Acta Paediatrica Hungarica, 24 (2), pp. 131–136 (1983)

Disaccharidases in coeliac disease

K Horváth, Gabriella Horn, Hedvig Bodánszky, Katalin Tóth and S Váradi

Second Department of Paediatrics, Semmelweis University Medical School, Budapest

In 30 children presenting with complaints characteristic of malabsorption in whom congenital enzyme deficiency could be excluded, determination of the enzymes lactase, saccharase and maltase was performed in the tissue sample obtained by jejunal biopsy; histology was also carried out in all cases. In 23 cases the diagnosis of coeliac disease could subsequently be confirmed, in the other 7 cases the diagnosis could neither be rejected nor established with certainty. All three enzymes had a decreased activity in cases displaying subtotal or total villous atrophy, the most sensitive among them being lactase: in 69% of cases no lactase activity could be shown while saccharase and maltase were absent in 29 respectively 4% of the cases.

No close correlation exists between the light-microscopic findings and the activity of enzymes since total absence of enzyme activity may be associated with only moderate villous atrophy. Lack of disaccharidase activity in the upper section of the small bowel does not necessarily mean disaccharide malabsorption exhibiting clinical symptoms, it only indicates a reduced capacity of disaccharide splitting.

It has been concluded that routine determination of disaccharidase activities is not justified within the diagnostic procedure of coeliac disease

Digestion of carbohydrates is ried out by a sequence of enzymatic cleaving procedures. The last step of these is the splitting of disaccharides to monosaccharides. The disaccharidases, the enzymes performing this process, are sited on the luminal surface of the epithelial cells lining the small bowel, in the neighbourhood of the microvillous structure [10].

Congenital absence of disaccharidases, in other words, congenital lactase, saccharase or isomaltase deficiency are rare conditions [8, 15]. Acquired forms are much more frequent. Secondary lactase deficiency is a common problem; it is frequently due to gastroenteritis [1] but may also be preceded by marasm, coeliac disease, cow's milk protein intolerance, immunodeficiency or a surgical intervention [14]. In adults, disaccharidase deficiency may evolve after gastric resection. Secondary saccharase and especially maltase deficiency are rather infrequent conditions.

In infancy, carbohydrate intake is mostly covered by the disaccharides lactose and saccharose and later a higher proportion of polysaccharides is consumed. The proportion of disaccharides within all carbohydrates ingested decreases to about 40% by the age of six to eight years [6].

The following tests can be used for establishing the diagnosis of disaccharidase deficiency:

demonstration of reducing compounds and measurement of pH in the stools;

chromatography of faecal carbohydrates;
oral carbohydrate loading;
measuring hydrogen concentration of expired air;
radioscopy after ingestion of a mixture of barium sulphate and lactose;
determination of disaccharidase activity in the jejunal mucosa.

The results of most of these tests are greatly influenced by other factors such as intestinal motility. Activity of the enzymes can be measured directly in homogenized tissue samples obtained by jejunal biopsy. This paper deals with experience gathered with the last-mentioned method.

Materials and Methods

Jejunal biopsy was carried out in 30 children admitted because of symptoms pointing to malabsorption. In addition to histological examination, activity of lactase, saccharase and maltase was determined. Mean age of the patients was 2.4 years with a range from eight months to ten years. In 23 the diagnosis of coeliac disease has been confirmed, the remaining 7 are being followed up. In other words, a third biopsy, definitely confirming the diagnosis, has not yet been done. The symptoms reported at admission by the parents are listed in Table I.

