Complex carbohydrate malabsorption in exocrine pancreatic insufficiency

Spiros D Ladas, Kostas Giorgiotis, Sotos A Raptis

Abstract
The magnitude of complex carbohydrate malabsorption in exocrine pancreatic insufficiency has not been well quantified in the past. The quantity of carbohydrate malabsorbed after a rice starch (100 g) meal in 20 patients with chronic pancreatitis (n=10) or pancreatic cancer (n=10) was therefore estimated. Patients had a three day stool fat collection (80 g/24 hour fat intake), a lactulose (20 g), and a rice flour (100 g) breath hydrogen test. Normal controls (n=29) had a postprandial H2 increase ≤14 ppm and malabsorbed (mean (SEM)) 1.12 (0.44) (range 0–11.10) g of the 100 g of carbohydrate ingested. Patients malabsorbed significantly more carbohydrate (11.36 (2.23) (range 9.90–32.60) g, F1,47= 29.92, p<0.001). The number of patients with fat (>7 g, n=8) or carbohydrate (increase in H2≥20 ppm, n=10) malabsorption was not different (χ²=0.01, p=0.75). There was a significant correlation between faecal fat and amount of malabsorbed carbohydrate (r=–0.60, F1,17=9.70, p=0.006) and faecal fat and stool wet weight (r=–0.57, F1,18=8.67, p<0.009), but not between stool wet weight and amount of malabsorbed carbohydrate (r=0.28, F1,17=1.45, p=0.25). Although patients with exocrine pancreatic insufficiency malabsorb 10%–30% of the ingested complex carbohydrate, the main determinant of stool wet weight could be faecal fat.

(Gut 1993; 34: 984–987)

Although malabsorption of fat and protein have been extensively investigated, malabsorption of complex carbohydrate has not attracted much attention in patients with exocrine pancreatic insufficiency. Based on pioneer work by Fogel and Gray, the notion that symptomatic carbohydrate malabsorption is uncommon in patients with chronic pancreatitis has not been challenged until recently, when it has been noticed that patients with exocrine pancreatic insufficiency may malabsorb complex carbohydrate.

As the magnitude of this carbohydrate malabsorption has not been investigated, the aim of the present study was to quantify the extent of complex carbohydrate malabsorption in patients with chronic pancreatitis and cancer of the pancreas.

Methods

SUBJECTS
Twenty ambulatory patients (16 men, four women) with a mean (SEM) age of 50–70 (2.36) (range 39–72) years, suffering from chronic idiopathic pancreatitis (n=10) or pancreatic cancer (n=10) and suspected malabsorption syndrome, participated in the study (Table I).

None of the patients were alcoholic or had any history of small intestinal disease, gastric operation, or small bowel resection and had not lost more than 10% of body weight in the six months preceding the study. Diagnosis of pancreatic disease was made by both computed tomography (CT) and endoscopic retrograde cholangiopancreatography (ERCP) in all patients and documented at laparotomy in those with pancreatic cancer. Twenty nine normal volunteers (18 men, 11 women) with a mean (SEM) age of 36–66 (2.28) (range 20–60) years served as controls. None of the patients or the normal volunteers had received antibiotics in the two weeks before the test period.

All 49 subjects participated in this study after giving written informed consent. The protocol was approved by the ethics committee on human studies of the Department of Internal Medicine, University of Athens, in December 1985.

TESTS PERFORMED

Quantitative faecal fat excretion
All 20 patients were placed on a 2200 kcal diet containing 80 g/day of fat. This diet was consumed for six days. Stools were quantitatively collected for the last three days (72 hours) of the test. After stool weight had been measured, they were analysed for fat content by the Van de Kramer method. Stool wet weight and fat content were expressed as g/24 hours. The excretion of normal subjects is less than 7 g/24 hours.

Table I

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Complex carbohydrate malabsorption

After an overnight (12-14 hours) fast all subjects drank a solution of 20 g lactulose in 250 ml of water. Three days later the same subjects again fasted and then ate a standard meal of rice cake made of 100 g rice flour, one egg, butter (7 g), and baking powder (5 g). This meal has been shown to be totally absorbed producing less than 20 parts per million (ppm) of peak breath H₂ concentration, when consumed by normal volunteers.19-20

After the ingestion of the lactulose drink or the rice flour meal end expiratory breath samples were collected in 50 ml polyethylene syringes at time 0 and 15 minute intervals thereafter over a 5-5 or seven hour period for the lactulose or the rice flour test respectively. During the test periods subjects were instructed not to smoke11 or eat anything12 but drank water ad libitum. Breath H₂ concentration was measured with a research chromatography (Hewlett-Packard 5750G) equipped with a thermal conductivity detector. The operating conditions have been published elsewhere.19 The minimum H₂ concentration detectable was 3 ppm, which gave a recorder deflection of 2 mm.

