Activity of duodenal disaccharidases in relation to normal and abnormal mucosal morphology

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Abstract

Endoscopic duodenal biopsy specimens from 100 predominantly adult Caucasian patients under investigation for gastrointestinal symptoms were used to establish reference ranges for lactase, sucrase, and maltase in the duodenum. Duodenal and jejunal disaccharidase values were compared and the association between disaccharidase activity and morphology in the duodenum was examined. Mean lactase activities were about 40% lower in the duodenum compared with the jejunum; maltase was reduced to a lesser extent; and sucrase activities were much the same in the two sites. Lactase deficiency was found in 24 patients of whom 14 (58%) had duodenal disease. The presence of moderate to severe duodenal lesions was associated with a significant decrease in all disaccharidase activities, while only lactase was reduced in mild lesions. Twelve patients had normal lactase activity, despite the presence of duodenal disease.

It is concluded that specific reference ranges for duodenal mucosal disaccharidase activity are required as this is less than that of jejunum. Reduced duodenal disaccharidase activity is usually but not invariably associated with morphological abnormality.

Numerous studies have been performed to determine the normal disaccharidase activities in jejunal mucosa removed from near the ligament of Treitz using such instruments as the Crosby capsule.¹ The disaccharidase activities of jejunal mucosa have also been related to various histological abnormalities of the mucosa, including, particularly, coeliac disease and infections such as giardiasis.^{2,3} Over recent years formal jejunal biopsy has been almost completely replaced by endoscopic duodenal biopsy in the Royal Adelaide Hospital. Endoscopic biopsy material has been found satisfactory for establishing the diagnosis of most mucosal abnormalities, including coeliac disease.^{4,5} There are only a few studies, however, which have attempted to determine the reference ranges for duodenal disaccharidase activities or relate these to disease states.^{6,7} Differences could be anticipated between jejunum and duodenum because differences in histology are present, including, for example, villous height, lamina propria cell content, and Brunner's gland

tissue.⁸ The presence of peptic duodenitis is also important because it affects the proximal duodenum.

The aim of this paper was to report the disaccharidase activities found in 100 consecutive duodenal biopsy specimens in which the estimation was requested and to compare them with jejunal disaccharidase activities reported in a comparable study by Jennings *et al.*² The histology of the duodenal biopsy specimens taken at the same time was reviewed. The relation between the histology and disaccharidase activities was examined.

Methods

This study was carried out at the Royal Adelaide Hospital (RAH) and the Institute of Medical and Veterinary Science (IVMS), Adelaide, South Australia. One hundred and two duodenal endoscopies were performed on 100 consecutive patients for whom disaccharidase activities were requested. Several biopsy specimens were taken from the second part of the duodenum of each patient. Some were placed in formalin for histological examination and the remainder were wrapped in aluminium foil and placed on dry ice for transport to the pathology laboratory where they were transferred for storage at -70°C until disaccharidase estimates were done.

The clinical indication for an estimate of disaccharidase activity as stated on the request form was noted. Disaccharidase activity was assessed using a modified method developed by Dahlqvist⁹ and described in detail by Jennings *et al.*² Units of activity were expressed as μmol of disaccharide hydrolysed/minute/g wet weight of tissue at 37°C .

DERIVATION OF REFERENCE RANGES

Absolute ranges, means, and standard deviations for each disaccharidase activity were calculated, and *t* tests were used to compare groups of patients. Reference ranges were established from probit plots. A probit plot linearises a normal distribution to where the slope of the line is a function of variance. Subpopulations with different variance within the total population have different slopes when plotted. A probit plot entails summing the number of patients with each disaccharidase value and expressing them as percentage cumulative frequencies. These are plotted on arithmetic probability paper against the corresponding disaccharidase value.

Probit plots were made of lactase, sucrase,

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Distribution of disaccharidase values.

and maltase values for the total population. When lactase values were plotted, two subpopulations emerged. The subpopulation with higher lactase values was replotted and this plot, along with the plots of sucrase and maltase values for the total population, was used to establish reference ranges. A 90% confidence interval was selected to demarcate the reference range for each disaccharidase value.

