Intestinal malabsorption in cystic fibrosis

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SUMMARY An oral solution containing lactulose and L-rhamnose was administered to six patients with cystic fibrosis. Intestinal absorption of both sugars was assessed by measurement of their urinary excretion. The lactulose:L-rhamnose excretion ratio was raised, supporting the hypothesis of an intestinal component to the malabsorption of cystic fibrosis.

While the role of pancreatic insufficiency in the pathogenesis of the malabsorption syndrome of cystic fibrosis has long been recognised, more recently an intestinal component to the malabsorption has been proposed.¹

The small intestinal permeability to probe molecules is widely used in the study of small intestinal absorptive function. One such test showed that after oral ingestion of D-xylose patients with cystic fibrosis have higher blood concentrations of D-xylose than controls.² These results were not substantiated, however, by steady state perfusion experiments in isolated in vivo lengths of jejunum.³ It was proposed that other mechanisms, such as altered gastrointestinal motility, decreased hepatic metabolism, or decreased renal excretion, might explain the raised blood D-xylose concentrations in cystic fibrosis.³

Another test compares the intestinal permeability to the monosaccharide L-rhamnose and the disaccharide lactulose by simultaneously measuring their urinary excretion after oral ingestion of a solution containing both sugars.⁴ The normal intestine is much less permeable to lactulose than to L-rhamnose, so that the lactulose:L-rhamnose excretion ratio (with both quantities expressed as a percentage of the oral dose ingested) is approximately 0.05.⁴ In children the upper limit of normal is considered to be 0.07.⁵ By studying alterations in the absorption of one substance relative to another, errors due to altered gastrointestinal motility, distribution after absorption, and renal excretion should be minimised.⁴ In this study the lactulose:L-rhamnose test was performed in six patients with cystic fibrosis.

Patients and methods

Six patients (four boys and two girls) with a mean

age of 12 years (range 8–15 years) participated in the study. All had the typical history of cystic fibrosis and raised concentrations of sweat electrolytes at the time of diagnosis. All patients were taking pancreatic enzyme substitutes.

After an overnight fast each patient ingested an oral load (80 ml) containing lactulose (5.3 g in 7.5 ml of 'Duphalac' syrup) and rhamnose (0.75 g). All urine passed over the next five hours was collected, its volume recorded, and a sample, preserved with merthiolate, frozen and stored for analysis.

Urine samples were analysed for lactulose and L-rhamnose by quantitative thin layer chromatography with five upward developments on silica gel layers (Schleicher and Schull F1500), with methanol/butanol 1-ol/water, 30/30/30, vol/vol as the solvent for the first two developments, butanol 1-ol/ethanol/acetic acid/water, 60/30/10/10, vol/vol as the solvent for the third and fifth developments, and butanol 1-ol/ethyl acetate/pyridine/acetic acid/water, 5/70/15/10/10, vol/vol as the solvent for the fourth development, using raffinose and fucose as internal standards. The sugars were measured by dipping in 1.4% wt/vol 4 aminobenzoic acid in 3.5% vol/vol orthophosphoric acid in methanol and heating for 10 minutes at 120–130°C, measuring the resulting colour by densitometry.

Each patient's height (m) and weight (kg) was measured and body mass index (height/weight²) calculated. Forced vital capacity, forced expiratory volume in one second, and the ratio between these measurements was also measured in each patient. For the purpose of comparison, forced vital capacity was calculated as a percentage of that expected for patient's height.⁶

Standard statistical methods were used in attempting to correlate the lactulose:L-rhamnose excretion ratios with the clinical variables.

Results

The six subjects excreted 13–111 mg (median value 26.8 mg) lactulose and 19–89 mg (median value 26.5 mg) L-rhamnose in the five hours. The lactulose:L-rhamnose ratio was derived from the five hour sugar excretions expressed as a percentage of the oral dose. In these subjects excretion ratios were

Table Urinary lactulose and L-rhamnose excretion expressed as a percentage of the oral dose ingested and the lactulose:L-rhamnose excretion ratios

Case No	% Recovery		Lactulose:L-rhamnose excretion ratio
	Lactulose	L-rhamnose	
1	2.11	11.98	0.176
2	0.36	3.66	0.098
3	0.57	2.48	0.23
4	0.45	4.31	0.10
5	0.57	3.42	0.167
6	0.26	3.28	0.079

0.079–0.23 (median value 0.13) (Table). All of these ratios exceed 'normal' values.⁵

There was no significant correlation between the level of the lactulose:L-rhamnose excretion ratio and body mass index ($r=-0.0594$), forced vital capacity, ($r=-0.717$), or forced expiratory volume in one second: forced vital capacity ratio ($r=-0.217$) in these patients.

Discussion

This study supports the hypothesis that there is an intestinal component to the malabsorption of cystic fibrosis. The mechanism of this intestinal dysfunction is yet to be elucidated. It seems unlikely that alterations in carrier mediated transport mechanisms are important, as mediated processes contri-

bute little to the absorption of lactulose and L-rhamnose.⁴ It has been proposed that the presence of abnormal mucus overlying the intestinal mucosa may alter transport kinetics.³

The clinical implications of this intestinal mucosal dysfunction in cystic fibrosis remain to be explored. In this small group of subjects the lactulose:L-rhamnose excretion ratio did not correlate with any of the simple clinical variables selected.

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References

- 1 Morin CL, Roy CC, Lasalle R, Bonin A. Small bowel mucosal dysfunction in patients with cystic fibrosis. *J Pediatr* 1976;**88**:213–6.
- 2 Schaad U, Kraemer R, Gaze H, Hadorn B. One hour blood xylose in cystic fibrosis. *Arch Dis Child* 1978;**53**:756–7.
- 3 Frase LL, Strickland AD, Kachel GW, Krejs GJ. Enhanced glucose absorption in the jejunum of patients with cystic fibrosis. *Gastroenterology* 1985;**88**:478–84.
- 4 Menzies IS, Laker MF, Pounder R, *et al*. Abnormal intestinal permeability to sugars in villous atrophy. *Lancet* 1979;ii:1107–9.
- 5 Ford RPK, Menzies IS, Phillips AD, Walker-Smith JA, Turner MW. Intestinal sugar permeability: relationship to diarrhoeal disease and small bowel morphology. *Journal of Pediatric Gastroenterology and Nutrition* 1985;**4**:568–74.
- 6 Cotes JE. *Lung function*. 4th ed. London: Blackwell Scientific Publications, 1979.

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Gastrografin in acute meconium ileus equivalent

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SUMMARY Twenty five (37%) patients with cystic fibrosis attending our clinic have experienced acute meconium ileus equivalent. In one year 37 of 40 episodes were treated with single dose oral Gastrografin with an 81% success rate, 75% being treated as outpatients. Patients found this treatment preferable to other recommended treatment.

Meconium ileus equivalent is an important complication of cystic fibrosis that reports have suggested occurs in 10–20% of patients.^{1,2}

Treatment is primarily preventative, using N-acetylcysteine, laxatives, and, in some cases, adjustment of pancreatic enzyme supplements. Surgery during acute attacks carries a high mortality and morbidity from bleeding, poor wound healing, and postoperative chest infections³ and should be avoided through effective medical treatment. N-Acetylcysteine given both by nasogastric tube and by enema three times daily³ and Gastrografin enemas⁴ have been used successfully but are unpleasant and require admission to hospital. There is little published information about oral Gastrografin in relief of acute meconium ileus equivalent.