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Intervention and Diagnosis Measures Based on Influencing Factors of Lactose Intolerance

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Abstract:

Lactose intolerance (LI) is a common condition that often manifests as an inability to properly consume milk and dairy products, resulting in diarrhea, vomiting, and fever. Dietary treatments at this stage are broadly categorized into two approaches: avoidance or control of lactose intake, and supplementation with additional supplements. However, most of the papers are studies conducted on lactose-intolerant neonates. There are gaps in treatments or palliative programs for adolescent and adult patients. This paper analyzes the classification of different types of LI and the factors affecting them, introduces several diagnostic measures, summarizes the existing treatments, and concludes the possibility of advancing the case of neonatal LI treatment to adolescents and adults. It aims to provide a clear background for future exploration of treatment and mitigation methods for LI, providing more dietary choices and more suitable lifestyles for adolescents and adults with LI. However, there is a lack of discussion on treatments for LI other than dietary modifications, especially the measure of using probiotics, which is an area for future research to focus on.

Keywords: lactose intolerance, factor, intervention

1. Introduction

Lactose intolerance (LI), known as lactose malabsorption, is one of the common gastrointestinal symptoms. It is caused by the lack of lactase enzyme in the body, unable to digest degradation of lactose, so that lactose in the intestinal tract. The bacterial decomposition occurs when lactose fermentation leads to the production of gases and acid, resulting in disorders of the intestinal environment [1].

LI can be hereditary or due to an acquired intestinal disorder. Based on the causes, LI can be categorized into 3 types, congenital lactase deficiency (CLD), secondary lactase deficiency (SLD), and primary lactase deficiency (PLD) [2]. CLD refers to the low or lack of lactase activity from birth, caused by the autosomal recessive gene in the body. CLD relatively rarely happens. SLD refers to the temporary low activity of lactase due to the damage of small intestinal epithelium for various reasons. This is mostly due to acquired infectious conditions such as infectious diarrhea, celiac disease, and immunoglobulin deficiency [3]. PLD, also known as adult-type LD, is caused by the gradual decrease of lactase activity with age. The time of occurrence varies with race and region, without the influence of other diseases, and is the most common type.

LI affects a wide group of patients and is considered a common condition worldwide. According to the findings of Christian L. Storhuag et al, the global prevalence estimate of lactose malabsorption was 68% [4], which is over half of the worldwide population. About two-thirds of people in Asia suffer from LI, and the proportion of people with varying degrees of LI in China is already as high as 85% [4]. Infants, children, and adolescents generally have a higher incidence and are the susceptible groups. Also, LI may reappear in some middle-aged and elderly people as they age.

Lactose is found in a variety of foods, such as milk and milk products, which are essential nutrients in human life, providing nutrients for human growth and development, and playing an important role in bone development. Treatment of LI involves reducing or restricting lactose-containing foods, with symptoms altered by changes in the amount of dairy and lactose in the diet. However, a less-lactose or lactose-free diet may interfere with calcium absorption, which can have adverse effects on the body, such as suffering from malnutrition, osteoporosis, and other conditions.

Dietary treatments at this stage of research include reducing or eliminating dietary lactose, exogenous lactase supplementation, application of probiotics, prebiotics, and calcium and vitamin D supplementation [5]. LI in newborns is overstudied, but there is a lack of treatment

or palliative programs for adolescent and adult patients. Moreover, there is a lack of discussion of therapeutic measures other than dietary modification, such as the use of probiotics and lactase supplementation.

This paper will systematically analyze the causes of LI, evaluate the advantages and disadvantages of the current diagnostic methods, and propose new therapeutic measures and protocols, aiming to provide more dietary choices and more suitable lifestyles for adolescents and adults with LI.

2. Influencing Factors

Based on the three types of LI mentioned above, the causative factors can be synthesized into genetic factors, geographical differences, human-made influences, and bacterial or viral infection factors. Of course, these do not represent all the causes and factors in the pathogenesis of LI and are meant to represent the main influencing factors.

2.1 Genetic Factors

CLD is a rare and severe autosomal recessive disorder caused by pathogenic mutations in the gene encoding lactase, generally due to a frameshift or missense mutation in the region coding for LPH, resulting in a truncated protein characterized by absent or reduced lactase activity at birth [6]. It usually manifests as severe intractable watery diarrhea after the infant's first breastfeeding or formula feeding, which can lead to dehydration, renal tubular acidosis, growth retardation, and hypercalcemia, and can be life-threatening if left untreated [5].

Similarly, patients with PLD with a gradual decline in lactase activity with age are associated with reduced lactase gene expression. During human evolution, lactase persistence developed independently in different parts of the world, and in some human races, lactase activity may usually persist into adulthood [5]. Most patients with this type of lactose intolerance can tolerate a certain amount of lactose and therefore do not need to avoid milk or dairy products altogether, but the amount of lactose that can be tolerated varies between individuals.

