Lactose Absorption and Mucosal Disaccharidases in Convalescent Pellagra and Kwashiorkor Children

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Prinsloo, J. G., Wittman, W., Kruger, H., and Freier, E. (1971). *Archives of Disease in Childhood*, 46, 474. **Lactose absorption and mucosal disaccharidases in convalescent pellagra and kwashiorkor children.** Oral lactose and glucose/galactose loading tests were done in Bantu children convalescing from kwashiorkor and pellagra. Small bowel biopsies and disaccharidase estimations were performed in all except 2 patients. Lactose absorption was more impaired and intestinal lactase levels were lower in the pellagra than in the kwashiorkor group. The fact that diarrhoea after admission to hospital was less common in pellagra than kwashiorkor was ascribed to a lesser lactose load due to the early introduction of a mixed diet in the former group, in comparison with milk feeds only in the latter group. The absence of troublesome diarrhoea while on moderate quantities of lactose in the diet, in the presence of low intestinal lactase levels, but evidence of lactose malabsorption after loading, has a bearing on preventive and therapeutic nutrition programmes in non-Caucasian children. Lactase deficiency is not necessarily synonymous with symptomatic lactose intolerance if the threshold is not exceeded. Concern is expressed that excessive caution against the use of milk may lead to a worsening of infantile malnutrition in developing countries.

During the past few years there have been several reports of lactose intolerance among non-Caucasian people (Cuatrecasas, Lockwood, and Caldwell, 1965; Cook and Kajubi, 1966; Bayless and Rosensweig, 1966; Davis and Bolin, 1967; Chung and McGill, 1968; Alzate, González, and Guzmán, 1969; Bayless and Huang, 1969; Haemmerli and Kistler, 1966; Jersky and Kinsley, 1967; Bolin, Crane, and Davis, 1968), and the possibility of either a genetic (Cook and Kajubi, 1966; Bayless and Rosensweig, 1966; Chung and McGill, 1968; Alzate *et al.*, 1969; Bayless and Huang, 1969; Haemmerli and Kistler, 1966; Jersky and Kinsley, 1967), or an induced (Cuatrecasas *et al.*, 1965; Davis and Bolin, 1967; Bolin *et al.*, 1968; Bolin and Davis, 1970) deficiency due to lack of milk intake was raised. The practical significance of lactose intolerance in children suffering from protein-calorie malnutrition was indicated first by Dean (1957) and later by Bowie, Brinkman, and Hansen (1963, 1965). In our area kwashiorkor patients also had low intestinal lactase levels, though generally diarrhoea was not as severe as reported

from other centres (Prinsloo *et al.*, 1969). The medical history of pellagra children revealed diarrhoea to be a complaint in about 16% of the patients (Prinsloo *et al.*, 1968). However, from superficial judgement it does not appear to be a clinical problem after admission to hospital, even when milk forms part of their diet. This seems paradoxical, firstly in view of the reported high incidence of lactase deficiency in non-Caucasians, and secondly since diarrhoea is generally considered to be one of the main features of pellagra.

The patients with childhood pellagra seen by us do not as a rule appear severely ill and they have few if any systemic complaints. The serum albumin levels are usually lower than normal but not nearly as severely depressed as in kwashiorkor (Prinsloo *et al.*, 1968). It therefore seemed possible that lactose tolerance could be less depressed in pellagra than in the more severely malnourished kwashiorkor patients. No published reports of intestinal lactase levels or lactose tolerance tests done on children suffering from pellagra could be found. It was therefore decided to evaluate lactose absorption and intestinal disaccharidase

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levels of pellagra children and to compare the results with those obtained in kwashiorkor.