DEFINITIONS, CALCULATIONS, AND STATISTICS

Carbohydrate malabsorption was defined as an increase of breath H₂ concentration ≥ 20 ppm over the base line. The amount of carbohydrate malabsorbed was estimated by comparing the area under the breath hydrogen curve (BH₂AUC) after the rice flour meal with that after lactulose.9-14 Lactulose, a non-absorbable disaccharide, is rapidly metabolised on entering the colon by the colonic flora into H₂, CH₄, CO₂, and short chain fatty acids. The H₂ produced in the colon is absorbed and excreted roughly linearly in the breath. It has been shown that there is a rough linear correlation between breath H₂ excretion rate and the quantity of malabsorbed carbohydrate.11,14 As it has been assumed that equal amounts of lactulose or other carbohydrate malabsorption will produce equal changes in breath H₂ excretion,9 rice starch malabsorption has been calculated as g malabsorbed carbohydrate according to the formula:

\[
\text{BH₂AUC-rice} - \text{BH₂AUC-lactulose} \times 20 \text{ g}
\]

The BH₂AUC was calculated by the trapezoid rule.10-16 Results in the text and figures are presented as mean (SEM). The statistical significance of the results was assessed by one way analysis of variance (ANOVA), χ² test and regression analysis as appropriate.11 Probabilities of <0.05 were regarded as significant.

Results

All subjects consumed the lactulose drink within five minutes and the rice flour pancake within 15 minutes. Most of them complained about the taste of lactulose and the amount of the pancake but consumed it all.

Figure 1 shows the mean (SEM) breath H₂ curve, after lactulose or the rice flour meal, of normal volunteers. The mean postprandial increase in breath H₂ after the rice flour meal was 2-93 (0-72) (range 0-14) ppm. When comparing the area under the breath H₂ curve after the rice flour meal with that of lactulose, normal subjects malabsorbed 1-12 (0-44) (range 0-11-10) g of carbohydrate.

Tables I and II show diagnoses, stool fat, and wet weight, as well as breath H₂ excretion data of the 20 patients and Figure 2 shows the mean (SEM) breath H₂ curves after lactulose or rice

![Figure 1: Mean (SEM) breath H₂ curves of 29 normal volunteers after ingestion of lactulose (20 g) or rice flour (100 g).](http://gut.bmj.com/cover.png)

**Figure 2: Mean (SEM) breath H₂ curves of 29 normal volunteers after ingestion of lactulose (20 g) or rice flour (100 g).**
flour ingestion. One patient was an occasional non-H₂ producer, as he did not produce breath H₂ after lactulose, but he had an increase in H₂ of 9 ppm after the rice flour meal. His faeces produced significant amounts of H₂ when they were incubated in vitro with lactulose. Patients malabsorbed significantly more carbohydrates (11.36 (2.23) range 8.90–32.60 g) compared with normal volunteers (F₁,₄₀=29.92, p=0.001).

The number of patients with carbohydrate (increase in H₂ ≥20 ppm, n=10) or fat (≥7 g/24 h) malabsorption was not significantly different (χ²=0.10, p=0.75). Patients with an increase in H₂ ≥20 ppm malabsorbed 18·30 (2·60) g of carbohydrate and those with >7 g/24 hours of faecal fat malabsorbed 15·55 (1·90) g of fat.

There was a significant correlation between faecal fat and amount of malabsorbed carbohydrate (y=3.25+0.88x, r=0.60, F₁,₁₇=9·70, p=0·006) (Fig 3), as well as between faecal fat and stool wet weight (y=146·70+7·13x, r=0.57, F₁,₁₈=8·67, p<0·002), but not between stool wet weight and amount of malabsorbed carbohydrate (r=0·28, F₁,₁₇=1·45, p=0·25).

Discussion

Recently it has been shown that normal volunteers efficiently absorb an oral load of 100 g of rice starch with minimal generation of breath H₂.¹⁸ These results proved to be reproducible in the present study, indicating that a cut off value of ≥20 ppm of H₂ is a safe indicator of rice starch malabsorption. Kerlin et al.⁴ were the first to use the rice flour breath H₂ test to study complex carbohydrate malabsorption in diseases of the pancreas and small intestine. They have shown that patients with chronic pancreatitis or pancreatic cancer may malabsorb carbohydrate,⁵ but the amount malabsorbed had not been quantified. Even more recently Hammer et al.⁶ measured the magnitude of faecal carbohydrate excretion in five patients with exocrine pancreatic insufficiency. They showed that three of the five patients had excessive faecal excretion of carbohydrate and organic acids.

