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Original Article

Lactose intolerance in the differential diagnosis of uneasy infants

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Abstract

Aim: Intestinal lactase deficiency is the most common carbohydrate malabsorption and digestive disorder. If lactase deficiency coexists with gastrointestinal symptoms such as abdominal distension, flatulence, abdominal pain, diarrhea, vomiting and nausea, then the term "lactose intolerance" is used clinically. Uneasiness and excessive crying are frequently seen in the first 3 months of life and constitute nearly 20% of the patients who are referred to a pediatrician. This study aims to perform a retrospective analysis of the complaints of patients who have been diagnosed with lactose intolerance.

Material and Methods: The files of patients, who were diagnosed with lactose intolerance between October 2017 and May 2018 in Defalife Hospital Pediatrics Outpatient Clinic, were retrospectively reviewed.

Results: A total of 38 patients, consisting of 23 males and 15 females are included to the study. The mean age of the patients was 5.51±3.47 months (age range 1 to 18 months). 31% of the patients diagnosed with lactose intolerance were admitted to the hospital due to uneasiness and excessive crying, and all of the patients were previously diagnosed as having infantile colic.

Conclusion: This study concludes that conducting tests for lactose intolerance might be beneficial in children that are presented to the hospital due to unexplained crying after the fourth month, at which time there is an expectation of seeing an improvement in colic behavior.

Keywords: Lactose intolerance; infantile colic; cow's milk protein allergy.

INTRODUCTION

Lactose is the primary carbohydrate that plays a role in infant nutrition. It consists of glucose and galactose. The lactase enzyme that is secreted from the brush border of the small intestine is necessary for lactose absorption and digestion, while intestinal lactase deficiency is the most common carbohydrate malabsorption and digestive disorder (1). There are 4 different forms of lactase deficiency: i.e. congenital, lactase non-persistence (LNP), secondary and neonatal. If lactase deficiency coexists with gastrointestinal symptoms such as abdominal distension, flatulence, abdominal pain, diarrhea, vomiting and nausea, then the term "lactose intolerance" is used to clinically describe the condition (2).

Uneasiness and excessive crying are frequently seen in the first three months of life and apply to nearly 20% of the patients who refer to a pediatrician. The prevalence of excessive crying in infants has been reported as being 14-30% in various studies (3,4). More specifically, infantile colic is a behavioral phenomenon characterized by inconsolable periods of crying in 1 to 4-month old infants (5). Although there is a consensus on excessive crying not having only one cause, the criteria for diagnosing infantile colic have been revised, the most recently with Rome IV criteria, and the parameters of excessive crying have been defined. Although the term colic refers to acute and unexplained abdominal pain, its pathophysiology has not yet been completely understood and it is also unclear whether there is an underlying gastrointestinal cause or not (6).

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This study retrospectively analyzes the complaints of patients who were diagnosed, at admission, with lactose intolerance due to LNP. They were then followed and treated in the general pediatrics outpatient clinic of our hospital.

MATERIAL and METHODS

We retrospectively evaluated the records of the patients who were diagnosed with lactose intolerance due to LNP between October 2017 and May 2018 at Defalife Hospital Pediatrics Outpatient Clinic. For the diagnosis of lactose intolerance, in addition to typical clinical complaints such as abdominal distension, flatulence, abdominal pain, diarrhea, vomiting and nausea, infants with feces of pH≤5.5 and reducing substance +2 and higher, and infants who exhibit improvement with lactase and/or lactose free formula over 4-6 weeks, as well as patients who do not have a history of upper or lower respiratory tract infection, were demographically verified. All of the patients were routinely tested for milk and egg-specific immunoglobulins, fecal occult blood and immunoglobulin E (IgE), as part of differential diagnosis of a cow's milk protein allergy. Regardless of the laboratory results patients with multiple system involvement such as gastrointestinal, skin and respiratory, who did not respond to lactose free and/or lactase treatment and the patients with severe atopic dermatitis, anemia, hypoproteinemia and growth hesitation were referred to another center for provocation tests for cow's milk allergy, celiac disease and non-celiac gluten sensitivity. Feces pH and reducing substances were studied manually. Merck 109535 pH-indicator strips were used for feces Ph and GBL Benedict's tests were used for reducing substances. The newborns and the patients who have a history of premature birth and chronic disease were excluded. Patients' characteristics including age, gender, birth weight, type of feeding, previous diagnosis, physical examinations and some laboratory results were reviewed for all patients. Among the forty six patients who fulfilled the criteria, six patients were excluded due to the fact that their complaints developed after rotavirus infection. Two other patients were excluded due to preterm birth of thirty four weeks.