Patients and Methods

Bantu children recovering in hospital from typical kwashiorkor (10 patients) and classical pellagra without oedema (12 patients) were investigated. Patients who suffered from overt secondary infections as well were excluded. Oral lactose loads (2.0 g/kg body weight) and glucose/galactose (1.0 g/kg body weight of each) were administered during the convalescent phase. In 19 patients the tests were done within 3 weeks of admission to hospital and in 3 patients between 3 and 6 weeks after admission. An interval of 2 to 6 days separated the two sugar loads in order to allow possible diarrhoea caused by the sugar ingestion to subside. Capillary blood samples were collected in the fasting state and at half-hourly intervals for 1½ hours after the sugar loads. The blood glucose concentration was determined colorimetrically with the aid of the glucose oxidase method (C. F. Boehringer, Mannheim, Germany, test kit). The maximum blood glucose increment was calculated from the highest rise above the fasting level during the test (Haemmerli and Kistler, 1966). An attempt was made to classify patients into 'absorbers' and 'non-absorbers' according to their blood glucose increments after the sugar loads. The arbitrary dividing line used by different investigators varied (Welsh, Rohrer, and Walker, 1966; Chandra, Pawa, and Ghai, 1968; Bolin and Davis, 1970; Huang and Bayless, 1967; Bayless and Rosensweig, 1966; Dubois *et al.*, 1970; Cook, 1967; Desai *et al.*, 1970; Jussila, 1969). The majority, however, considered an increment in blood glucose concentration of more than 20 mg/100 ml above the fasting level after a standardized oral sugar load as being indicative of 'absorption'. Thus patients who had a blood glucose rise of more than 20 mg/100 ml above the fasting value at any stage during the test were designated 'absorbers' and those with lesser increments, 'non-absorbers'. Small bowel biopsies were also done during the convalescent phase in all except 2 patients. The biopsies were taken with a Watson infant-size capsule from the jejunum near the region of the ligament of Treitz after the capsule had traversed the duodenum. The position of the capsule was verified fluoroscopically with an image intensifier. The mucosal specimens were immediately weighed, frozen, and analysed for disaccharidases and protein content. Enzyme and protein estimations were done according to the methods of Dahlqvist (1964) and Lowry *et al.* (1951), respectively. Disaccharidase activities were expressed as units (μ mole disaccharide hydrolysed per minute) per g protein. The body weight of each patient was recorded on admission and expressed as a percentage of the 'expected' weight (Boston 50th centile—Nelson, 1964).

Statistical analysis. The blood sugar increments of the two groups after lactose as well as after glucose/galactose loading were tested for significant differences by applying Wilcoxon-Mann-Whitney U test (Siegel,

1956). The same test was used in the case of the disaccharidase and mucosal protein concentrations of the two groups. The two-tailed Wilcoxon matched-pairs signed-ranks test (Siegel, 1956) was used to test for a significant difference in blood sugar increments after lactose and glucose/galactose ingestion within the same group. In all tests a probability level of less than 5% ($p < 0.05$) was regarded as significant.

Results

The sex, age, body weight on admission, percentage expected weight of the patients, and the blood glucose increments after the sugar loads can be seen from the Table. The blood glucose increments after lactose were poor in both the pellagra and kwashiorkor groups, average peak levels being less than 25.0 mg/100 ml. The response of the pellagra group after lactose was less than that of the kwashiorkor group and the maximum increments of the 2 groups differed significantly ($p < 0.01$). The blood glucose increments of both groups after glucose/galactose intake were better than after lactose. Several patients, however, especially in the kwashiorkor group, still had unsatisfactory increments, but no significant difference was found between the values of the two groups ($p > 0.05$ – 0.10). The maximum blood glucose increments of the kwashiorkor patients were similar both after lactose and after glucose/galactose and did not differ significantly. In the pellagra patients, however, the maximum increments after lactose were much less than after glucose/galactose, and the difference was highly significant ($p < 0.001$).

After the lactose load there were no 'absorbers' in the pellagra group but 5 'absorbers' in the kwashiorkor group, whereas after glucose/galactose ingestion 9 of the 12 pellagra and 5 of the 10 kwashiorkor patients were 'absorbers'. Of the 5 kwashiorkor patients who were lactose 'absorbers', 2 failed to 'absorb' glucose/galactose. This is difficult to explain but might have been due to delayed gastric emptying in these 2 patients.

