LACTOSE INTOLERANCE: HEREDITARY OR ACQUIRED? EFFECT OF PROLONGED MILK FEEDING

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SYNOPSIS

Twenty-one children from a Girls' Home, aged $2\frac{1}{4}$ to 10 years, were investigated to find the incidence of lactose intolerance. Milk in amounts equivalent to that in Western diets was then introduced into their diet over a period of one year. At the end of this period, the incidence of lactose intolerance was investigated again to find whether any change had occurred as a result of the high milk diet. It was concluded that although there was apparent benefit from this mode of diet, resulting in marked weight gain, there was no objective evidence that the lactose tolerance was improved in the majority of the children. There was, however, some suggestion from this study that, given a much longer period of high milk intake, slow improvement in lactose tolerance is possible. Despite the lack of direct evidence for this, several recent publications on human subjects and animal experiments stressed the important association between milk intake and lactose tolerance, even though a genetic basis is believed by most to be the cause of primary lactose intolerance.

INTRODUCTION

In recent years there has been increasing interest in the phenomenon of lactose intolerance due to intestinal lactase deficiency occurring in apparently healthy subjects. An increased incidence has been described in various ethnic groups, including Negroes (Cuatrecasas *et al*, 1965; Cook and Kajubi, 1966), Greek Cypriots (McMichael *et al*, 1966), Australian Aborigines (Elliot *et al*, 1967), Indians (Desai *et al*, 1967), Chinese (Davis and Bolin, 1967; Chung and McGill, 1968), Thais (Troncale *et al*, 1967) and South American Indians (Alzate *et al*, 1969).

There has been controversy over the aetiology of primary lactase deficiency. Most authors have argued in favour of a genetic basis for this deficiency (McMichael *et al*, 1966; Cook and Kajubi, 1966; Chung and McGill, 1968; Bayless and Christopher, 1969). An adaptive basis for lactase deficiency was proposed by Cuatrecasas *et al* (1965) and Davis and Bolin (1967). This acquired deficiency could result from lack of continued substrate challenge—in the form of low levels of milk consumption after weaning—producing a gradual adaptive decline in enzyme activity.

A study was undertaken in Singapore to determine the incidence and age of onset of lactose intolerance in an indigenous Asian population (Bolin *et al*, 1970). Detailed histories of milk consumption from birth were taken in this study, and this was related to the presence or absence of lactose intolerance to show whether there was a positive correlation between lactose tolerance and continued milk consumption after weaning. In this survey, 98 subjects hospitalised for non-gastrointestinal disease, from 1 to 42 years of age, were studied; there were 73 Chinese, 15 Malays and 10 Indians. The results showed that there was a high incidence of lactose intolerance amongst these three ethnic groups, and this was found to be due to an isolated deficiency of lactase. Amongst the group who had been drinking milk continuously since weaning, the incidence of primary lactose intolerance was low compared to the group who had abstained from milk since weaning. The evidence from this study seemed to support an adaptive rather than a genetic cause for primary lactose intolerance, and that lactase deficiency was acquired from lack of substrate (milk) challenge in the majority of our subjects.

In the light of this finding of a relationship between lack of milk ingestion and lactose intolerance, it was proposed that a further survey be made to confirm this relationship. Accordingly, milk in equivalent amounts to Western diet was introduced into the diet of a group of children for a period of one year. Before and after milk introduction to this group of children, their lactose tolerance status was studied, and the results then compared to find if any change has occurred.

METHOD

For ease of supervision of the enforced milk diet, it was proposed that a group of children from

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an institution be studied, and 21 children from Toa Payoh Girls' Home were thus chosen. This consisted of 17 females and 4 males, aged between 2¼ yr. and 10 yr. They have all been weaned from a milk diet, and the amount of milk consumed since weaning has been small. Before lactose tolerance tests were done to survey the incidence of lactose intolerance, haemoglobin concentration and stool examination for ova were done. Whenever there was anaemia and worm infestation, these were corrected, as it has been shown that anaemia and worm infestation could affect the test (Bolin *et al*, 1971 i). The main survey consisted of a glucose tolerance test followed by a lactose tolerance test and lactose barium meal for each child. For the first two tests, capillary blood samples were taken fasting, at 15, 30, 45, 60 and 90 min. after glucose or lactose ingestion. The dose of glucose was 25 gm. in 150 ml. water, except in those under 25 kg. body weight, where the dose was 1 gm./kg. body wt. The dose of lactose was 50 gm. in 300 ml. water, except in those who were under 25 kg., where the dose was 2 gm./kg. body wt. Blood glucose was measured by a glucose oxidase method. Lactose intolerance was diagnosed if the maximum rise in blood glucose was less than 20 mg. per 100 ml. blood after lactose and more than 20 mg. per 100 ml. blood after glucose. In the lactose barium meals, mixtures of 'Micropague' barium sulphate suspension and lactose were given and the procedure carried out according to Laws and Neale (1966). The films were classed as normal or abnormal according to dilution of barium, dilatation of small intestine and transit time of barium to the colon (Kho and Bolin, 1969). The results were then correlated with the lactose tolerance test.

