Archives of Disease in Childhood, 1984, **59**, 735–738

Incomplete intestinal absorption of fructose

C M F KNEEPKENS, R J VONK, AND J FERNANDES

Department of Paediatrics, University Hospital, Groningen, Netherlands

SUMMARY Intestinal D-fructose absorption in 31 children was investigated using measurements of breath hydrogen. Twenty five children had no abdominal symptoms and six had functional bowel disorders. After ingestion of fructose (2 g/kg bodyweight), 22 children (71%) showed a breath hydrogen increase of more than 10 ppm over basal values, indicating incomplete absorption: the increase averaged 53 ppm, range 12 to 250 ppm. Four of these children experienced abdominal symptoms. Three of the six children with bowel disorders showed incomplete absorption. Seven children were tested again with an equal amount of glucose, and in three of them also of galactose, added to the fructose. The mean maximum breath hydrogen increases were 5 and 10 ppm, respectively, compared with 103 ppm after fructose alone. In one boy several tests were performed with various sugars; fructose was the only sugar incompletely absorbed, and the effect of glucose on fructose absorption was shown to be dependent on the amount added. It is concluded that children have a limited absorptive capacity for fructose. We speculate that the enhancing effect of glucose and galactose on fructose absorption may be due to activation of the fructose carrier. Apple juice in particular contains fructose in excess of glucose and could lead to abdominal symptoms in susceptible children.

Intestinal D-fructose absorption has been studied less extensively than that of the other two monosaccharide components of the human diet, D-glucose and D-galactose. Its absorption is assumed to take place by energy independent, facilitated transport,[1] but evidence of active intestinal transport of fructose has been found in the rat.[2 3] Concern regarding fructose ingestion is directed more towards its toxic metabolic effects than towards limitations of absorption.[1 4] Ravich *et al* [5] recently investigated fructose absorption in adult volunteers by means of the breath hydrogen test and found that in most subjects absorption of 50 g given as a 20% solution was incomplete. Fructose absorption has not previously been studied in children.

Fructose is used with increasing frequency in a number of foods, especially beverages. Since its incomplete absorption may lead to recurrent abdominal pain, we decided to investigate fructose absorption in children, measuring the hydrogen concentration in expired air after a fructose challenge.

Subjects and methods

We studied 31 children aged between 1 month and 16 years 9 months (mean 7·7 years). Twenty five children were completely free of gastrointestinal symptoms but six had functional abdominal complaints. None of the children had received antibiotics or cytotoxic treatment in the days before the tests. The parents gave informed consent and some were present during the test.

Fructose was given as a 20% solution at a dose of 2 g/kg body weight (maximum 50 g) after a fast of at least six hours. Duplicate breath samples were taken immediately before administration of the fructose solution and at 30 minute intervals thereafter for two and a half hours, using a modification of the method of Douwes *et al.*[6] The samples were stored in vacuum tubes. The hydrogen concentration of the samples was assessed using a Hewlett Packard HP 5880 gas chromatograph and a thermal conductivity detector. A 50 cm stainless steel column filled with molecular sieve 5A was flushed with nitrogen, 12 ml per minute. The oven temperature was 60°C and the detector temperature 300°C. Any abdominal symptoms present during the test were noted. The results were corrected for the basal breath hydrogen value which ranged from 4 to 23 ppm in 30 children and was 114 ppm in one. The peak increase in breath hydrogen was determined: a peak increase of more than 10 ppm was considered indicative of incomplete absorption of fructose.[7] Seven children were

also challenged with a solution containing the same amount of fructose, but combined with an equal dose of glucose. In three of them the test was repeated with galactose added instead of glucose. The total sugar concentration was kept at 20%. Finally, a boy aged 16 years with irritable bowel symptoms volunteered for a number of tests with different solutions.

Results

Results in the two groups, (the 25 normal children and six with functional bowel symptoms) are presented in Fig. 1. Twenty two of 31 children (71%) absorbed the fructose test solution incompletely. Only four children showed moderate peaks in breath hydrogen of between 10 and 20 ppm over basal values; breath hydrogen peaks in the others ranged from 22 to 250 ppm. Four children experienced symptoms during the test—abdominal pain in three and abdominal pain, diarrhoea, and flatulence in the fourth; their peak breath hydrogen values were 105, 106, 250, and 85 ppm, respectively.