The intestinal disaccharidase levels, the sucrase/lactase ratios, and the mucosal protein concentrations are also shown in the Table. The lactase concentrations of the pellagra patients were lower and their sucrase/lactase ratios higher than those of the kwashiorkor group. The difference between the values of the two groups was highly significant ($p < 0.005$) in the case of lactase concentrations, and significant ($p < 0.02$) in the case of the sucrase/lactase ratios. There were no significant differences, however, between the sucrase, isomaltase, maltase, and mucosal protein concentrations of the two groups.

Maximum Blood Glucose Increments of Patients After

Patient	Sex	Age (mth)	Weight (kg)	% Expected Weight*	Maximum Blood Glucose Increment During First 90 minutes After:			
					(a) Lactose	A† or NA‡	(b) Glucose/ Galactose	A† or NA‡
Kwashiorkor								
1	M	24	6.28	50.0	13	NA	7	NA
2	M	15	7.62	67.5	9	NA	11	NA
3	M	30	7.75	56.9	17	NA	82	NA
4	M	84	15.54	63.3	13	NA	50	NA
5	M	36	10.75	73.6	18	NA	16	NA
6	M	16	7.15	66.5	24	A	15	NA
7	M	17	8.58	75.1	32	A	11	NA
8	M	36	14.09	96.4	21	A	28	NA
9	M	24	8.44	67.2	66	A	25	NA
10	M	36	9.83	67.3	32	A	34	NA
Average value		31.8	9.60	68.38	24.50		27.90	47.4
Pellagra								
11	M	96	12.27	45.0	8	NA	38	NA
12	F	144	27.95	70.3	1	NA	17	NA
13	F	84	17.27	72.9	14	NA	33	NA
14	F	48	15.00	91.4	10	NA	31	NA
15	M	108	13.86	46.3	12	NA	40	NA
16	F	121	30.00	83.9	2	NA	55	NA
17	F	108	18.86	65.2	16	NA	26	NA
18	M	108	16.13	53.9	18	NA	16	NA
19	F	144	17.72	44.6	20	NA	27	NA
20	F	84	18.86	79.6	20	NA	18	NA
21	M	96	22.95	76.6	13	NA	53	NA
22	M	120	23.64	72.4	5	NA	51	NA
Average value		105.1	19.54	66.8	11.58		33.75	40.2

* Boston 50th centile.

A† Absorber (see text).

NA‡ Non-absorber (see text).

§ Units = micromoles disaccharide hydrolysed/min/g protein

Comments

It can be seen from the Table that, in general, both groups of patients absorbed lactose poorly and that the pellagra group fared worse with a total absence of 'absorbers'. On the whole the pellagra group was able to absorb glucose/galactose better than lactose and also more efficiently than the kwashiorkor group, though the maximum increments of the two groups showed no significant differences. The greater inability of the pellagra patients in comparison with the kwashiorkor group to handle lactose is further evidenced by their blood glucose increments after lactose as well as their intestinal lactase levels. On both counts they had lesser average values than the kwashiorkor patients and the differences were significant. It is well known that blood glucose increments after loading tests may also be affected by the time of gastric emptying. It seems improbable, however, that the pellagra patients as a group could have had delayed absorption with lactose loading and not with glucose/galactose loading. Furthermore, considering a lactase level of over 10 units/g protein

as normal (Dahlqvist, 1967), only 3 kwashiorkor patients had normal values while those of all the pellagra patients were abnormal. If the 3 normal values of the kwashiorkor group are excluded and the rest of the group is compared with the pellagra children, there is little difference in the lactase concentrations. It should be pointed out, however, that absolute enzyme values show great variations while the ratio of the different enzymes remain more or less constant in normal subjects (Prader and Auricchio, 1965). Thus the sucrase/lactase ratio has been considered a more reliable index, and a value of 4.0 or less suggested as normal (Prader and Auricchio, 1965; Welsh, 1968). Adopting this standard, all the patients except one were lactase deficient, and the pellagra group again had values furthest away from normal. The more severe lactase depression of the pellagra group was selective since the other disaccharidases did not differ significantly between the two groups.