Lactase values for the subpopulation with low lactase were also replotted and a 90% confidence interval was selected to ascertain whether the 90% confidence intervals for normal and low lactase values were separate. Jennings *et al* used different criteria for selection of reference ranges,² precluding direct comparison with ours. They set the upper limits as the highest value for each disaccharidase activity. Lower limits were related to the presence or absence of jejunal pathology, although slightly different criteria were used for each disaccharidase.

HISTOLOGY

The biopsy specimens for histopathological examination were fixed in formalin, processed, orientated and embedded in paraffin wax. Ribbons of 4 μ m sections were cut at three different levels through each block. These were stained with haematoxylin and eosin and extra ribbons were stained with alcian blue at pH 2.5 and periodic acid-Schiff reagent pretreated with diastase. The sections were reviewed by both authors.

The following features were assessed subjectively: (1) villus:crypt ratio; (2) surface epithelial changes—cell height, nuclear shape, and nuclear position were noted and the changes graded as mild, moderate, or severe; (3) lamina

propria cellularity—increase in cellularity was graded as mild, moderate, or severe. The presence of neutrophils as well as mononuclear cells, including plasma cells was noted.

Duodenal pathology was summarised in the following manner:

- (a) *a mild lesion*—comprising mild epithelial and lamina propria inflammatory changes with a normal or only slightly changed villus:crypt ratio;
- (b) *a moderate lesion*—comprising a pronounced change in villus:crypt ratio accompanied by inflammatory changes;
- (c) *a severe lesion*—comprising a complete loss of villi accompanied by pronounced inflammatory changes.

Results

The ages of the patients ranged from 7 to 76, mean 39 years. Four patients were under the age of 15. Fifty nine patients were female and 41 were male (1.4F:1.0M). Patients were Caucasian with the exception of two, who gave their country of origin as Africa and India, respectively. Gastroduodenoscopy was performed for various complaints, with coeliac disease or giardiasis suspected in many patients. The predominant presenting signs and symptoms were diarrhoea, weight loss, abdominal pain and low folate concentrations.

The frequency distribution of disaccharidase activities of the total population is shown in the figure.

The means, reference ranges, and absolute ranges of the duodenal disaccharidase values for the total population are presented in table 1, together with available data on jejunal disaccharidase activities from Jennings *et al*.²

According to the reference ranges for duodenum, we found lactase deficiency in 24 (24%) patients, sucrase deficiency in five (5%) patients, and maltase deficiency in eight (8%) patients.

Patients could be placed into four categories based on lactase values and histological appearances. Group A comprised 64 patients who had normal histology and normal disaccharidase activities. Group B comprised 10 patients with normal histology and low lactase activity but normal sucrase and maltase activities. Group C comprised 12 patients with duodenal pathology and normal disaccharidase activities. Group D comprised 14 patients with duodenal pathology and low disaccharidase activities. The 10 patients in group B included patients with primary lactase deficiency.

The two non-Caucasian patients had all disaccharidase values above the population means. Of the 26 patients with duodenal pathology, 12 had a mild lesion, nine had a moderate lesion, and five had a severe lesion. *Giardia* infection was shown in one patient who also had a mild lesion.

Disaccharidase values in relation to duodenal pathology are shown in table 2.

When a mild lesion was present, only the mean lactase value was significantly lowered compared with mean disaccharidase activities

Table 1 Disaccharidase values* in duodenum and jejunum†

	Mean (SD)		Reference range‡		Absolute range (minimum-maximum value)	
	Duodenum	Jejunum§	Duodenum	Jejunum	Duodenum	Jejunum
Lactase	5.7 (3.2)	10	3-14	7-30	0.5-19	0.5-30
Sucrase	16.3 (5.8)	17	6-26	9-40	2-35	1-39
Maltase	28.8 (10.3)	40	13-44	19-75	4-58	0.5-75

* μ mol of disaccharide hydrolysed per minute per gram wet weight of tissue at 37°C.

†Jennings *et al*.²

‡Jejunal and duodenal reference ranges are not directly comparable.

§Standard deviations not available.