There was no significant correlation between fructose induced breath hydrogen production and age (r=0·159; Student's *t* test). Only one of 17 children under 9 years of age, however, absorbed fructose completely, compared with seven of 14 children over 9 years of age (Fig. 1).

Seven children underwent a second test in which an equal amount of glucose was added to the fructose. Breath hydrogen excretion was significantly higher for the fructose solution alone (peak

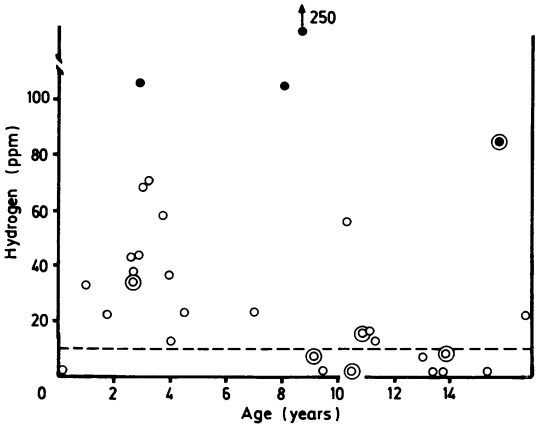

Fig. 1 *Fructose breath hydrogen test in 31 children. Peak increase in breath hydrogen in relation to age.*

Closed circles represent children with abdominal symptoms during the test and open circles those without symptoms.
Open and closed concentric circles represent children with functional bowel disorders with and without symptoms respectively.
The dashed line is the upper limit of the normal peak increase in breath hydrogen, indicating complete absorption.

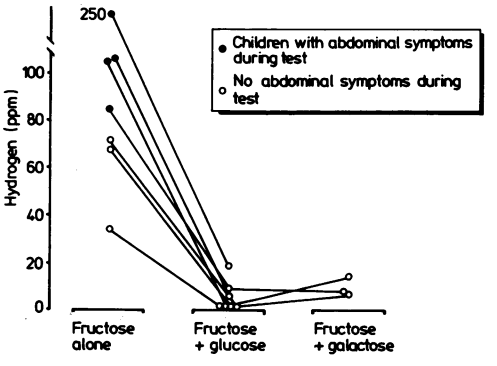

Fig. 2 *Effect of the addition of an equal amount of glucose or galactose on the peak increase in breath hydrogen in 7 children.*

Table *Peak increases in breath hydrogen and symptoms after different test solutions in a boy aged 16 years*

Substrate	*Dose*		*Breath hydrogen increase (ppm)*	*Symptoms*		
	g	*ml*		*Cramps*	*Flatulence*	*Diarrhoea*
Disaccharides						
Lactose	50	250	0	+	−	−
Sucrose	100	500	0	±	−	−
Fructose alone						
Fructose	50	250	85	+	+	+
Fructose	25	125	27	NN	NN	NN
Fructose	50	500	86	+	+	−
Fructose combined with other solutes						
Fructose + glucose	50+50	500	9	+	−	−
Fructose + glucose	50+25	375	17	+	+	−
Fructose + glucose	50+10	300	37	+	+	−
Fructose + galactose	50+50	500	8	+	−	−
Fructose + urea	50+16·3[‡]	500	86	+	−	+

* +=present; −=absent; NN=not noted (the patient claims never to be free of abdominal pain).
‡ Calculated osmolarity equal to that of the fructose plus glucose solutions.

value 103 ppm; range 34 to 250 ppm) than for the fructose plus glucose solution (5 ppm; range 0 to 19 ppm) (Fig. 2). The fructose plus galactose test gave similar results; the maximum breath hydrogen increase was 10 ppm, range 7 to 14 ppm (Fig. 2). The results of tests with different carbohydrate solutions which were performed in one patient are shown in the Table.