MILK INTRODUCTION

From the 1st of September, 1969, milk was introduced into the diet of this group of children. This was supplied in powder form and had to be reconstituted every morning in a standard way (2½ oz. to a pint) so that each pint would contain 25 gm. of lactose. Each child was given this amount as her daily portion, which was taken in several doses together with her meals. This enforced milk diet was strictly supervised by members of the staff of the Girls' Home, and was continued for a year. A monthly weight chart was kept on each child during this period.

On completion of this period of milk intake, lactose tolerance tests were done again. Although the results of this final test were used mainly for our conclusions, an interim lactose tolerance test was also done after the 4th month of milk intake, simply to find whether this relatively short period could induce any changes.

Comparing the Effects of Pure Lactose and Milk

After the main survey was completed, by the end of September 1970, a short survey was made on the same group of children to compare the effects of pure lactose ingestion and milk ingestion. Apart from this, the aim was to find the approximate quantity of lactose or milk which would give rise to symptoms, such as abdominal cramps, distension, loose stools and diarrhoea. No blood glucose estimations were done. Graduated doses of lactose was first given to each child to find the amount which would cause symptoms within 4 hours of ingestion. During each session, the lactose solution was consumed at one sitting, within 15 min. usually, and the symptoms, if any, were recorded. Beginning with 12·5 gm. lactose, this was gradually stepped up to the dose which would give rise to symptoms in a significant number of subjects. Similarly, milk containing equivalent amounts of lactose, beginning with ½ pint, was given, and then stepped up gradually until the amount which would cause symptoms.

RESULTS (Table I)

Lactose Tolerance Tests before Milk Introduction

All the children were found to have normal glucose tolerance tests, the maximal rise being greater than 20 mg.%.

In the lactose tolerance tests, however, 13 of the 21 children were found to be intolerant, with an overall incidence of 62%. Analysis according to age groups showed that all these 13 children were above 5 yrs. of age. Of the remaining 8 who were lactose tolerant, only 2 were above 5 yrs. and all the 6 children who were under 5 yrs. were tolerant.

Comparing the lactose barium meal findings with the lactose tolerance tests, it was found that, apart from 2 instances, 17 of the 19 cases done showed good correlation.

Lactose Tolerance Tests after Milk Introduction

At the end of one year of enforced milk diet, it was found that 17 of the children were lactose intolerant, an incidence of 81%. These 17 included 12 of the 13 children who were intolerant at the beginning of the study. Of the 8 children who were found tolerant at the beginning, only 3 remained so at the end of the year of study. These 3 cases were all under 5 yrs. of age. The other 5 children who became intolerant after 1 year were relatively older by comparison.

TABLE I

RESULTS OF LACTOSE TOLERANCE TESTS

No.	Age Yrs.	Sex	Race	Lactose T.T. (1)	Lactose T.T. (2)	Lactose T.T. (3)	G.T.T.	Lactose Barium.
1	3	F	Chinese	30	20	10	82	—
2	3	F	Chinese	60	32	36	77	Normal
3	4¼	F	Chinese	40	22	8	26	—
4	5½	F	Indian	5	6	0	28	Abnormal
5	5½	F	Indian	29	14	12	80	Normal
6	6	F	Chinese	2	0	8	57	Abnormal
7	2¼	M	Indian	23	40	55	28	Normal
8	2½	M	Chinese	25	14	29	57	Normal
9	4¼	M	Indian	28	5	16	64	Normal
10	5½	M	Chinese	1	18	11	20	Normal
11	6½	F	Indian	2	13	9	36	Abnormal
12	6½	F	Chinese	12	6	7	49	Abnormal
13	7½	F	Indian	2	4	0	57	Abnormal
14	7½	F	Chinese	21	30	12	53	Abnormal
15	8	F	Chinese	5	0	4	50	Abnormal
16	8¾	F	Indian	0	6	0	26	Abnormal
17	9¼	F	Chinese	11	3	0	42	Abnormal
18	9½	F	Chinese	3	4	11	20	Abnormal
19	9¾	F	Chinese	0	12	22	26	Abnormal
20	10	F	Chinese	0	11	0	67	Abnormal
21	10	F	Chinese	0	5	0	33	Abnormal

Under the lactose tolerance tests, the three columns refer to maximum rise in blood glucose in mg.%. Column (1) refers to figures before milk, (2) at the 4th month, and (3) after 1 year of milk ingestion. The lactose-barium meal results are taken before milk ingestion, and they should be correlated with the lactose tolerance tests in column (1) only.