RESULTS

The demographic characteristics and some laboratory results of the patients included in the study are provided in Table 1. The study included a total of 38 patients: 15 females and 23 males. The mean ages of the patients was 5.51±3.47 months (age range 1 to 18 months). Weight, height and head circumference values of our patients at the time of diagnosis are given in Table 1 together with standardized body mass indexes. Specific immunoglobulins (milk, egg) were all negative and none of the patients had positive results for fecal occult blood. The mean IgE was found to be 8.43±7.52 kU/l. The mean values of hemoglobin and eosinophils are 11.51±1.62 g/dl, 2.86±2.78 x 103/mm3 respectively. None of our patients had eosinophilia and none of them was exclusively breastfed. All of them are partially breastfed or formula fed. Nine patients had atopic dermatitis, 9 patients had rash, and 6 patients had abdominal distention at the time of diagnosis, according to their physical examination. All patients with complaint of uneasiness were previously diagnosed infantile colic. When we classify the patients

Table 1. Demographical and clinical characteristics of children with lactose intolerance

	Children with lactose intolerance (n=38)
Gestational age (months)	5.51±3.47
Gender	
Male (n %)	23 (60.5)
Female (n %)	15 (39.5)
Birth weight (total, g)	3108.82±399.49
Weight (kg)	7.37±2.04
Weight SDS	-0.27±1.03
Height (cm)	66.39±7.35
Height SDS	-0.18±1.23
Head circumference (cm)	42.65±2.20
Head circumference SDS	-0.57±0.93
BMI SDS	-0.22±1.42
Hemoglobin (g/dl)	11.51±1.62
Eosinophils (x 103/mm3)	2.86±2.78
Feces pH	5.39±0.21
IgE (kU/l)	8.43±7.52
Serum albumin (g/dl)	4.15±0.25
Feeding type (n)	
-breast-fed	-
-partially breast-fed	26
-formula-fed	12
Physical examination (n)	
-atopic dermatitis	9
-rash	9
-abdominal distention	6
Previous diagnosis (n)	
-infantile colic	18
-food allergy	4
-cow's milk protein allergy	2

Data show mean±SD values, BMI SDS, standardised body mass index

Table 2. Complaints of lactose intolerance patients upon admission to the hospital

Complaints upon admission to the hospital	Number (%)
Uneasiness, inconsolable crying	12 (31%)
Rashes on the face and body	9 (23%)
Non-healing rash, loose stool	9(23%)
Refusal to eat, vomiting	8 (21%)

according to their complaints at the time of diagnosis; the most common complaint was uneasiness and excessive crying with 31%. The least complaint was refusal to eat and vomiting. The other complaints are; non-healing rash, loose stool and rashes on the face and body. Table 2 shows the list of the complaints of the patients. After treatment our patients were followed up for 4 months and their symptoms did nor recur

