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Alimentary tract and pancreas

Controlled trial of bowel rest in the treatment of severe acute colitis

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SUMMARY In a prospective, randomised clinical trial, 47 patients with severe, acute, non-infective colitis treated with 60 mg intravenous prednisolone daily, received either bowel rest with parenteral nutrition or oral diet. Although those who received 'bowel rest' experienced a reduction in daily stool weight, there were no differences in the operation or mortality rates between the groups. Fourteen of the 27 patients with ulcerative colitis, but none of the 16 patients with Crohn's disease required urgent surgery. Bowel rest did not affect the outcome in severe ulcerative colitis treated with intravenous prednisolone. Ulcerative colitis and Crohn's colitis behaved differently in the acute attack.

Severe attacks of colitis are uncommon but potentially dangerous, particularly if urgent surgical treatment is needed.[1 2] Medical treatment of severe colitis relies upon intravenous corticosteroids and nutritional replacement. There has been considerable interest in the use of parenteral nutrition as a possible treatment to reduce mucosal inflammation. The concept of 'bowel rest' is theoretically attractive and one might expect that inflamed intestine would heal more quickly if relieved of mechanical trauma, intestinal secretions, and the antigenic challenge of food. The only controlled trial so far published was not encouraging[3] and the present trial was designed to study further the effect of 'bowel rest' in patients with severe attacks of non-infective colitis.

Methods

PATIENTS

A diagnosis of non-specific colitis was established by endoscopy and/or barium enema, in the absence of specific infection or possibility of antibiotic associated colitis.

Patients were admitted to the trial if they presented with an attack of colitis severe enough to necessitate admission to hospital and to require treatment with intravenous prednisolone. They were excluded from entry if, at the time of presentation, they exhibited colonic dilatation on a plain abdominal radiograph, perforation, or haemorrhage which necessitated immediate surgery.

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INITIAL PERIOD FOR ASSESSMENT AND RANDOMISATION

After entry to the trial, all patients were allowed only clear fluids by mouth for 36 hours. During this time, a 24 hour stool collection was completed, and blood removed for laboratory investigations. Intravenous fluids, protein and blood tranfusions were allowed if needed. Treatment with intravenous prednisolone 20 mg as a bolus eight hourly was started, and continued in all patients throughout the trial period. After the basal investigations, patients were randomised to receive either 'bowel rest', consisting of parenteral nutrition and water only by mouth, or oral diet, consisting of hospital meals supplemented as needed to maintain a satisfactory nitrogen and calorie input. Parenteral electrolyte solutions were allowed to restore and maintain fluid and electrolyte balance.

Randomisation, using random numbers, was undertaken separately at the two centres. As it is often difficult to distinguish between acute ulcerative or Crohn's colitis within two days of admission to hospital it was decided in planning the trial that stratification into these diagnositic groups should not be attempted on entry.

ASSESSMENT DURING THE FIRST SEVEN DAYS

The first day of the trial began after the 36 hour assessment period. During the next seven days

detailed daily observations were maintained using a special proforma from which the data in Tables 1 and 3 have been extracted. The need for urgent surgical treatment was decided by joint consultations between physicians and surgeons without reference to the treatment received. Full reassessment was completed after seven days in those patients who did not require surgery. The results of the two trial treatments were assessed by comparing the operation and mortality rates in the two groups at seven days and during the admission to hospital.

LATER ASSESSMENT

The intravenous prednisolone with or without bowel rest was continued for 10 days after which oral administration was started and the prednisolone dosage was then progressively reduced. The subsequent course of the patients during the admission was recorded.

STATISTICAL ANALYSIS

The data were not normally distributed and results are therefore expressed as median and range. The significance of differences between the trial groups has been determined using the Wilcoxon's rank sum test for non-parametric samples and the χ^2 test with correction for small numbers.

Results

(a) COMPARABILITY OF PATIENT GROUPS

Forty seven patients, 28 women and 19 men, were admitted to the trial. Twenty seven received bowel rest, and 20 received oral diet. The comparability of the two groups is shown in Table 1. The bowel rest group contained more men and more patients with a total colitis. Large variations in the clinical and laboratory data were seen between patients. This reflected their clinical course before treatment, some having a short lived, acute attack with raised temperature, sedimentation rate and white cell count, while others had more protracted disease with metabolic depletion manifest as weight loss, and reduced albumin and haemoglobin levels. Stool frequency also varied considerably, those with infrequent stools invariably having severe, distal disease.