Table I

Symptoms before admission to hospital of patients with established or suspected coeliac disease

Symptom	No.	Per cent
Impaired growth	30	100
Diarrhoea	13	43
Bulky maldigested stools	13	43
Meteorism	12	40
Loss of appetite	9	3
Vomiting	6	2
Abdominal pain	1	3.3
Oedema	1	3.3
Good appetite	1	3.3

Determination of the enzymes was carried out by the method of Dahlquist [5]. The tissue sample immediately after removal was homogenized at 0 °C and deep-frozen. The measurements were carried out within two weeks after obtaining the sample. The results were expressed in international units (1 IU = 1 μmol substrate/g wet tissue/min). For comparison, the data of Burgess [3] obtained from 112 children with a normal jejunal mucosa were used. These were 2–16 IU for lactase, 3–20 IU for saccharase, and 15–77 IU for maltase. Sampling of the tissue was performed by a Watson-capsule from a section between the duodenojejunal junction and 10 cm distally from this. The enzyme activities were compared with the degree of villous atrophy of the jejunum. Classification of the atrophy was done using the principle of Oehlert [12]. The following distribution was found according to the degree of villous atrophy: partial villous atrophy (PVA), stage II or III: 4 cases; subtotal or total villous atrophy (SVA respectively TVA): 26 cases.

Results

For each enzyme the results are grouped according to the degree of villous atrophy and the clinical diagnosis. In Figure 1 it can be seen that lactase activity was below the normal limit in all cases but one exhibiting SVA or TVA (96%); in fact, it was absent in 69% of such cases. Among the four cases affected by PVA one had no lactase activity whatever, in two the value was within the normal limits.

Saccharase activity was determined in all but two of the 26 patients

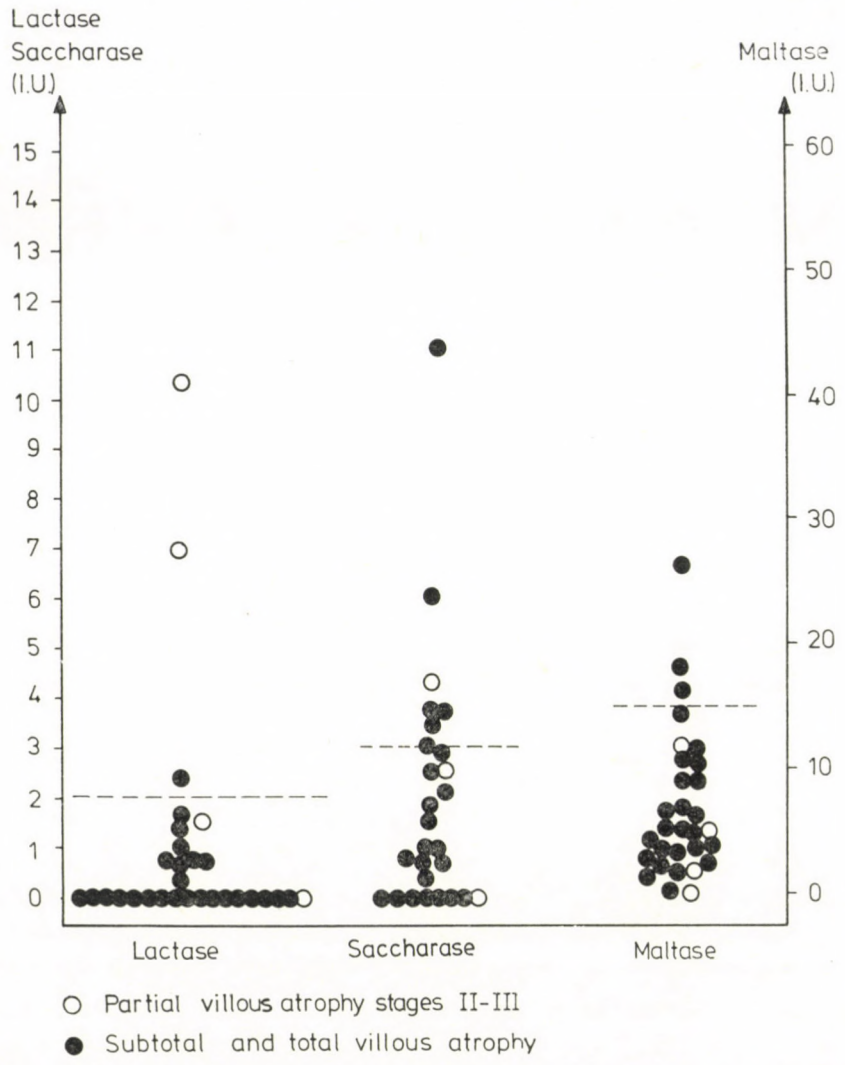

FIG. 1.

affected by subtotal or total villous atrophy. Absence of activity was demonstrated in 29%, an activity below the lower normal limit in 79% of cases (Fig. 1). Thus, saccharase is less sensitive to damaging factors than lactase. An abnormally low activity of saccharase was found in two cases out of the three with PVA.

