians, Newcomer et al. report that all of the subjects they studied who had malabsorption (6 to 62 years old) tolerated amounts of lactose equivalent to 240 to 300 ml of milk taken with a meal with no intestinal symptoms attributable to lactose. In contrast, lower tolerance levels are reported in older adults by Bayless et al. and in Peruvian children by Paige et al. Studies from other countries have reported a lack of symptoms in lactose-intolerant children comparable to those reported here.

A possible solution for circumventing intolerance to normal intakes of milk is to hydrolyze the lactose. Although studies such as those of Jones et al. report that lactose hydrolysis substantially increases milk tolerance in adults, other studies cast doubt on the efficacy of lactose hydrolysis in children. Paige and co-workers tested whole milk, 50% hydrolyzed lactose milk, and 90% hydrolyzed lactose milk in 22 black 13- to 19-year-old subjects with lactose malabsorption. Three of these teenagers reported symptoms to untreated whole milk and to 90% hydrolyzed lactose milk. None reported symptoms to 50% hydrolyzed lactose milk. Similarly, Kwon et al. reported that 28 of 45 teenagers with lactose malabsorption did not experience symptoms to 240 ml of whole milk or lactose-free milk. Ten of the others had inconsistent symptoms; some had symptoms to lactose-free milk only, some to both lactose-free milk and whole milk, and others to 240 ml but not 480 ml of whole milk. Seven subjects had consistent symptoms, but none had symptoms to 240 ml of milk, with or without lactose.

Milk in the Diet

The importance of milk in the American diet rests on its high nutrient content. The U.S. Department of Agriculture estimates that dairy products, excluding butter, contribute only 11% of the available food energy; however, they provide 75% of the calcium, 39% of the riboflavin, 35% of the phosphorus, 22% of the magnesium, 20% of the vitamin B₁₂, and substantial proportions of other nutrients. The question of the bioavailability of these nutrients in the presence of lactose malabsorption without symptoms of intolerance is, therefore, important. Unfortunately, little data are available. Significant malabsorption is unlikely if there are no symptoms; however, the chronic effects of subtle differences in bioavailability of various nutrients might be significant, especially under conditions of marginal intakes. There are substantial data on the “malabsorption of lactose,” but there are no studies estimating metabolizable energy in lactose-containing diets of children with lactose malabsorption. Less increase in blood glucose levels has been demonstrated in those with lactose malabsorption than in those with lactose absorption after milk ingestion. The possibility that slower but sustained digestion of lactose is responsible for these smaller increases remains unknown.

A metabolic study in which milk provided all dietary protein was designed by Calloway and Chenoweth and was conducted in lactose-tolerant and -intolerant adults. After adjustments for metabolizable energy were made, no effect on nitrogen balance was demonstrated. Unpublished results from this study indicate that calcium, phosphorus, and magnesium absorption also were not influenced by the presence of lactose.

Leichter and Tolensky, in a study on weaned rats that were fed lactose-containing diets, obtained suggestive evidence that lactose may reduce protein and fat absorption in animals with low lactase activity. Bowie reported the effects of lactose-induced diarrhea on nitrogen and fat absorption. Nitrogen absorption was depressed in those with lactose malabsorption who were fed milk compared to a disaccharide-free diet, but nitrogen retentions were similar with both diets. No differences in fat absorption were noticed. In a separate study by Bowie et al., absorption was studied by using xylose. No difference in xylose excretion was observed when malnourished, lactose-intolerant subjects were fed whole milk or a disaccharide-free formula. A recent study conducted in 2- to 8-month-old infants compared calcium and magnesium absorption when untreated milk, milk treated with lactase ten minutes before feeding, and a lactose-free milk were fed. Calcium and magnesium absorption was best (72% and 81%, respectively) with lactase-treated milk and poorest (calcium 37% and magnesium 39%) with lactose-free milk. The infants were presumably lactose tolerant.

Summary

Lactose intolerance is observed in black and Mexican-American children by age 3 years, and it probably occurs in other non-northern European ethnic groups at a similar age. However, intoler-
ance to the consumption of 250 ml of milk apparently is rarely seen in preadolescents. Current research on the response of adolescents to hydrolyzed lactose milk suggests that the symptoms observed in lactose-intolerant subjects after milk ingestion may be unrelated to lactose or may be mild enough to be of little practical significance. The effects of undigested lactose on nutrient absorption has received little attention, but preliminary data suggest that this is not a problem, except perhaps when overall intakes are marginally adequate.

SECONDARY LACTOSE INTOLERANCE

The predominant view at present is that primary lactose intolerance is genetically predetermined. The following observations support this view: its prevalence among apparently healthy populations, its absence among specific groups,36-38 the inevitable decrease with age in lactase activity in most mammalian species,39 and the apparently noninducible nature of the enzyme in humans.36,40 However, the environment’s role in accelerating the age of lactose intolerance, determining the severity of its expression, and increasing the prevalence within population groups has not been assessed. Few studies have been directed at a basic understanding of the physiology of the intestinal mucosal cells as it relates to lactose intolerance and malabsorption. Yet the importance of the environment is repeatedly demonstrated by the apparently transient decrease in lactase activity and intolerance to lactose commonly associated with gastrointestinal disease or significant malnutrition. This condition is classified as secondary lactose intolerance. Areas of concern in assessing its practical implications are (1) its significance in the treatment of malnutrition, which is common to gastrointestinal disease; and (2) the “reversibility” of this condition and its effects on the expression of a presumably, genetically determined decrease in lactase.