Table 1 *Trial groups at entry to the trial.*

	Bowel rest	*Oral diet*
Age	35·7 (19–56)	37·7 (17–72)
Sex	14F 13M	14F 6M
Disease extent		
Total	17	8
Substantial	5	9
*Left-sided	5	3
First attack	8 (30%)	5 (25%)
Relapse	19 (70%)	15 (75%)
Duration of attack (weeks)	8 (2–24)	4 (1–24)
Bowel frequency	5 (2–14)	6 (1–17)
Stool weight (g)	400 (100–1200)	300 (5–1250)
Weight loss (% of usual weight)	12·0 (0–32·5)	15·0 (1·3–34·7)
Haemoglobin (g/dl)	8·7 (5·6–14·4)	10·4 (5·6–16·1)
Albumin (g/l)	28 (20–38)	27 (21–45)
Fever > 38°C	15 (56%)	7 (35%)
ESR mm/h	60 (12–124)	62 (14–100)
WBC ($\times 10^9$/l)	7 (5·2–13·4)	4 (6·1–20·3)

* Inflammation involving the colon to the splenic flexure. Substantial indicates intermediate between total and left sided. All figures are median and range.

(b) COMPLICATION OF TREATMENT

One patient given parenteral nutrition developed a pneumothorax after catheter insertion. During the trial period there were no septic or metabolic complications of treatment.

(c) RESULTS AT SEVEN DAYS

After seven days, patients fell in to one of four groups. Those who improved rapidly were generally having less pain and diarrhoea with reduced fever and an improved appetite within 48 hours of starting treatment. At the other extreme were those patients who required urgent surgery within the first week of treatment. The remainder constituted two groups, those whose improvement was rather slower but who nonetheless attained remission and avoided surgery, and those who at seven days had made no progress or had deteriorated slowly. All these patients came to surgery later during the same hospital admission. It can be seen from Table 2 that there was no obvious difference in outcome between the two trial groups.

The clinical and laboratory data obtained after seven days' treatment appears in Table 3. The intravenous intake was assessed in 26 patients on day 7; the median was nitrogen 12·4 g (range 9·3–16·9 g) and energy, 2200 kcal (range 1400–2950). The oral intake was assessed in 14 patients on day 7. The median intake was 12·8 gN (range 6·4–18·4 g) and 1800 kcal (range 1200–2700) daily. There was no significant difference between the groups for any parameter measured. Within each group the stool weight and stool frequency decreased significantly in the bowel rest group ($p<0·01$) between days 0 and 7 but not in those receiving oral diet. The sedimentation rate was significantly reduced in both the trial groups ($p<0·01$). In the oral diet group, serum albumin concentrations increased significantly compared with day 0 ($p<0·02$). This difference cannot be ascribed to any difference in blood transfusion between the two groups. Among the other para-

Table 2 *Outcome at day 7*

	Bowel rest	*Oral diet*
Rapid improvement	10 (37%)	8 (40%)
Improvement	6 (22%)	4 (20%)
No change/worse	8 (30%)	7 (35%)
Surgery	3 (11%)	1 (5%)

Outcome at day 7

Table 3 *Clinical and laboratory data on day 7.*

	Bowel rest	*Oral diet*
Bowel frequency	3 (0–11)†	3 (0–15)
Stool weight (g)	180 (0–900)†	250 (0–790)
Haemoglobin (g/dl)	10·0 (5·1–14·5)	9·3 (6·6–14·5)
Albumin (g/l)	30 (24–40)	31 (24–40)*
ESR mm/h	34 (10–70)*	28 (5–61)*
WBC ($\times 10^9$/l)	9·9 (4·1–23·8)	13·2 (5·8–24·6)

*p<0·02
†p<0·01 compared with results on Day 0.

Table 4 *Outcome of treatment with bowel rest (BR) and oral diet (OD) in different types of colitis.*

	Ulcerative colitis		*Crohn's colitis*		*Indeterminate colitis*	
	BR	*OD*	*BR*	*OD*	*BR*	*OD*
Total	15	12	9	7	3	1
Medical treatment†	6	7	9	7**	1	1*
Surgery before day 7	2	1	0	0	1	0
Surgery after day 7	7	4	0	0	1	0
Deaths	1	1(+1)	0	0	0	0

*Each asterisk indicated one of the three patients who had bowel rest after initial lack of improvement.
†These patients responded to medical treatment and left hospital well.
The figure in brackets indicates the patient who died of a pulmonary embolus after discharge from hospital.

meters, although there was a tendency to improve in both groups, differences between day 0 and day 7 were not statistically significant.