Among patients with SVA or TVA all but three (88%) had a maltase value falling below the normal limit. Total absence of maltase, however, could only be demonstrated in a single patient (4%), i.e. maltase proved to be a resistant enzyme. In the patient with partial villous atrophy and manifest coeliac disease the deficiency in

maltose cleaving led to clinical symptoms, therefore a diet poor in maltose had to be prescribed during the initial phase of treatment.

Comparison of the figures shows that lactase is the most valuable and maltase the least vulnerable enzyme. In spite of the fact that all three enzyme activities were depressed or absent in the majority of patients affected by subtotal or total villous atrophy, no close correlation existed between the histological findings obtained by light microscopy and the enzyme activities, since decreased or absent activity could be observed even in cases with partial villous atrophy. Similarly, no age dependence could be observed in the groups with various degrees of villous atrophy.

Discussion

The disaccharidases are sited in the vicinity of the microvillous structure of epithelial cells lining the mucosal surface of the small bowel [10]. This adjacent situation makes them vulnerable to various damaging factors. In infancy and early childhood there is a marked proneness to mucosal abnormalities and secondary disaccharidase, chiefly lactase, deficiency after enteritis. Differentiation between mucosal damage due to enteritis and gluten sensitive enteropathy is not easy. In doubtful cases a diet containing no disaccharides and gluten may be indicated [1]. In case of lactase deficiency the ingested lactose cannot be split, it thus passes to lower sections of the small bowel, the unsplit sugar exerts its osmotic effect on the intestinal wall; the hypertonic solution in itself causes cellular damage and a decrease of disaccharidase activity [13]. The undigested sugar is then fermented by bacteria in the colon.

Christopher et al [4] investigated the pathomechanism of diarrhoea in 5 patients affected by lactase deficiency: after lactose ingestion they found the ileal fluid to have an osmolality of 300 mosm/l, and in the stools this value was 379 mosm/l. In their opinion, the diarrhoea was due to altered ileal secretion and colonic absorption. Bacterial fermentation of the unsplit lactose explains the higher osmolality in the stools and the fermentation products may inhibit the absorption of water in the colon.

Disaccharidase activity can be demonstrated all along the normal small intestine [2], the activity being lower in the distal sections. The damaging factors rarely cause mucosal damage all along the small bowel, in most cases there is only a reduction in sugar splitting capacity.

In coeliac disease, the villous damage is most pronounced in the upper part of the small intestine, the ileum is usually normal. Since biopsy is usually performed in the upper, damaged section, an abnormally low enzyme activity found here does not necessarily lead to clinical manifestation of disaccharide maldigestion and thus to diarrhoea. This was reflected also in our material: diarrhoea was mentioned in the history of only 13

cases (43%) out of 30 children with established or suspected coeliac disease.

In our experience, the mere demonstration of a decreased or absent disaccharidase activity in the jejunal biopsy specimen is no indication for a lactose-free diet. Elimination of lactose is only necessary at initiation gluten-free or the diet if diarrhoea has occurred in the history. Walker–Smith et al prescribe a lactose-free diet in coeliac disease only if diarrhoea appears immediately after an oral load of lactose [14]. In coeliac patients, biochemical deficiency of saccharase or maltase rarely leads to clinical manifestations.

Lactose malabsorption does not necessarily lead to diarrhoea. Conversely, it may be a frequent cause of abdominal pain. Liebman [cit. 9] performed lactose loading in 38 children with recurrent abdominal pain and in 11 of them he found a pathological curve. Four weeks of lactose-free diet resulted in disappearance of the complaints and so it was concluded that lactose intolerance may be a major factor in causing recurrent abdominal pain in children.