Lactose intolerance in malnutrition has been well described41-44; however, the relevance of this intolerance to milk feeding is controversial. Reddy and Pershad,26 in a study evaluating a milk-based diet in refeeding programs, conclude that this is a self-limiting problem and of little practical importance. An ongoing evaluation43 of a supplemental milk feeding program serving 32,000 rural Haitians and an accompanying program refeeding the severest cases of malnutrition (301 subjects) make the same conclusions. A favorable outcome was reported for 93% of the subjects in a refeeding program. Milk intolerance could not be excluded as a possible cause of failure in only 1% of the subjects. In a study reported by Prinsloo et al.,42 children refed on cow’s milk did not have more diarrhea than those fed formulas with glucose, sucrose, or D-maltose, although lactic acid excretion was high in children fed cow’s milk.

In the study by Bowie33 referred to earlier, lactose-induced diarrhea had no effect on nitrogen retention or fat absorption. He concluded that, as long as milk is the most widely available and cheapest source of good protein, it should be used. However, he does caution that children with severe diarrhea will require a lactose-free formula for a variable period of time. Mason et al.44 reported similar tolerances.

Mitchell et al.45 reported results of blind-controlled feeding trials evaluating prehydrolyzed lactose milk and a reconstituted whole milk. Thirty-five slightly undernourished Australian aboriginal infants were studied. No complications were seen in children fed either milk, but five of those fed whole milk failed to gain weight compared to only one in the hydrolyzed lactose milk group. Children fed the hydrolyzed lactose milk had a mean 70% larger weight gain than those fed the whole milk. Children with diarrhea or weights less than 90% of expected weight for age who were fed hydrolyzed lactose milk had statistically significant higher weight gains than comparable groups of children fed whole milk.

The effects of previous malnutrition or gastrointestinal disease on the prevalence of primary lactose intolerance is difficult to evaluate because few studies have attempted to quantitate the severity of observed intolerance or malabsorption. Paige and co-workers25 report no differences in prevalence between previously malnourished children and their siblings who had no history of significant malnutrition, although tolerance levels in both groups appear lower than observed in children in this country. Woteki et al.44 found the prevalence of lactose intolerance of Mexican-Americans similar to that reported by Sowers and Winterfeldt44 from rural Mexico. Stoopler et al.27 restudied children with lactose malabsorption seven months after an initial evaluation and found that 21% had normal lactose tolerance curves on retesting. In Britain, no correlation was found among continuing lactose intolerance, maximal increase in blood glucose level after a standard lactose test dose, intestinal lactase levels, and small intestinal morphology on reevaluation46 of 30 children 2 to 38 months old with a previous diagnosis of presumably secondary lactose intolerance.
Summary

Individuals using milk-based diets in refeeding programs occasionally report initial problems with diarrhea aggravated or precipitated by lactose. In this early phase, a hydrolyzed lactose or lactose-free milk may be optimal. Apparently, however, whole milk is successfully used for refeeding, unless there is severe diarrhea. This suggests that the milder cases seen out of the hospital may present less significant problems. The report by Mitchell et al., however, suggests that the milder cases seen out of the hospital may present less significant problems. Although unavailable lactose may not present major problems to fat and nitrogen absorption, the decrease in metabolizable energy may be enough to decrease the rate of weight gain, lengthen hospital stays, and therefore decrease the effectiveness of lactose in refeeding programs, unless compensated for in the total diet. Comparable studies should be repeated in hospital and supplementary feeding programs to determine whether or not potential effects on nutrient bioavailability are as significant as this study suggests.

CONGENITAL LACTOSE INTOLERANCE

The extremely low or absent activity of brush-border lactase in congenital lactose intolerance can be life-threatening because of the accompanying severe diarrhea and dehydration when lactose is fed. The condition is rare, but it is not unusual for secondary lactose intolerance to be misdiagnosed during the newborn period as congenital lactose intolerance. A definite diagnosis requires intestinal biopsy for histology and enzyme assay. Nonetheless, it is imperative that a lactose-free formula be provided as soon as the diagnosis is suspected because of the seriousness of the condition.

RECOMMENDATIONS AND CONCLUSIONS

The Committee's position remains unchanged. On the basis of present evidence it would be inappropriate to discourage supplemental milk feeding programs targeted at children on the basis of primary lactose intolerance. The Committee continues to encourage the development of nutritious and acceptable supplementary foods in areas with inefficient and uneconomical milk production. The use of milk should not be discouraged in the refeeding of malnourished children—except if they have severe diarrhea—as long as milk continues to provide the best and cheapest source of high-quality protein. However, the Committee cautions that some of these children will require lactose-free diets if recovery is to be achieved with minimal complications. It also urges that studies such as those of Mitchell et al., be continued in inpatient and outpatient facilities for reasons outlined here; that more attention be given to studies of environmental effects on enterocyte function, thereby increasing our understanding of the development of low lactase levels; and that efforts to provide effective, low-cost, supplemental foods to children be continued as part of comprehensive health planning for decreasing morbidity in children.

REFERENCES


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