2.2 Geographical Differences

The PLD mentioned above, known as adult-type hypolactasia (ATH), varies greatly in different racial populations, and it is a phenomenon of synergistic human gene, culture, and diet evolution [5]. Most Chinese, Africans, and half of the Spanish and Italians have LD. However, this is not the case for most northern Europeans who use milk and dairy products regularly [7]. According to Wu Yi's study, Western Europeans and Caucasians are more likely to carry the lactase gene, whereas Asians generally lack it [8]. This is closely related to the availability of milk products and other lactose-containing products in the living environment, as well as to local customs and cultures.

2.3 Human-made Influence

Due to insufficient lactase quantity and activity and poor lactose digestion and absorption, because they miss the optimal period of lactase development, LI can occur in preterm infants, especially those with a gestational age under 34 weeks. Fortunately, this type is mostly temporary and can improve on its own as the infant grows and the intestinal tract matures. However, the gastrointestinal development of infants is slow, and it takes longer for infants to recover from lactose intolerance on their own. In the meantime, infants are unable to absorb the nutrients from breast milk or milk powder because of lactose intolerance, so it takes even longer for lactose intolerance to heal on its own. Moreover, it cannot be ruled out that the infant has not recovered from the disease for other reasons. Therefore, changing milk powder and adding lactase can be used to help infants' intestines digest lactase, absorb nutrients, and promote development.

2.4 Bacterial or Viral Infection Factors

Secondary LI is mainly secondary to small intestinal epithelial cell breakdown, small intestinal mucosal disease, or certain systemic disorders, and usually occurs after severe gastroenteritis, most commonly after rotaviral enteritis [5]. As an example, rotavirus and Giardia are two common pathogens that damage the surface of the small intestine and cause temporary lactose intolerance. It also occurs after, for example, Crohn's disease or launching enterocolitis [9]. This type of LI can be attributed to infections from other diseases.

3. Diagnostic Methods

Current diagnostic methods for LI include fecal reducing sugar and pH measurements, urinary galactose measurements, lactose tolerance tests, hydrogen breath tests, etc. [10]. Each diagnostic method has its pros and cons and needs to be considered before use in the context of the specific patient situation and condition.

3.1 Fecal Reducing Sugar and pH Measurements and Urinary Galactose Measurements

The principle of fecal reducing sugar and pH measurement, as well as urinary galactose measurement, can be described as both lactose and galactose belonging to reducing sugar, and lactose is broken down to galactose in the intestine and absorbed directly in the small intestine. While 80% of the unmetabolized galactose is excreted from the urine [10], lactase metabolism can be reflected by the measurement of reducing sugar in the feces and urine. Fecal lactose is usually detected by the lead acetate ammonium hydroxide method. The presence of lactose in

the feces is indicated when there is a clear pink precipitate in the test tube. In addition, the pH test was immersed into the original fecal specimen and the pH value was read against the pH color card. Fecal pH ≤ 5.5 was defined as positive for lactose [7]. The First Hospital of Peking University and other organizations jointly reported that the incidence of LD in newborns was high, and the recovery time of stools was longer in lactose-intolerant children than in the tolerant group. Nevertheless, the differences in pH and urine galactose positivity between diarrhea and non-diarrhea groups of newborns were not statistically significant [6]. Therefore, the accuracy of this method in diagnosing LI needs to be further studied.

3.2 Lactose Tolerance Tests

The lactose tolerance test is used to diagnose lactose intolerance by detecting changes in blood glucose in plasma after ingesting a certain amount of lactose. If lactase is deficient and cannot break down lactose to produce glucose, serum glucose levels show a smooth curve, whereas lactose-tolerant individuals show marked peaks [7]. However, this test is more dangerous and painful for the patient, who has ingested a substance that the body may reject, which may lead to symptoms such as diarrhea, vomiting, etc.

3.3 Hydrogen Breath Tests

The hydrogen breath test utilizes the principle that because lactose is not completely broken down and absorbed by the small intestine, it directly enters the colon, and the hydrogen produced by colonic bacterial fermentation is exhaled through the pulmonary circulation. The concentration of hydrogen exhaled by the patient is detected, indirectly reflecting the digestion and absorption of lactose. According to Hou Ancun, the hydrogen concentration in the exhaled breath was expressed as PPM, and any difference between the peak hydrogen concentration in the exhaled breath and the basal hydrogen value exceeding 20 ppm within 3 h after lactose ingestion was considered positive, indicating the presence of LD [11]. However, when there is an overgrowth of small intestinal bacteria, the results of this test can be false-positive, misleading both physicians and patients.