(d) OVERALL RESULTS DURING HOSPITAL ADMISSION

A total of 16 patients (59%) in the bowel rest group responded to medical treatment and 11 (41%) required surgery. In the oral diet group, 12 (60%) responded to the trial treatment. Of the eight who did not respond, five patients required surgical treatment. The remaining three patients, two with Crohn's and one with indeterminate colitis, who did not initially respond to treatment received a period of bowel rest during which improvement occurred.

There were two deaths during the hospital admission, one in each group. One patient died from torrential haemorrhage from an asymptomatic duodenal ulcer on the third postoperative day, and the other from peritonitis and septicaemia after a caecostomy was undertaken for colonic dilatation. In a third patient the colitis failed to improve and she suffered gastric ulceration with acute haemorrhage which required gastrectomy, colectomy, and intensive care. She left hospital but died following a massive pulmonary embolus two weeks after discharge.

(e) RESULTS ACCORDING TO FINAL DIAGNOSIS

A final diagnosis was made at the end of the admission based on all the radiological and pathological data, including examination of a colectomy specimen when available. Table 4 shows the numbers of patients with ulcerative, Crohn's, and histologically indeterminate colitis in each group, and their outcome. Although there were no differences in outcome between bowel rest and oral diet, there were significant differences between ulcerative colitis and Crohn's colitis. Surgical treatment was required by 14 of 27 patients with ulcerative colitis but none of 16 with Crohn's colitis (p<0·01).

Table 5 *Outcome during follow up of those patients who responded to medical treatment during the trial.*

		Bowel rest		*Oral diet*	
	Total	*Remission maintained*	*Relapse*	*Remission maintained*	*Relapse*
Ulcerative colitis	13	2	4(2)	3	4(2)
Crohn's colitis	16	3	6(1)	2	5(0)
Total	29	5	10(3)	5	9(2)

Figures in parentheses indicate patients treated surgically.

Table 6 *Time of relapse in months after the end of the trial.*

	Bowel rest				*Oral diet*			
	<6	*6–12*	*12–24*	*>24*	*<6*	*6–12*	*12–24*	*>24*
Ulcerative colitis	3	0	1	0	2	0	0	2
Crohn's colitis	3	1	0	2	2	0	0	3

(f) LATE FOLLOW UP

The median length of follow-up was 43 months (range 27–64). During this period eight of 13 patients with ulcerative colitis and 11 of 16 with Crohn's colitis have relapsed. Four patients with ulcerative, and one with Crohn's colitis required surgical treatment for the relapse, the others settled with medical therapy. One patient died after a myocardial infarction while her colitis was still in remission. Tables 5 and 6 show the outcome of follow-up for these patients and the timing of relapse after the end of the trial period.

Discussion

Acute colitis requiring inpatient treatment is not common, and district general hospitals can expect to see only two to three such patients each year, one of whom may require urgent surgery.[1 4 5] Buckell *et al*[5] found that the mortality during medical treatment was 1·8%, but after urgent surgery 20% (five of 25) of patients died. In another more recent survey in British district general hospitals, Ritchie *et al*[1] found a surgical mortality rate of 24% (eight of 33) in similar cases and a French series has shown a mortality of 35%.[2] Corticosteroids remain the mainstay of medical therapy, but despite intravenous administration of large doses about 25% of patients with acute colitis continue to require surgical treatment during the hospital admission.[6] The development of possible additional effective medical measures to reduce the need for urgent surgery is clearly desirable.

The assessment of the severity of an attack of colitis is difficult to assess. Truelove and Witts[7] used five parameters, bowel frequency, temperature, pulse rate, haemoglobin, and ESR, and designated attacks as mild, moderate and severe. Lennard-Jones *et al*[8] found that a combination of the bowel frequency and body temperature in the first 24 hours after admission to hospital provided the best predictive value as to whether a patient would respond to medical therapy or not but neither the haemoglobin nor ESR were of help in predicting the failure of medical treatment. The problem of any classification which uses several criteria is that in many cases, not all the criteria are fulfilled at the same time.

