

Breath hydrogen analysis in patients with ileoanal pouch anastomosis

E Bruun, J N Meyer, J J Rumessen, E Gudmand-Høyer

Abstract

The possible influence on functional outcomes of hydrogen production in the ileoanal pouch after restorative proctocolectomy was investigated by means of lactulose H₂ breath tests. Eight of 15 patients had significant increases in breath hydrogen after 10 g lactulose. One patient declined to participate in further investigations, the remaining seven responders had no evidence of small bowel bacterial overgrowth after glucose H₂ breath tests. The ability to produce hydrogen by anaerobic fermentation of lactulose in the pouch was unrelated to the age of the patients or of the pouch. Seven of eight responders had successive breath tests after ingestion of lactulose 20 g and wheat starch 100 g. Five of seven had significant increases after lactulose but none after wheat starch. The overall function of the pouch continence, spontaneity of defecation, and 24 hour stool frequency was significantly better in responders than in non-responders. The absence of H₂ production of 100 g wheat starch may indicate either increased absorption or defective fermentation.

(Gut 1995; 37: 256-259)

Keywords: ulcerative colitis, ileoanal pouch, hydrogen breath tests, carbohydrates, functional results.

Proctocolectomy combined with ileal pouch-anal operation has become the procedure of choice in the surgical management of colitis ulcerosa and familial polyposis.¹ The patients maintain a transanal voluntary defecation and do not have to suffer the inconveniences and psychological impact of ileostomy and the nuisance from a perineal cicatrix.

Morphological studies have shown that the adaptation of the terminal ileum to its neorectum function is accompanied by a progressive transformation to a colonic type mucosa in nearly 50% of the cases.²⁻⁴ Intraluminally, the ratio of anaerobe to aerobic bacteria, as well as the total count, increases compared with the findings both in controls and in patients with ileostomy.^{5,6} The functional outcomes after pouch surgery, however, have neither been clearly correlated to the mucosal morphology nor to the faecal bacteriology.^{4,5}

The anaerobic bacterial fermentation of both endogenous mucus and undigested carbohydrates normally occurs in the large intestine resulting in the end products short chain fatty acids (SCFAs), carbon dioxide, hydrogen, and methane.⁷ The changed ileal flora after restorative proctocolectomy results

in increased production of SCFAs in the pouch, but the possible influence of increased concentrations of SCFAs on the functional outcomes has not yet been fully investigated.^{5,6,8,9}

The aim of this study was to investigate in vivo by means of hydrogen breath tests^{10,11} the extent to which the ileal pouch manifests colonic fermentation after ingestion of lactulose and wheat starch.

Patients

All patients participated in the study after giving written informed consent. The protocol was in accordance with the Helsinki II declaration and approved by the local ethical committee.

Fifteen patients between 15 and 63 years (median 27) at the time of restorative proctocolectomy were examined between 13 and 109 months (median 58.8) after the closure of the protective loop ileostomy. There were nine women and six men with the diagnosis of ulcerative colitis histologically verified on specimens taken from the colon after total colectomy. All patients had a triplicated S pouch with a spout not longer than 4 cm and a covering loop ileostomy constructed at the operation. After closure of the loop ileostomy they could all defecate spontaneously. Two patients eventually found it more convenient to control the pouch function by catheterisations alone. Clinical evidence of ileitis of the pouch ('pouchitis') was not seen in the patients participating in the study neither previously nor at the time of investigation. No patient had received antibiotics within a month before the tests.

Methods

After an 11 hour overnight fast duplicate end expiratory breath samples were taken before ingestion of 10 g lactulose made up to 100 ml tap water and thereafter at intervals of 15 minutes for minimum of six hours as described in detail elsewhere.^{11,12} The patients were outpatients and smoking and sleeping was not permitted. Mouth rinsing was performed with 0.1% chlorhexidine solution before the test meal. H₂ concentrations were measured on a GMI (Renfrew, Scotland) H₂ monitor. A sustained rise of 10 ppm or more was considered significant for H₂ production in accordance with earlier studies.^{11,13} PPM_{max} was defined as maximal rise of H₂ concentration from lowest previous values. Bacterial overgrowth of the small intestine was excluded if ingestion of 50 g glucose did not effect hydrogen production within six hours. A cut

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Accepted for publication
19 December 1994

off value of 20 ppm was our laboratory's standard procedure for diagnosing this condition in clinical practice.

