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Small intestinal transit in diabetics

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Summary

Small intestinal transit was assessed in diabetic patients and healthy controls by measuring the breath hydrogen appearance time after the ingestion of lactulose. Transit in diabetics with autonomic neuropathy was significantly slower than in diabetics without neuropathy and controls. Delayed transit is probably due to vagal denervation. These slower transit times would allow bacteria to proliferate, which might explain why some diabetics have diarrhoea. The test cannot be used in patients with bacteria in the small bowel because these may metabolise lactulose and release hydrogen prematurely.

Introduction

Gut symptoms in diabetics are usually associated with autonomic neuropathy.[1] Diabetic diarrhoea may sometimes be associated with small intestinal bacterial overgrowth, and symptoms can be relieved by antibiotics.[2 3] Bacterial colonisation of the small bowel may result from changed intestinal motility.

Transit through the small intestine is difficult to study, although various methods have been described.[4] Recently Bond and Levitt have advocated measuring the breath hydrogen appearance time after the ingestion of a non-absorbable carbohydrate.[5] This simple non-invasive technique measures the time taken for a bolus of the carbohydrate to reach bacteria in the ileocaecal region.

We have used this technique to compare small intestinal transit times in normal people and diabetics with and without autonomic neuropathy.

Patients and methods

Twelve well-controlled, insulin-dependent diabetics (mean age 45 years) were studied together with eight healthy controls matched for age and sex. None were receiving any drugs apart from insulin. The diabetics were assessed for evidence of autonomic neuropathy.[6] None of the diabetics had diarrhoea, and all had had normal results in the ^{14}C-glycocholic acid test, a sensitive test of bacterial deconjugation of bile acids in the small bowel.[3] This was considered important because small-bowel bacteria can metabolise lactulose[7] and would release hydrogen prematurely, invalidating the hydrogen test as a measure of small-bowel transit. To assess the validity of the hydrogen test two additional patients were studied: one had multiple jejunal diverticula before and after a course of tetracycline; the other was a diabetic with diarrhoea, a positive ^{14}C-glycocholic acid test result, and a previous symptomatic response to antibiotics (metronidazole).[3]

After an overnight fast all subjects were given a solution of lactulose to drink (13 g lactulose as Duphalac syrup (20 ml) diluted with water to 130 ml). Breath samples were obtained every 10 minutes by end-expiratory sampling[7] and analysed for hydrogen content using the apparatus described by Bergman *et al.*[8] Sampling was continued with the subject inactive until a definite and sustained rise in breath hydrogen concentration was observed. This point was defined as the hydrogen appearance time.

Results

Six of the diabetics had good evidence of changed autonomic function in addition to a clinical history suggestive of autonomic

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neuropathy. The remaining diabetics had normal autonomic function and were free of other complications.

The hydrogen appearance times for each subject in the three groups are shown in fig 1. No significant differences were observed, between diabetics without autonomic neuropathy (mean = 69·8 min) and controls (mean = 70·8 min). The diabetics with autonomic neuropathy, however, had a significantly delayed hydrogen appearance time (mean = 140·2 min) compared with the controls (P = < 0·01) and the other diabetics (P = < 0·01) (Wilcoxon sum of ranks test). Repeat studies were performed in six subjects (see table). The correlation between both studies for all subjects was significant (r = < 0·01; Spearman rank test).

A typical graph of breath hydrogen output is shown in fig 2. This also shows the pattern of hydrogen appearance in the patient with jejunal diverticula before and after antibiotics. The very early and rapid appearance of hydrogen indicated bacterial overgrowth in the upper small intestine. After antibiotics no rise in breath hydrogen output was observed, indicating inhibition of bacteria in the colon as well as in the upper small intestine. A similar pattern was observed in the single diabetic with evidence of bacterial overgrowth in the small gut.

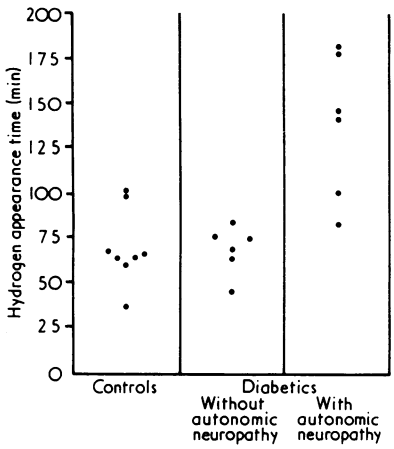

FIG 1—Hydrogen appearance times.

Reproducibility studies on hydrogen appearance time (minutes)

	Controls			Diabetics		
Subject No ..	1	2	3	4	5	6
First study	65	100	65	102	184	143
Second study ..	70	95	60	110	186	130

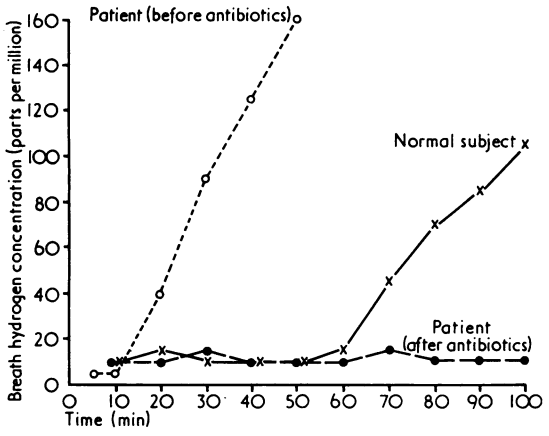

FIG 2—Hydrogen excretion in normal subject and patient with jejunal diverticulosis before and after antibiotics.

Discussion

It is difficult to investigate transit through the small intestine, and studies in diabetics have been few. McNally *et al*,[9] using balloon kymography, showed reduced intestinal motility in diabetics with autonomic neuropathy compared with values in diabetics without neuropathy and controls. The findings of radiological studies vary, some reporting an increased transit time, others a decrease.[10]

The use of the breath hydrogen appearance time provides a simple method of estimating the transit time of a bolus of fluid through the small intestine. The rise in the amount of breath hydrogen observed when the non-absorbed carbohydrate reaches the colonic bacteria is easily measured. Reproducibility in this series was good, and our results for normal controls were similar to those of Bond and Levitt.[11] The transit time depends on the quantity of lactulose given and cannot be applied to the transit of normal postprandial intestinal contents.

Our results strongly support the concept that small intestinal transit is delayed in diabetics with autonomic neuropathy. Slow intestinal transit could allow bacteria to proliferate in the lumen and this seems to explain diarrhoea in some diabetics.[3] Unfortunately, the test is invalidated by the presence of small-gut bacteria capable of metabolising lactulose. The diabetics we studied had no evidence of bacterial overgrowth in the small intestine in that they all had negative ^{14}C-glycocholic acid tests and had normal or delayed rather than premature excretion of hydrogen.

We would speculate that diabetics with bacterial overgrowth have even more sluggish small intestinal transit, but we cannot prove this with the present method. These findings contrast with those in a study in which we failed to show any significant delay in the gastric emptying of solid meals in diabetics with autonomic neuropathy.[6] All three diabetics with the longest hydrogen appearance times had normal gastric emptying rates. Thus possibly, whereas slow intestinal transit is probably caused by vagal denervation, the stomach can empty solid meals at a normal rate even when it is deprived of some of its vagal supply.

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