Discussion

Carbohydrate malabsorption has been studied increasingly by means of the breath hydrogen test. All carbohydrates, including starch, can serve as a substrate for the colonic flora to produce hydrogen. The amount of hydrogen produced depends on the amount of carbohydrate not absorbed.[8] As there are considerable individual differences, however, in the capability of hydrogen formation, the test results can be interpreted only semiquantitatively. Twenty two of 31 children (71%) failed to absorb fructose completely at a dose of 2 g/kg body weight. These results are not significantly different from those of Ravich *et al*,[5] who found incomplete absorption of 50 g of fructose as a 20% solution in 10 of 14 adult volunteers (71%). Accordingly, we did not find a significant relation between breath hydrogen excretion and age, although most children absorbing fructose completely, were more than 9 years old (Fig. 1).

The dosage of fructose used in these tests is, in fact, non-physiological. Nevertheless, healthy children are able to absorb the same dose of lactose or sucrose completely and the amount used is widely accepted for the investigation of carbohydrate malabsorption. One child, who was unable to absorb 50 g of fructose completely, showed no rise in breath hydrogen excretion after the ingestion of 100 g of sucrose, which contains about the same amount of fructose (Table). In addition, 'predigested' sucrose, that is fructose in combination with glucose, was completely absorbed in six of seven children undergoing the test (Fig. 2). (The same holds true for the combination of fructose and galactose.) Accordingly, sucrose ingestion seldom leads to abdominal symptoms, and sucrose digestion and absorption has been shown to be complete in almost all children tested.[9] Thus, sucrase is rarely a limiting factor in the absorption of the fructose moiety of sucrose.

To elucidate the mechanism by which glucose improves fructose absorption, additional tests were performed in one boy (Table). It may be postulated that the improved fructose absorption is due to dilution of the fructose solution rather than to glucose per se. The larger volume of the solution may lead to delay in gastric emptying, thus slowing down the availability of fructose to the intestinal mucosa. Alternatively, absorption may be improved by the 'solvent drag' effect of glucose uptake. Neither dilution of the fructose solution, however, nor addition of urea, another rapidly absorbed compound, stimulated fructose absorption (Table). Another possibility is a direct stimulating effect of glucose on the intracellular conversion of fructose in the mucosa, increasing the concentration gradient of fructose. There is no evidence, however, that galactose is metabolised in the intestinal mucosa;[10 11] if this were the case the effect of galactose on fructose absorption might be expected to be different from that of glucose, and this is in contrast with our findings. Moreover, even small amounts of glucose should have an effect on fructose uptake. Milla *et al*[10] found that glucose improved fructose absorption, in rat jejunum, but this effect was only present if glucose was added at low concentrations (2 mmol/l compared with 20 mmol/l for fructose) and disappeared at higher (56 mmol/l) glucose concentrations. We found a clear dose-effect relation however between glucose and breath hydrogen excretion, indicating another mechanism. Glucose and galactose share one mucosal membrane carrier and it is possible that the improved effect is mediated by this carrier, possibly resulting in activation of the fructose carrier. Further investigations are needed to elucidate the mechanism by which fructose absorption is promoted by other monosaccharides.

Malabsorption of fructose leading to chronic abdominal symptoms in adults has been described.[12] Barnes *et al*[13] recently described a 12 year old girl who showed an excess in breath hydrogen excretion after ingestion of fructose (even in small amounts) and sucrose. In contrast with our children, this girl may exhibit a specific defect in fructose absorption. Ravich *et al*,[5] who found a similar prevalence of incomplete fructose absorption, reported gastrointestinal symptoms in five of six volunteers who absorbed a 10% fructose solution incompletely. The frequency of symptoms in our children was lower but it should be remembered that scoring of abdominal symptoms is difficult in children, and therefore unreliable.

The question arises whether incomplete absorption of fructose is implicated in recurrent abdominal pain in susceptible children, as has been reported for lactose[14 15] and for the diet sweetener sorbitol.[16] Fructose-containing foods include fruits, fruit juices, and honey.[17] Most fruits contain about equal quantities of glucose and fructose, however, which would make incomplete absorption of the fructose moiety improbable. Exceptions are apples (fructose 5·0

g/100 g; glucose 1·7 g/100 g), pears (fructose 5·0 to 6·5 g; glucose 2·5 to 2·6 g), and honey (fructose 40·5 g; glucose 34·2 g).[17] The fructose and glucose content of apple juice is comparable with that of apples, that is about 6 g fructose and 2 g glucose per 100 ml.