Although the breath H₂ test is sensitive and non-invasive and widely applied for the study of carbohydrate malabsorption, there are certain problems in the interpretation of its results. It is assumed that the H₂ producing bacteria are limited to the colon and that the fermentation of carbohydrates occurs rapidly on entering the caecum. There is a wide interindividually varying, however, in breath H₂ excretion, when given a constant dose of lactulose repeatedly. It is also assumed that all complex carbohydrate malabsorbed are converted to H₂ with the same degree of rapidity as is the case with lactulose. There are indications that certain complex carbohydrates such as fibre are converted to H₂ more slowly and less completely than lactulose⁵ resulting in an underestimation of the amount entering the colon. Another problem that researchers face when using breath H₂ tests is their duration. Many volunteers complain of feeling fasted for more than six hours. As a result, most experiments end after six to eight hours, when the breath H₂ concentration has not returned to the fasting value. All these assumptions and practical problems concerning the breath H₂ test have been discussed in detail by Bond and Levitt¹⁴ and Levitt et al.² who suggest that 'quantitative data of the breath H₂ test should be considered to be estimates of malabsorption of fermented material rather than precise quantitative measurements of polysaccharide malabsorption'. Despite its limitations, the breath H₂ test is the only acceptable non-invasive method to estimate complex carbohydrate malabsorption in humans.¹⁵,¹⁶

In the present study, it has been shown that 50% of the patients with chronic pancreatitis or pancreatic cancer had evidence of polysaccharide malabsorption (increase in H₂ ≥20 ppm) and malabsorbed 10%–30% of the ingested complex carbohydrate. This finding challenges the notion that carbohydrate malabsorption is uncommon in patients with chronic pancreatitis.¹³ Recent experimental data support our results suggesting that faecal pancreatic type isomylase activity is lower in patients with chronic pancreatitis and pancreatic cancer who have moderate to severe exocrine pancreatic insufficiency when compared with normal subjects.¹⁷ In these patients gastric acidity does not affect faecal pancreatic isomylase activity, but faecal salivary type isomylase activity is raised in patients with gastric hypoaecidity, indicating the important role of H₂ receptor antagonist administration with pancreatic supplements.

All our patients who had evidence of fat malabsorption (faecal fat ≥7 g/24 hours) malabsorbed complex carbohydrate (increase in H₂ ≥20 ppm) and as well, and there was a significant correlation between faecal fat and amount of malabsorbed carbohydrate. This correlation is explained if there is a parallel reduction of pancreatic lipase and colipase combined with low pancreatic type isomylase secretion. Indeed, Moriyoishi et al.¹⁸ have shown that there is a good positive correlation between faecal pancreatic isomylase activity and grade of pancreatic exocrine insufficiency as assessed by the secretin test.¹⁹

The second important finding from this study is the significant correlation between faecal weight and stool fat. Similarly a significant correlation between these two variables can be calculated from the data shown in Table I in the study by Kerlin et al.¹ (y=117·99+5·58x, r=0·81, F₁,₁₅=27·72, p<0·001) who investigated rice flour absorption in patients with chronic pancreatitis, and from the data shown in

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**Figure 3: Correlation of stool fat (g/24 h) with the amount of carbohydrate malabsorbed (g) (y=3·25+0·88x, r=0·60, F₁,₁₇=9·70, p=0·006) in 20 patients with chronic pancreatitis or pancreatic cancer. Dotted lines represent the upper range of normal values.**
Table I (patients 1 to 19) in the study by Bo-Linn and Fordtran (y = 38.54 + 7.07x, r = 0.89, F1,17 = 67.57, p < 0.001) who investigated faecal fat concentration in patients with pancreatic steatorrhoea. Figure 4 shows the correlation between faecal wet weight and stool fat of the pooled data derived from these two studies as well as the present study. This significant correlation between faecal fat and wet weight indicates that malabsorption of fat could be the main determinant of faecal weight in patients with mild to moderate exocrine pancreatic insufficiency. Despite this evidence, patients with severe exocrine pancreatic insufficiency (faecal fat 40–120 g/day) may have osmotic diarrhoea due to carbohydrate malabsorption. In patients with mild to moderate pancreatic insufficiency, however, there is no correlation between the amount of complex carbohydrate malabsorbed and stool wet weight. This is explained if malabsorbed polysaccharides are fermented to short chain fatty acids, most of which are rapidly absorbed, decreasing the colonic osmotic pressure and thereby preventing an increase in faecal water.

In conclusion, we have shown that patients with chronic pancreatitis or pancreatic cancer, who have mild to moderate fat malabsorption, may malabsorb up to one third of the ingested carbohydrate. These malabsorbed carbohydrates are probably metabolised by the colonic flora to short chain fatty acids and subsequently absorbed by the colon, so that malabsorbed fat could be the main determinant of faecal weight.

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This paper has been presented in part at the fifth meeting of the International Association of Pancreatology (Athens-Greece, 1992) and published in abstract form in the International Journal of Pancreatology 1992; 12: 93A. It was also awarded the 3rd Janssen Pharmaceutica prize by the Hellenic Society of Gastroenterology during the first United European Gastroenterology week (Athens-Greece, 1992).

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