Mouth to pouch transit time was defined as the interval between ingestion of 10 g lactulose test carbohydrate and the initial sustained rise in breath hydrogen.¹¹

Patients with a significant H₂ rise after ingestion of lactulose 10 g had successive breath tests in random order after lactulose 20 g and after 100 g gluten containing wheat starch given as bread prepared and characterised as previously reported.^{14 15} Breath samples were taken for seven hours after wheat starch. Side effects to the tests were scored and recorded by the patients during the tests.

The elapsed time between tests was a minimum of six days. Functional outcomes after pouch surgery were based on data from the last follow up visit. Although all patients were routinely interviewed personally by one of us (EB), assessments of pouch function were conducted independently from this study. The objective criteria of pouch functioning¹⁶ were used to classify the patients retrospectively.

Statistical analysis

Grouped data were expressed as median (range), and differences between measurements were assessed by the Mann-Whitney U test. Fisher's exact probability test was used to test whether two independent groups differed in proportion. Significance of association was assessed by Spearman's rank correlation. Statistical significance was taken as $p < 0.05$.

Results

Eight patients who responded to ingestion of lactulose with increases in breath hydrogen were denoted as responders (Fig 1). One responder refused further investigation, but the remaining seven responders were not found to have small bowel bacterial overgrowth by the glucose breath tests.

Seven patients failed to respond, non-responders, and were primarily evaluated in

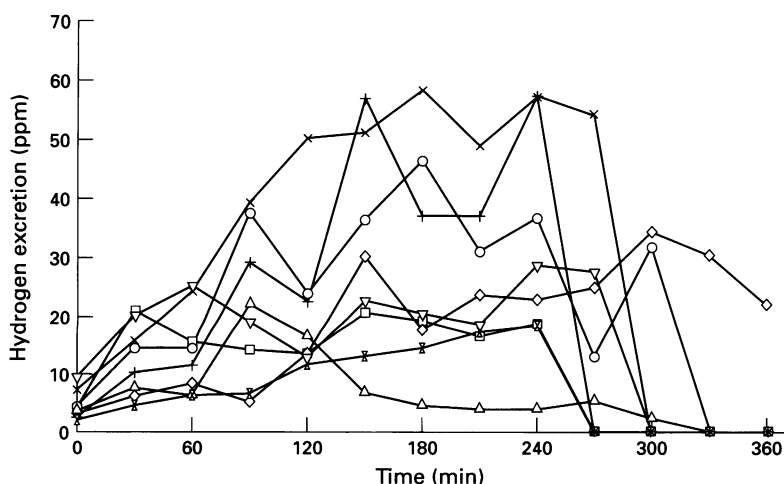


Figure 1: Concentration of hydrogen excreted expressed as parts per million (ppm) after ingestion of lactulose (10 g). The lines suggest that the flora had changed towards a fecaloid ('colonic') milieu in the ileal pouch. Patients are identified by the same symbols throughout the study - that is, 8: x, 9: v, 10: +, 11: o, 12: □, 13: x, 14: ◇, 15: △.

Functional outcomes of pouch surgery. Relation to hydrogen production after ingestion of lactulose

Patients (n)	Determinants of pouch function					
	I	II	III	IV	V	
1	+	+	-	10		No response
2	+	+	+	8		No response
3	-	+	+	Tubulates		No response
4	-	+	+	Daily		No response
5	+	+	-	5		No response
6	+	+	+	10		No response
7	+	+	+	5		No response
8	+	+	+	5		17
9	+	+	+	6		20
10	+	+	+	5		55
11	+	+	+	3		43
12	+	+	+	6		17
13	+	+	+	3		51
14	+	+	+	10		27
15	+	+	+	4		19

I: Spontaneity of defecation; II: ability to defer defecation more than 15 minutes; III: continence; IV: maximal stool frequency per 24 hours; V: Δ ppm_{max} after ingestion of lactulose 10 g. Sustained breath H₂ increases >10 ppm are considered significant.

the context of sample variation by calculating the exact 0.95 confidence limits of the observed frequency of 0.47. Based on binomial distribution the limits were 0.21 to 0.73, which is significantly higher than the limits 0.002 to 0.07 deduced from the rate 0.02 taken as an expression of the general population.¹⁰

Responders versus non-responders showed no significant difference as regards age, $p > 0.34$, or length of follow up after closure of the protecting loop ileostomy, $p > 0.19$. Light to moderate abdominal discomfort with borborygmus, flatulence, and diarrhoea was experienced by six of seven non-responders and four of eight responders. The difference in proportion was not significant, $p = 0.36$.