3.4 Exclusions

It is important to note that milk product allergy and LI while having the same symptoms, are actually two different conditions that need to be carefully recognized. Milk product allergy is a food allergy, a cell-mediated immune disorder. Due to the specificity of the food, food allergies are diverse and frequent. Patients with milk protein allergy have diarrhea that stops when they switch to breast milk or stop using milk, while patients with LI, especially infants, are intolerant to both breast milk and cow's milk [7]. In the case of a dairy allergy, the immune system perceives certain milk proteins as harmful, which triggers the production of immunoglobulin E (IgE) antibodies to neutralize the proteins, also known as allergens. To assess for a milk allergy, a medical professional will perform a skin test, which means that the skin will be slightly pricked and the pricked area will be exposed to a small amount of the protein derived from the milk. If there is an allergic reaction, a raised bump (hives) may appear on the test site of the skin. Of course, milk allergy can co-exist with lactose intolerance.

4. Interventions

Based on the available research, it is known that there are two main treatments: avoidance of lactose intake and additional supplementation measures after intake. The former includes the application of lactose-free (low) milk powder [7], while the latter includes the addition of lactase drops to milk products [9], supplementing patients with oral probiotics, or replacing milk products with yogurt.

4.1 Dietary Modification

In the therapeutic approach of applying lactose-free (low) milk powder, since the complete exclusion of dairy products is detrimental to growth and development, lactose-free dairy products and low-lactose dairy products are more advantageous compared to the exclusion of dairy products as they do not reduce the intake of the nutrients. Some countries define "low-lactose" as less than 1 g of lactose per 100 g of product and "lactose-free" as less than 10 mg of lactose per 100 g of product [5]. However, there is no global consensus on the regulation of lactose-free.

In addition to the preparation of lactase-enriched lactose-free or low-lactose formulas, an alternative to lactose is the use of glucose polymers, which are most often digestible maltodextrins and glucose syrups, and others such as sucrose [5]. Glucose polymers are produced by the hydrolysis of different types of starch, common ones such as potato and rice. Although starch, maltodextrin, glucose, and lactose all have a similar energy, they are digested and absorbed at different rates, and there is a lack of research on whether these lactose substitutes can completely replace lactose nutritionally. Moreover, glucose polymers, because they have a higher glycemic index than lactose, may induce a higher glycemic response and contribute to diseases such as diabetes.

4.2 Lactase Supplementation

On the other hand, applying additional supplementation measures after lactose intake is a widely used method for LI patients, especially infants. According to ZHA et al. in the experiment, 180 mg of lactase drops were added to

each feeding of breast milk or preterm infant formula in the experimental group; while in the control group, 180 mg of heat-inactivated lactase drops were added to each breast milk or preterm infant formula feeding. Infants in both groups were intervened and observed for at least 2 weeks. It turns out that there was no statistically significant difference in the proportion of children with abdominal distension between the two groups at the time of enrollment and after 1 week of intervention. However, after 2 weeks of intervention, the rate of abdominal distension decreased to 2.6% in the lactase-treated group and 24.3% in the control group, which was lower in the lactase-treated group than in the control group, and the difference was statistically significant [9]. It can be seen that lactase treatment normalizes the intake of breast milk and formula in infants, so as children and adults, with LI.

4.3 Probiotics

Probiotics can safely and effectively reduce lactose intolerance symptoms and hydrogen excretion. Probiotics can synthesize digestive enzymes, which, together with those synthesized by the animal body, participate in the digestion of nutrients in the intestinal tract, stimulate the secretion of digestive enzymes by the animal body, reduce the depth of the crypts of the small intestine, increase the height of the villi, increase the surface area of the small intestine, and promote the absorption of nutrients in the intestinal tract. It maintains intestinal health by regulating the host's mucosal and systemic immune function or by regulating the balance of intestinal flora and promoting nutrient absorption, thus producing single microorganisms or a mixture of microorganisms with a clear composition conducive to health effects. There are huge differences in lactase activity of different probiotics. According to Facioni MS et al, among the eight probiotic strains, (Bifidobacterium longum, Bifidobacterium animalis, Lactobacillus bulgaricus, Lactobacillus rohita, Lactobacillus acidophilus, Lactobacillus rhamnosus, Saccharomyces boulardii and Streptococcus thermophilus), the degree of improvement in the symptoms of lactose intolerance, of which Bifidobacterium animalis is one of the most well-studied and effective strains [12]. However, according to current research, the therapeutic principle of probiotics is unclear and may be related to the effect on lactase.

5. Conclusion

By studying three types of LI: CLD, SLD, and PLD, and analyzing the four possible causes of LI, namely, genetic, geographic, anthropogenic, and bacterial or viral infections, this paper presents the values of current research overview of LI. The three available diagnostic methods of lactose tolerance testing and hydrogen breath as well as exclusions that differ from dairy allergies are provided, as are three therapeutic methods of lactose-free (low) product application, lactase supplementation, and probiotics. Its contribution is to provide a comprehensive discussion of topics related to LI. Nonetheless, this paper is still missing an explanation of dairy allergenicity and an exploration of the principles of probiotics. Pointing out gaps in research on the mechanistic role of probiotics, future research should aim to discover more non-dietary therapeutic options and suggest new therapeutic possibilities by understanding the principles of probiotics.

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