Table 2 Disaccharidase values in normal duodenum compared with values in mild, moderate, and severe mucosal lesions

	<i>Normal</i>		<i>Mucosal lesion</i>					
	<i>n = 74</i>		<i>Mild (n = 12)</i>	<i>Moderate (n = 9)</i>		<i>Severe (n = 5)</i>		
Lactase	6.5	(2.8)	3.9	(2.2)	3.8	(3.1)	0.9	(0.2)
Sucrase	17.2	(5.6)	16.3	(3.8)	11.9	(7.0)	4.0	(1.4)
Maltase	31.03	(12.3)	26.42	(10.0)	22.78	(11.4)	5.8	(1.0)

in normal duodenum ($p < 0.01$). Pathological changes had to be moderate before mean sucrase and maltase values were also significantly lowered ($p < 0.01$; $p < 0.05$ for sucrase and maltase, respectively). Mean lactase, sucrase, and maltase values were not significantly different in patients with mild lesions compared with those with moderate lesions, but were significantly lower in severe lesions compared with moderate lesions ($p < 0.01$; $p < 0.05$; $p < 0.01$ for lactase, sucrase, and maltase, respectively).

Discussion

This study does not include a true control group as all patients were under investigation for gastrointestinal symptoms. In view of the uncertain correlation, especially in children, between disaccharidase values, lactose tolerance test data, and actual reported intolerance to lactose^{10,11} we established reference ranges independent of such data, finding a clear separation between the confidence limits for normal and low lactase activities.¹² The literature does not concur on the definition of normal and abnormal disaccharidase values¹³ and different assay techniques, groups of subjects and sites of biopsy are some of the variables which require cautious interpretation of interstudy comparisons.¹⁴⁻¹⁶

The study by Jennings *et al* provides, in some respects, a good direct comparison between disaccharidase values in the duodenum and jejunum, because that study was also done at the RAH-IMVS complex on patients drawn from the same population (albeit separated by 12 years) and using an assay method identical with that used in the present study.²

There is a difference between the two studies with regard to method of biopsy (suction capsule as opposed to endoscopic biopsy), but it is uncertain whether this affects disaccharidase values.^{17,18} Nevertheless, data in table 1 indicate that mean lactase values in the duodenum are reduced by about 40%. Maltase is reduced to a lesser extent, and sucrase activities in the two sites seem to be similar. Bergoz *et al* found that duodenal disaccharidase activities were, in general, reduced by about 40% compared with those in the jejunum,¹⁸ but his results differed from ours in that he found that sucrase and maltase were significantly reduced but lactase, although reduced, was not significantly so. The site of biopsy in the duodenum may be important, but data on the variability of disaccharidase values along the duodenum are not concordant.^{6,13,14} There is general consensus,

however, that duodenal biopsy specimens are adequate for diagnosing disaccharidase deficiencies.¹⁵

The low incidence of giardiasis in this study compared with that found by Jennings *et al*² may reflect an increased awareness and earlier treatment of giardiasis by general medical practitioners.

The incidence of primary lactase deficiency varies according to ethnic origins,¹⁹ but our incidence of patients with low lactase activity and normal histology of 10% compares with the 7% of adults and 6.25% of juveniles of similar ethnic origins reported in other studies.^{2,11} Patients with primary lactase deficiency would fall into this group, although some may be cases of true secondary deficiencies.²

The presence of duodenal pathology does not always predict low lactase values, but disaccharidase values in patients with duodenal pathology were significantly lower than those in patients with normal histology, with lactase activities declining before those of sucrase and maltase.

Berg *et al* found a significant correlation between pathology at the ligament of Treitz and disaccharidase values³ but Calvin *et al*, in their study of the jejunum and on surveying the literature, found the association between disaccharidase values and mucosal injury in both children and adults to be unconvincing.¹¹ Harrison and Walker-Smith found that in biopsy specimens taken between the fourth part of the duodenum and the first loop of the jejunum, there was a negative correlation between lactose tolerance test data, clinical lactose intolerance, small intestinal morphology and lactase activity.¹⁰

In our study mild lesions were more frequently associated with normal disaccharidase activities, while moderate or severe changes were more frequently seen in patients with low disaccharidase activities.

Part of the difficulty in establishing the existence of a correlation must be the uncertainty of determining what constitutes a deficiency state. Discordant histology and enzyme activity could also be due to spotty mucosal change.⁷

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