The Table gives the functional outcomes of pouch surgery. The maximal 24 hour stool frequency in patients who evacuated spontaneously was unrelated to the time elapsed since closure of the loop ileostomy, $r_s = 0.22$.

Maximal 24 hour stool frequency in responders could not be shown to differ from non-responders, $p = 0.20$.

Mouth to pouch transit times varied considerably around a median = 60 minutes (Fig 1). No significant correlation between mouth to pouch transit times and 24 hour defecation frequency could be shown, $r_s = 0.03$.

Two of the responders failed to increase breath hydrogen after ingestion of 20 g lactulose (Fig 2). No significant peaks of breath hydrogen after ingestion of 100 g wheat starch were apparent in lactulose responders (Fig 3). Determinants of pouch function compared with the clinical data showed that seven of eight responders complied completely to the objective criteria for good pouch function in contrast with only one of seven non-responders, $p = 0.02$ (Table).

Discussion

This study suggests that the functional outcomes after pouch surgery according to objective criteria are related to the occurrence of hydrogen excretion in the pouch after lactulose ingestion. This relation has not been suggested before and implies that a colon like bacterial

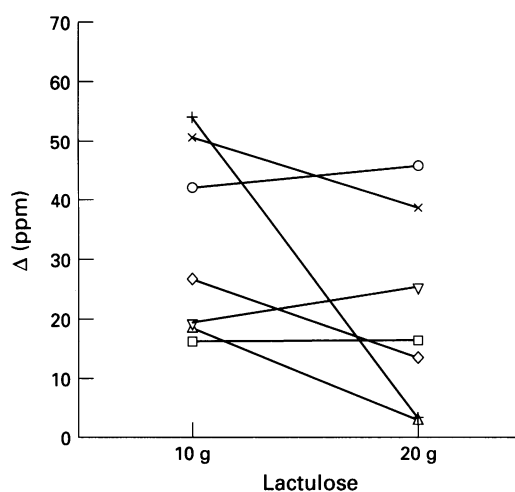


Figure 2: Paired findings of Δ ppm after ingestion of 10 g and 20 g lactulose.

fermentation in the pouch may influence the functional outcomes favourably (Table). Obviously the inverse relation between stools per day and faecal concentrations of total SCFAs or the individual SCFAs acetic, propionic, and butyric acids recently shown in 14 ileal pouch-anal anastomosis patients may reflect the same change in flora.⁹ In another study ingestion of a test meal to investigate the possible influence of small bowel transit time after colectomy and pouch construction four of 12 pouch patients also failed to produce hydrogen,¹⁷ which did not differ significantly from our proportion, $p=0.52$ (Fisher's exact test, two tailed). However, the possible relations to functional outcomes were not evaluated.

Pouch function in terms of stool frequency has a tendency to improve with time, but in agreement with our findings not significantly so after one year.¹⁶ A contributory cause might be that the pouch capacity that is usually found to be inversely related to stool frequency mainly increases during the first year of function.¹⁹ In addition to pouch capacity and pouch flora, compliance, epithelial function, pouch motility, proximal enteric bacterial flora, and course after surgery are also considered as determinants of pouch function.¹⁶

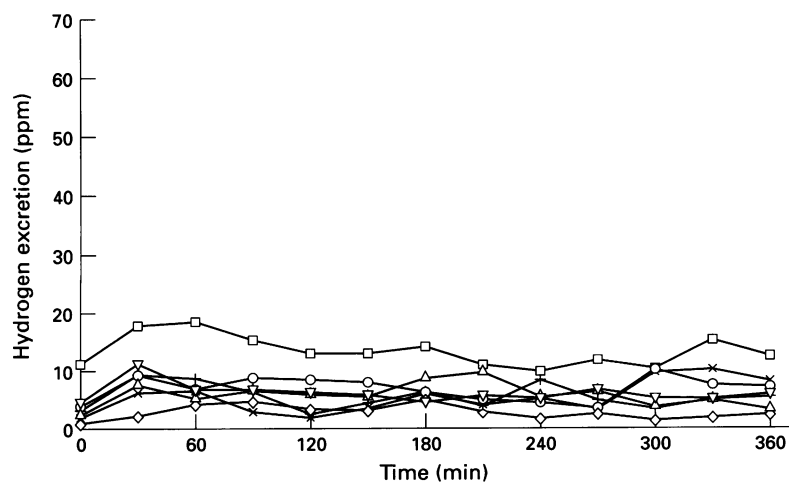


Figure 3: No significant hydrogen spikes were seen after ingestion of wheat starch (100 g) in seven lactulose responders.

