

Lactose Intolerance in Childhood

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Lactose (4-0-B D-Galactopyranosyl- α -D-glucose) is the principal carbohydrate in mammalian milk with concentrations varying from 4.8% in cow's milk to values as high as 7.2% found in human milk¹. It is interesting however, to note that there is no detectable lactose in the milk of certain species such as sea lions, walrus or Seals². The lactose present in milk needs to be hydrolyzed into its components, glucose and galactose, by the intestinal brush border disaccharidase enzyme lactase. It appears ontogenetically, that both lactose and lactase appeared in humans at approximately the same point in evolution over a 100 million years ago³. It is uncertain as to why lactase was selected for persistence in the wake of several other carbohydrate splitting enzymes, but an interesting biological advantage of lactose over glucose may be that it provides twice the caloric intake at almost half the osmotic penalty. Although lactase is the last of the disaccharidases to develop in the fetal intestine⁴, most newborn infants are born with normal amounts of brush-border lactase. The levels of intestinal lactase however, decrease after weaning in most races except Scandinavian and northern European population⁵. The reasons for these genetic differences in lactase persistence are uncertain. Continued lactase activity is however, not considered to be dependent upon dietary factors such as the level of milk intake and resultant brush border enzyme induction. It is possible however, that lactase persistence offered a potential protection against the development of nutritional rickets in sun-deprived northern climates, with a consequent 3-5% survival advantage⁵. An alternative view of the survival advantage conferred by hypolactasia in malarial endemic areas, has relatively little support⁶.

Although congenital hypolactasia is rare⁷, several Asian studies have revealed high rates of hypolactasia in childhood⁸⁻¹⁰. Whereas, Nose et al had shown demonstrable lactase deficiency in Japanese children by 5 years of age, nearly 85% had low lactase by the age of three years. Similarly, nearly 80% of children in Thailand were found to be lactase deficient by 2 years of age⁹. The same proportion in Taiwanese infants was 10%¹⁰. Although environmental factors may play a major role, genetic determination of lactase insufficiency is equally important. Overall, however, lactase deficiency is most commonly associated with protein-energy-malnutrition (PEM)^{11,12} or acquired infections. On a global scale diarrheal disorders, frequently if occurring in young children, are the most common disorders associated with acquired lactase deficiency and lactose intolerance^{13,14}.

In most cases, the brush border disaccharidases bear the brunt of the infectious diarrhea and particularly in young infants, there may be an ensuing period of secondary lactase deficiency. The latter cosequence and its diagnosis are clearly important, as dietary modifications may be required in affected children. It is important therefore, to critically evaluate the methodology used to diagnose lactose intolerance in these situations, as these have been frequently used to estimate the prevalence and severity of lactose intolerance.

The most definitive test of lactose intolerance is intestinal biopsy and assay of mucosal disaccharidases¹⁵, but this is clearly impractical for routine use. While a simpler method of multifunctional assay for lactase activity in intestinal fluid has been described¹⁶, it also requires intestinal intubation and is cumbersome. The indirect lactose tolerance test employing an oral lactose load, is impractical in children and potentially dangerous because of the risk of exacerbation of diarrhea. The simpler estimation of stool pH (<5.0) and the demonstration of >0.3% reducing substances in the stools though a useful screening method, is far from perfect as it depends upon the

type and quality of dietary carbohydrate and requires a fresh stool specimen¹⁷. The most commonly used “gold-standard” test for reestimation of lactose intolerance is the estimation of breath hydrogen excretion, after an oral dose of lactose, but does require special equipment and may not be as reliable in young infants¹⁸. While the latter test is frequently used in adults given an oral load of 20 g lactose, it is debatable whether intolerance of such large lactose loads (exceeding 2 g/kg/day) may have any clinical relevance with daily practice, as the amounts of milk required to simulate such lactose intake are clearly unphysiological¹⁹. It should thus be noted that the presence of excessive breath hydrogen excretion on an intake of supraphysiological amounts of milk, Cannot be translated into clinically significant lactose intolerance. It has been shown that physiological amounts of milk are well tolerated in malnourished children at risk of lactose intolerance²⁰, barring those with severe kwashiorkor²¹. Brown et al demonstrated satisfactory tolerance of low dose milk feeds in malnourished Bangladeshi children with lactose intolerance²² and in a similar recent study by Rosado et al from Mexico²³, both rural and urban lactose intolerant children were shown to comfortably tolerate physiological amounts of milk.

The aforementioned data clearly calls into question the widespread practice of replacement of milk feed with special lactose-free formulations in children with diarrheal disorders or malnutrition and suspected lactose intolerance. While the institution of special lactose-free or lactose-reduced formulations is commonplace in the developed world, such diets are expensive and clearly impractical for most developing countries. In the absence of satisfactory dietary alternatives, the elimination or reduction of milk intake in the diet may lead to disastrous nutritional consequences. Recent evidence however, indicates that such dietary manipulations may be neither necessary nor beneficial in most cases with acute diarrhoea. Although, a preliminary evaluation of available evidence of continued feeding of cow's milk-based diets in children with diarrhead suggested a 30% consequent increase in stool output²⁴, two recent metaanalyses have addressed this issue in detail and found no effect on stool output of a continued intake of modified cow's milk based formulations^{25,26}. This data calls the widespread practice of dilution and modification of milk feeds in children after diarrhea, into serious question.

It should be pointed out however, that despite the satisfactory tolerance of physiological lactose-loads by most children after diarrhea, there are subsets at increased risk of complications with continued lactose intake. These include severely malnourished children and those with prolonged diarrhea²⁷. in the latter study, Penny et al demonstrated clinically significant worsening of diarrhea and continued high purging rates in relatively well nourished infants receiving a lactose intake exceeding 5 g/kg/day. We have corroborated the above findings with a demonstration of adverse nutritional and diarrheal outcome in severely malnourished children with prolonged diarrhea receiving a traditional rice-lentil (Khitchri) diet alongwith dilute buffalo milk, providing a lactose intake of 3 g/kg/day²⁸. There is evidence however, that replacement of the milk intake with equivalent substitutes such as yogurt²⁹ or fermented milk³⁰ may be well tolerated in such children. There is additional evidence that the lactose load of milk can be substantially reduced by the addition of cereals to the diets³¹. Using the combined approach, we have recently demonstrated that a combination of khitchri and yogurt can be effectively used in children with acute diarrhea and lactose-intolerance, with a comparable efficacy to expensive soy-based, lactose-free formulations. A similar dietary combination was also found to be equally efficacious in the dietary management of severely malnourished children with persistent diarrhea and documented lactose intolerance. These data provide objective evidence that even in the subset of severely malnourished children with lactose intolerance following diarrhea, it is possible to administer relatively inexpensive and well tolerated milk-substitutes and traditional diets. Such an approach provides the means of successful ambulatory enteral nutritional therapy for complicated diarrhea of infancy.

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