In the present series some patients presented with a high fever, frequent bloody stools, and a raised ESR, but no anaemia or hypoalbuminaemia. Conversely, other patients with more protracted attacks, perhaps resistant to topical or oral steroid treatment, presented with profound anaemia and hypoalbuminaemia, but only moderate stool frequency, and normal pulse rate, temperature and ESR. Stool frequency in particular varied widely, tending to reflect the extent of disease. There can be little doubt, however, that the patients in this trial had severe disease. Thirty nine of the 47 patients had disease involving most or all of the colon, and only eight had disease limited to the left side. The median weight loss was more than 12% of usual body weight, the median haemoglobin was about 10 g/dl, the albumin less than 30 g/l and the ESR about 60 mm/h. Despite intravenous prednisolone, 16 of 47 patients (34%) required urgent surgical treatment, a figure comparable with other series.[5 6]

The randomisation procedure, done separately in the two trial centres, produced groups of different size. The other main differences were the number of patients with total colitis, 17 (63%) in the bowel rest group and 8 (40%) in the oral diet group, and the number of patients with a fever, 15 (56%) in the bowel rest and seven (35%) in the oral diet group. Both these factors have been shown to be associated with a greater risk of failure of medical treatment[8 9] and may indicate a rather sicker population.

This trial showed no benefit from bowel rest in ulcerative colitis; nine of 15 patients required urgent surgical treatment compared with five of 12 in the oral diet group. One patient died postoperatively in each group.

The numbers in the trial were small because severe acute ulcerative colitis is uncommon. To show that bowel rest might reduce the operation rate from the 30% observed in most series to 10% at a significance level of $p<0{\cdot}05$ in nine out of 10 trials, 127 patients would be needed in each group.[10] Such a large trial using a complicated and potentially dangerous treatment, with detailed clinical and laboratory observations, was regarded as impracticable on a multicentre basis. In the event, 60% of patients with ulcerative colitis needed urgent surgical treatment in the bowel rest group and 42%

of those in the oral feeding group. These figures reflect the selection of only the most severely ill patients for the trial. The observed difference of 18% in favour of the oral diet group has a standard error of ±19% and 95% confidence limits of −19% to +55%. We cannot therefore exclude a possible advantage in favour of bowel rest in a larger trial of up to 19% although our results showed a trend against this treatment.

The results in Crohn's colitis were in marked contrast to those in ulcerative colitis. No patient required surgery in either group and there was no death. It is therefore not possible to distinguish between the results in the two trial groups, although it is of interest that two patients with Crohn's colitis received parenteral nutrition after failing to respond to steroids and an oral diet, and subsequently achieved remission. Although an uncontrolled study[11] has suggested that remission of acute attacks of Crohn's disease can be achieved using parenteral nutrition, the remissions were not long lived, and the place of parenteral feeding as a primary treatment for Crohn's disease remains under review.

In the only other controlled trial, Dickinson *et al*[3] also noted a difference in the response to medical treatment by patients with ulcerative colitis and Crohn's colitis. Of 27 patients with ulcerative colitis, 13 needed surgery compared with only two of nine patients with Crohn's colitis. These authors also concluded that bowel rest exerted no primary therapeutic effect in ulcerative colitis, but they were not able to draw a conclusion about this mode of treatment in severe acute Crohn's colitis because of small numbers.

From the relatively long follow up of those patients who did not require surgical treatment, in every patient for more than two years and in some for more than five years, it is apparent that about one third of the patients relapsed within six months and about two thirds within the period of follow up. There was no difference in the two trial groups. Of the eight patients with ulcerative colitis whose disease relapsed, four were treated surgically. Thus by the end of the follow up period, 18 of 27 patients with ulcerative colitis admitted to the trial had undergone surgery. Among those with Crohn's colitis, 11 of 16 patients relapsed after successful medical treatment, but in contrast with those with ulcerative colitis, only one of the 16 patients in the trial was treated surgically throughout the follow up. The relatively benign course of acute Crohn's colitis observed here corresponds with the overall experience at St Mark's Hospital.[12] These results suggest that in future trials, and in routine practice, there is an advantage in distinguishing between ulcerative colitis and Crohn's colitis as early as possible in the course of the illness.

This trial does not suggest that bowel rest, using parenteral nutrition, influences the inflammatory response in ulcerative colitis but no conclusion is possible for patients with Crohn's colitis. In severely malnourished patients who cannot take food orally or by nasogastric feed for any reason, parenteral nutrition may be indicated in severe acute ulcerative colitis on purely nutritional grounds[13] but not as a primary treatment for the disease.

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