The lack of H_2 increase in the pouch after wheat starch ingestion may show the inability of the pouch to ferment this important, and partially resistant food carbohydrate. In this small study, it cannot be totally excluded that the results are a consequence of the variability and sensitivity of the H_2 breath test method. The possibility of more efficient, adaptive starch absorption cannot be excluded either, because incomplete absorption of wheat starch ranges between 2–20% in healthy adults as measured by means of H_2 breath tests.^{14 15} It is important to test this last possibility because it may have consequences for interpretation of starch data from ileostomy models.^{12 19 20}

Two of the responders failed to show an increase in breath hydrogen after ingestion of 20 g lactulose. The explanation might be that the capacity of the pouch flora to ferment the substrate was overridden by osmotic diarrhoea. This is supported by the clinical experience that even the adapted pouch ecology is sensitive to the load of substrates.

It is well known that faecal stasis caused by a stricture of the ileoanal anastomosis might mimic the clinical entity pouchitis.⁴ The desire to self catheterisations and irrigations shown by patients 3 and 4 might be interpreted as a compensatory act to ameliorate a functional stenosis and so far no cases of pouchitis have been recorded. On the other hand, the only patient among non-responders with a good functional outcome, patient 7, developed a 'pouchit' half a year after this study, which was possibly caused by a low grade stricture at the angulation of the spout.

The functional outcomes of patient 14, were not clearly understood at completion of the study. A pronounced paradoxical contraction of the puborectalis muscle was shown later by electromyography, however, and a benign multicystic ovarian mass embedded in dense adhesions requiring salpingo-oophorectomy recently was shown by laparotomy.

Morphological changes of the mucosa neither seem to influence functional outcomes nor the absorptive functions normally maintained by the terminal ileum.^{2 4 5} Forty five per cent of 20 patients studied 26 months after pouch surgery had colonic metaplasia and all had chronic inflammation in pouch biopsies.² The findings were in agreement with other studies and they were as found elsewhere unrelated to the clinical results and unrelated to occurrences of pouchitis.⁴ Studies of the Koch's pouch show that the pouch mucosa in the long term – that is, six to 10 years after surgery – becomes fully adapted to the faecal stasis and is no longer hyperregenerative.²¹ This study shows that the changes in pouch flora required for hydrogen production by anaerobic fermentation of carbohydrates do not only depend on the time elapsed from the pouch construction.

It has been hypothesised that SCFAs become energy sources while colonic metaplasia has taken place, and that the lack of these acids may lead to pouchitis.²² Metaplasia only appears in half of the patients, however, and hydrogen production in the pouch

probably appears in more than half of the patients and pouchitis in less than half of the patients. Clearly, we need to clarify the mutual relations between colonic metaplasia, concentration of SCFAs, hydrogen production, and the relations to small intestine adaptation above the pouch as well.

Concentrations of SCFAs may reflect mouth to pouch transit times; therefore information about pouch capacity is also important for the understanding of the objective determinants of pouch function in both patients with and without pouchitis.

In conclusion, the changes toward a colon like pouch flora, which permit hydrogen production by anaerobic fermentation of carbohydrates is not a matter of time elapsed since the pouch operation.

A good function of the pouch is significantly related to the ability of the pouch to produce hydrogen after ingestion of lactulose. The importance of both qualitative and quantitative determinants of pouch function should be tested in prospective studies.

Parts of this work have been presented at the EURESTA general meeting, Segovia, October 1992 (abstract: E Bruun, J Nielsen Meyer, J J Rumessen and E Gudmand-Høyer. Breath Hydrogen (H_2) Analysis in Patients with S-Pouch-anal Anastomosis. FLAIR Concerted Action No 11, P 25).

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