DISCUSSION

Nearly 70% of the population of the world suffers from lactose intolerance. Since this presentation is associated with the gradual decrease in genetically programmed lactase expression when the mother is no longer able to breastfeed, it is known as LNP or hypolactasia (7,8). The age of symptom onset and prevalence vary depending on ethnicity and the dietary habits of a community. While the prevalence of lactose intolerance due to LNP in North European countries, which have high dairy product consumption, is 2-5%, it is 17% in Finland and Northern France, 50% in South America and Africa, and 90-100% in Southeast Asia (9). Although it can be said that Caucasian children younger than 5 years of age with lactose intolerance due to LNP are asymptomatic with a higher clinical tolerance, it has also been reported that the condition can be seen in younger patients in communities with a high prevalence of the disease (10-12). In studies conducted at the molecular level, it has been demonstrated that lactase activity started to decline around one year of age in Thai children, whereas the activity declined between the ages of 10 to mid-20s in Finnish children (13-14). It has been shown in previous studies that lactase expression in enterocytes is at the maximum level in the first months of life and then declines following the transition to supplementary food and weaning (15,16). It is for that reason that patients who were one year old and younger were included in the study. In Turkey, the rate of babies who are only given breast milk in the first 6 months is 2.4% (17). None of the patients in this study were only given breast milk, but they were being given formula or supplementary food.

In order to exclude cow's milk protein allergy (CMPA), which is clinically similar and should definitely be ruled out with a differential diagnosis in the infantile period, a detailed medical history was obtained from all of our patients. They were also tested for milk and egg-specific immunoglobulin, IgE, and fecal occult blood. Our patients did not have any signs that supported the presence of CMPA. CMPA progresses with more severe and systemic signs and, contrary to the common opinion, lactose can be tolerated in this disease (18). Our patients exhibited a dramatic clinical response to weaning from lactose or the use of lactase.

In the diagnosis of lactose intolerance, the hydrogen breath test is the least invasive and the most helpful test, although it is not very practical (19,20). In the presence of a clinical suspicion, complaints that are aggravated upon adding lactose to the diet, or that show a response to 2-weeks of lactose free diet, are also diagnostic (21). In order to diagnose our patients, we also considered the presence of a response to 4-6 weeks of lactose free diet and evaluated a reducing substance in the feces and feces pH. These are indirect markers of lactose malabsorption in patients under the age of two. Since reducing substance positivity to 0.25% is considered normal, patients with 0.50% and higher (+2 and higher) were selected for reducing substance positivity (22,23).

A total of 23% of the patients exhibited atopic dermatitis in their physical examination. Although conducted studies have shown that nearly 50% of children with CMPA have atopic dermatitis, the existence of atopic dermatitis alone is insufficient to make a reliable CMPA diagnosis (24). In accord with our study, Rudzeviciene et al. (25) have shown that 40.9% of children with atopic dermatitis exhibit lactose malabsorption.

The mean age of diagnosis was 5.51±3.47 in our patients. A total of 31% of the children were brought to the hospital due to uneasiness and excessive crying. These patients had been previously diagnosed with infantile colic due to excessive crying. However, the mean age of diagnosis partly ruled out infantile colic as it is generally self-limiting to around 4 months. Although infantile colic can be seen up to 6 months, its self-limiting etiopathogenesis in the first 4 months is an unknown phenomenon (26). Stahlberg et al. (27) have shown that lactase does not have an effect on the duration and symptoms of infantile colic. Similarly, Miller et al. (28) have shown that the use of lactase is ineffective in the treatment of colic. Although there are studies that show the opposite, lactase is not recommended in colic treatment (2,29). In our study, parents indicated that the uneasiness and excessive crying of their children showed improvement following treatment. Refusal to eat, vomiting, diarrhea, nausea, and non-healing rashes are the clinical signs expected with lactose intolerance, and some of our patients also exhibited these complaints.

CONCLUSION

Our study has some limitations. Since our study is retrospective genetic studies could not be performed for definitive diagnosis. In addition, patients who were referred to another hospital for milk provocation test could not be followed up. Consequently, babies can exhibit a partial malabsorption of the carbohydrate contained within breast milk or baby formula in the first year of their life. This physiological malabsorption, which stems from a deficiency due to slow enzyme maturation, can lead to colic in infants. During the 3rd month, when enzyme deficiency improves, clinically matches the month when infantile colic also subside (30). It is therefore concluded that performing tests for lactose intolerance due to LNP

could be beneficial in children who exhibit unexplained crying after the 4th month, at which time it is expected to see an improvement in colic behavior. However, prospective long-term studies, conducted with more patients, are necessary to support these findings.

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