In older children, adult type hypolactasia or late onset lactase deficiency must be taken into consideration. In such cases the initially normal lactase activity of infancy decreases with age. The condition is common in certain races. In Japan, for instance, lactase deficiency was revealed in 30% of three year old children and in 89% of adults by the H_2 breath test based on the observation that bacterial fermentation of lactose in the colon produces molecular hydrogen [11]. In this condition the lactase deficiency exists in the presence of a normal histology of the jejunal mucosa.

Congenital lactase deficiency has to be distinguished from lactose intolerance with lactosuria, a condition characterized by specific clinical symptoms appearing after lactose ingestion. The latter condition is not due to deficient enzyme activity but to the mucosal leakage of lactose.

A comparison of the light microscopic findings with the enzyme activities obtained from the same sample allowed the conclusion that with increasing villous atrophy the activity of the disaccharide-splitting enzymes decreases. The most vulnerable was lactase, in accordance with data obtained by others, but no explanation of the phenomenon can be offered. It can, however, be seen from Table I that the correlation between histology and enzyme activity is unclear since moderate villous atrophy may occur with total deficiency of the enzymes and, conversely, normal activity is compatible with severe atrophy of the villi.

Electron microscopy of the microvillous structure will perhaps be able to establish some relationship between morphology and function [7]. For the diagnosis of coeliac disease, jejunal biopsy before and after gluten withdrawal and the estimation of faecal fat excretion are fully sufficient; thus, routine disaccharidase assays are not necessary for the purpose.

References

1. Anderson CM, Gravey M, Burke V: Coeliac disease. Some still controversial aspects. Arch Dis Child 47:292, 1972
2. Antonowitz J: Development and distribution of lysosomal enzymes and disaccharidases in human fetal intestine. Gastroenterology 67:51, 1974
3. Burgess EA: Techniques of investigation. In: Diseases of the Small Intestine in Childhood, ed. Walker-Smith JA, Pitman Medical Publications. London 1979, p. 82
4. Christopher NL, Bayless TM: Role of the bowel and colon in lactose induced diarrhea. Gastroenterology 60:845, 1971
5. Dahlquist A: Method for assay of intestinal disaccharidases. Anal Biochem 7:18, 1964
6. Gray GM: Carbohydrate digestion and absorption. Role of the small intestine. N Engl J Med 292:1225, 1975
7. Harrison M, Walker-Smith JA: Reinvestigation of lactose intolerant children: lack of correlation between continuing lactose intolerance and small intestinal morphology, disaccharidase activity and lactose tolerance test. Gut 18:48, 1977
8. Holzel A, Schwarz V, Sutcliffe KV: Defective lactose absorption causing malnutrition in infancy. Lancet 1:1126, 1959
9. Liebman WM: Recurrent abdominal pain in children: Lactose and sucrose intolerance, a prospective study. Pediatrics 64:43, 1979
10. Miller D, Crane RK: The digestive function of the epithelium of the small intestine I. An intracellular locus of disaccharide and sugar phosphate ester hydrolysis. Biochim Biophys Acta 52: 281, 1961
11. Nose O, Iida Y, Kai T: Breath hydrogen test for detecting lactose malabsorption in infants and children. Prevalence of lactose malabsorption in Japanese children and adults. Arch Dis Child 54:436, 1979
12. Oehlert W: Pathologie des Magen-Darm-Traktes. Schattauer Verlag, Stuttgart-New York 1978, p. 326
13. Teichberg S, Lifshitz F, Pergolizzi R, Wapnir RA: Response of rat intestine to a hyperosmotic feeding. Pediatr Res 12:720, 1978
14. Walker-Smith JA: Sugar malabsorption. In: Diseases of the Small Intestine in Childhood, ed. Walker-Smith JA, Pitman Medical Publishers, London 1979, pp. 250–278
15. Weijers HA, Van de Kamer JH, Mossel DRA, Dicke WK: Diarrhoea caused by deficiency of sugar-splitting enzymes. Lancet 2:296, 1960

Received August 3, 1982

K Horváth MD
Tűzoltó u. 7
H-1091 Budapest, Hungary