Thus, taking into account the quantities of the foods mentioned that children are likely to consume, apple juice could be of particular relevance with regard to incomplete fructose absorption. Apple juice has been shown to induce excess hydrogen formation in adult volunteers.[18] The excessive ingestion of apple juice and fructose enriched dietary products may lead to abdominal complaints in susceptible children and should therefore be discouraged.

References

[1] Gitzelmann E, Steinmann B, Van den Bergh G. Essential fructosuria, hereditary fructose intolerance and fructose-1,6-diphosphatase deficiency. In: Stanbury JB, Wyngaarden JB, Fredrickson DS, eds. *The metabolic basis of inherited disease.* New York: McGraw-Hill, 1983: 118–37.

[2] Gracey M, Burke V, Oshin A. Active intestinal transport of D-fructose. *Biochim Biophys Acta* 1972;**266**:397–406.

[3] Macrae AR, Neudoerffer TS. Support for the existence of an active transport mechanism of fructose in the rat. *Biochim Biophys Acta* 1972;**266**:137–44.

[4] Boot-Handford R, Heath H. Identification of fructose as the retinopathic agent associated with the ingestion of sucrose-rich diets in the rat. *Metabolism* 1980;**29**:1247–52.

[5] Ravich WJ, Bayless TM, Thomas M. Fructose: incomplete intestinal absorption in humans. *Gastroenterology* 1983;**84**:26–9.

[6] Douwes AC, Fernandes J, Rietveld W. Hydrogen breath test in infants and children: sampling and storing expired air. *Clin Chim Acta* 1978;**82**:293–6.

[7] Barr RG, Watkins JB, Perman JA. Mucosal function and breath hydrogen excretion: comparative studies in the clinical evaluation of children with nonspecific abdominal complaints. *Pediatrics* 1981;**68**:526–33.

[8] Bond JH, Levitt MD. Quantitative measurement of lactose absorption. *Gastroenterology* 1976;**70**:1058–62.

[9] Douwes AC, Fernandes J, Jongbloed AA. Diagnostic value of sucrose tolerance test in children evaluated by breath hydrogen measurement. *Acta Paediatr Scand* 1980;**69**:79–82.

[10] Milla PJ, Muller DPR, Harries JT. Glucose stimulates fructose absorption: clinical implications in health and disease. *Arch Dis Child* 1977;**52**:429.

[11] Ockerman PA, Lundborg H. Conversion of fructose to glucose by human jejunum. Absence of galactose-to-glucose conversion. *Biochim Biophys Acta* 1956;**105**:34–42.

[12] Anderson DEH, Nygren A. Four cases of long-standing diarrhoea and colic pains cured by fructose-free diet; a pathogenic discussion. *Acta Med Scand* 1978;**203**:87–92.

[13] Barnes G, McKellar W, Lawrance S. Detection of fructose malabsorption by breath hydrogen test in a child with diarrhoea. *J Pediatr* 1983;**103**:575–7.

[14] Barr RG, Levine MD, Watkins JB. Recurrent abdominal pain of childhood due to lactose intolerance. A prospective study. *N Engl J Med* 1979;**300**:1449–52.

[15] Lebenthal E, Rossi TM, Nord KS, Branski D. Recurrent abdominal pain and lactose absorption in children. *Pediatrics* 1981;**67**:828–32.

[16] Hyams JS. Sorbitol intolerance: an unappreciated cause of functional gastrointestinal complaints. *Gastroenterology* 1983;**84**:30–3.

[17] Hardinge MG, Swarner JB, Crooks H. Carbohydrates in foods. *J Am Diet Assoc* 1965;**46**:197–204.

[18] Hickey CA, Calloway DH, Murphy EL. Intestinal gas production following ingestion of fruits and fruit juices. *Dig Dis* 1972;**17**:383–9.

Correspondence to Dr C M F Kneepkens, Department of Paediatrics, University Hospital, 59 Oostersingel, 9713 EZ Groningen, Netherlands.

Received 26 April 1984