Only 1 of the 13 children found initially to be intolerant became tolerant after 1 year. In this instance, a glance at the tests done at the 3 stages (before milk, 4th month after milk and one year after milk intake) showed that there was a gradual improvement in the lactose tolerance tests, the maximum rise in blood glucose being 0 mg., 12 mg. and 22 mg.% respectively. This child was aged 10 yrs., and she was the only example of a significant response to the enforced milk diet.

Lactose and Milk Ingestion Compared

Using graduated doses of plain lactose solution and milk containing equivalent amounts of lactose, it was found that none of the 21 children given the smaller doses (up to 18 gm. lactose or ¾ pint of milk per child per sitting) developed symptoms within 4 hours of ingestion. But when 25 gm. of lactose or 1 pint of milk was taken, about ¼ of the children developed abdominal pain or loose stools. This confirmed that intolerance to milk was due to its lactose content, and symptoms usually occurred when a large amount of milk (1 pint or more) was taken at one time.

Weight Changes

There was an average weight gain of 3·5 kg. per child during this period of milk intake. This compared favourably with a control group of children of similar age in the same Home, the average gain being 2·0 kg. over the same period.

COMMENTS

The aim of this study was to find whether enforced milk intake introduced to the diet of a group of children for a period of one year would have any effect on their lactose tolerance status. The results were not entirely clear-cut, though it is reasonable to conclude that one year's continued high milk intake does not convert a subject from intolerance to tolerance. Of the 13 children found intolerant before milk introduction, 12 remained so despite high milk intake after 1 year. It should be noted that this group of children were relatively older than the others who were found tolerant to lactose. The increasing incidence of lactose intolerance with rise in age found in this survey is in accord with the previous study by Bolin *et al* (1970) over a larger number of children.

If the adaptation theory as proposed by Cuatrecasas and Bolin is valid, then it seems that once the enzyme lactase is grossly deficient, as is the case in subjects with primary lactose intolerance, continued substrate (milk) challenge for a period of one year is insufficient to cause the enzyme level to increase (i.e. to adapt) in response to the high milk diet. Experiments on rats (Bolin *et al*, 1969; Bolin *et al*, 1971 ii) showed that there was a close relationship between lactase levels and lactose intake. Rats with normal lactase levels, when fed on lactose-free diet, were soon found to be enzyme deficient, but when lactose was introduced to their diet over a period, the lactase levels gradually increased to their normal values. In human subjects, it is plausible that, given a long enough period of high milk intake, a state of lactose tolerance could be achieved eventually. Bolin *et al* (1968) have reported that a number of Asian students studying in Australia developed abdominal symptoms when they took on a high milk diet. However, after several years of habitation in Australia, these symptoms diminished in severity or even subsided entirely. One of the children in the present study, a 10 yr. old girl, had an improved lactose tolerance after the high milk diet. It is quite likely that, given a longer period of intake, more subjects could be converted to tolerance. This has yet to be confirmed by more extensive studies over longer periods. Short term enforced lactose feeding over a few weeks has been shown recently from a study on Thai subjects to have no effect at all on the lactose status (Keusch *et al*, 1969).

In the present series, only 3 children were shown to have been consistently tolerant to lactose, and they were all under 5 yr. of age. It would be interesting to follow up these children to find whether continued milk intake could maintain a state of tolerance beyond childhood. Since such studies entail prolonged follow-up over a number of years, reports of this kind must necessarily be uncommon. Indeed, the present authors are not aware of such reports. At any rate, a recent study from another angle (Bolin and Davis, 1970) compared the incidence of lactose intolerance in Asians who were born in Australia and have adopted a Western diet since birth, with a control group of students from Southeast Asia and they showed a significant difference between these two groups of Asians, the incidence of intolerance in the Australian-born Asians being much lower.

Whether primary lactose intolerance is purely due to a genetic cause or is acquired through lack of substrate stimulation has not been clearly resolved. Dietary habits, especially milk intake, have been shown by several papers, mainly from Australia, to play an important role in certain subjects. It is probable that both factors, heredity and adaptation, play a role in its etiology, though in most reports, usually only one factor was stressed.

In the recent paper from Singapore (Bolin *et al*, 1970), the authors stressed the importance of considering the relationship between milk ingestion and lactose tolerance when food is offered to another country as part of a foreign aid programme. If milk or milk products are offered to a country with a high incidence of lactose intolerance, the recipients may not be grateful to this kindly gesture. In the light of recent studies, it would be more logical if the offered milk be aimed at the young children, who have been shown to be able to benefit from it. If this is given in divided doses, as shown from the present study, the majority of children, including the older ones, will be able to tolerate a high milk diet over a long period. The marked increase in weight compared with a control group of children in this study reinforced this view.

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