These findings seem to be contradictory to our earlier remarks, namely that diarrhoea is neither a common complaint nor frequently encountered

Sugar Loads, and Mucosal Disaccharidase Activities

Disaccharidase Units§					Mucosal Protein (mg/g wet weight)
Lactase	Sucrase	Sucrase/Lactase	Isomaltase	Maltase	
		Ratio			
24.5	99.5	4.1	123.5	349.0	86.1
19.5	93.0	4.8	99.0	296.0	96.3
3.9	30.0	7.7	44.0	86.0	108.0
2.3	43.2	18.8	59.0	143.0	103.0
2.8	69.0	24.6	100.0	305.0	80.0
3.5	17.7	5.1	25.0	79.0	123.0
10.4	35.7	3.4	54.0	159.0	97.5
6.1	36.0	5.9	44.0	99.0	107.0
7.3	58.0	7.9	87.0	184.0	118.0
3.2	18.7	5.8	43.5	157.0	81.0
8.35	50.08	8.81	67.90	185.7	99.99
1.3	42.0	32.3	60.0	138.0	111.0
5.4	77.5	14.4	101.0	256.0	89.5
2.3	50.5	22.0	76.5	217.0	86.0
1.3	37.4	28.8	62.6	155.0	102.0
2.1	74.0	35.2	86.0	224.0	98.0
3.0	64.0	21.3	87.0	183.0	136.0
4.7	38.0	8.1	52.0	101.0	104.0
3.1	46.7	15.1	77.5	172.0	100.5
2.1	46.5	22.1	60.0	104.0	138.0
2.0	30.2	15.1	37.6	84.0	116.0
—	—	—	—	—	—
—	—	—	—	—	—
2.73	50.68	21.44	70.02	163.4	108.10

after admission to hospital in pellagra children. The explanation of this phenomenon is most probably due to the fact that after admission to hospital pellagra patients, being older and less acutely ill, are allowed in addition to milk a general ward diet, whereas kwashiorkor patients initially receive milk feeds only. The lactose tolerance of pellagra patients is consequently not as severely stressed as in the case of kwashiorkor patients. If the pellagra patients had been given milk only, such a high lactose load in the presence of their lower lactase levels would almost certainly have led to similar or more severe diarrhoea than found in kwashiorkor patients. In the present experiment stools were unfortunately not collected from all the patients. Subsequently stools were collected from 8 kwashiorkor and 11 pellagra children after identical glucose/galactose and lactose loads. The average stool weights of the kwashiorkor group after glucose/galactose and lactose were 182.5 g and 195.5 g/day respectively, while comparable values for the pellagra group were 212.0 g and 333.3 g/day. These results are further evidence

of a greater lactose intolerance of patients recovering from pellagra than those recovering from kwashiorkor.

In conclusion, it is evident that there was lactose intolerance in pellagra as well as kwashiorkor subjects as exemplified by loading tests and intestinal lactase concentrations. In our experience troublesome diarrhoea is not often encountered in pellagra children while they are on a moderate lactose intake (milk as part of their diet). Furthermore, as previously shown (Prinsloo *et al.*, 1969) most kwashiorkor patients tolerate milk feeds well and diarrhoea usually subsides within 2 weeks of admission to hospital. These findings have a practical bearing on preventive and therapeutic measures in malnutrition (at least where severe and prolonged diarrhoea is not a general accompanying feature). Considering the expense involved in compiling lactose-free formulae and the availability as well as the success of milk in establishing convalescence in malnourished children, we are concerned that probable excessive caution against the use of milk in nutrition programmes for non-

Caucasian children in developing countries (Bayless and Huang, 1969; McCracken, 1970) may lead to a worsening of the state of affairs. Lactose intolerance found after lactose loading need not in practice necessarily be symptomatic if the threshold is not exceeded. Desai *et al.* (1970) aptly pointed out that though diarrhoea developed in 62% of Indian subjects after a load of 50 g lactose, 90% of the population could tolerate at least 20 g lactose, the amount present in 450 ml cows' milk.

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