# CLINICAL RESEARCH

# Elemental diet as primary treatment of acute Crohn's disease: a controlled trial

C Ó'MORÁIN,   A W SEGAL,   A J LEVI

## Abstract

Acute exacerbations of Crohn's disease are usually treated with prednisolone or potentially more toxic immunosuppressive drugs or by surgery. In pilot studies replacing the normal diet by a protein free elemental diet also induced remission. A controlled trial was therefore conducted in which 21 patients acutely ill with exacerbations of Crohn's disease were randomised to receive either prednisolone 0·75 mg/kg/day or an elemental diet (Vivonex) for four weeks. Assessment at four and 12 weeks showed that the patients treated with the elemental diet had improved as much as and by some criteria more than the steroid treated group.

Elemental diet is a safe and effective treatment for acute Crohn's disease.

## Introduction

Nutritional treatment was initially included in the management of Crohn's disease because patients are often poorly nourished as a result of reduced intake and hypercatabolism. Total parenteral nutrition has been used to induce remission in this disease on the basis that it "rests the bowel." We believe that Crohn's disease consists of two main components: an underlying predisposition to ulceration of the gut, and a secondary immunological reaction to the passage of large amounts of foreign protein through the damaged gut wall. In an attempt to treat this secondary aspect we gave patients an elemental diet which contains all essential nutrients but is free of all protein, nitrogen being supplied in the form of amino acids.[1] The results were encouraging enough to warrant a prospective controlled trial of the efficacy of the treatment. We report the results of that trial, in which the therapeutic effect of an elemental diet as sole treatment of acute Crohn's disease was compared with the response to prednisolone, the most effective conventional treatment.

## Patients and methods

Crohn's disease was diagnosed on the basis of typical clinical and radiological features and diagnostic or compatible histological findings. The disease was considered to be in an active phase (a) if the patient had at least one of either weight loss of more than 2 kg in the previous month, diarrhoea (three or more loose stools a day), abdominal pain resulting in severe limitation of activity, abdominal wall or perianal fistulas, or a temperature exceeding 38°C for one week or (b) if at least two of the following laboratory measurements were abnormal: haemoglobin concentration (<12·5 g/dl in men, <10·5 g/dl in women), erythrocyte sedimentation rate (>20 mm in first hour), and serum albumin concentration (<35 g/l). Patients must not have received specific treatment in the past and were excluded if they had contraindications to the use of prednisolone. Any patient whose condition deteriorated to an extent that necessitated a change of treatment, as judged by two physicians, was withdrawn.

*Patients selected*—Twenty one patients (14 men, 7 women) were admitted to the trial (see table I). All were ill enough to require hospital admission. Rectal biopsy specimens were characteristic in four and compatible with the diagnosis of Crohn's disease in another four, in whom there were also relevant clinical and radiological features. Thirteen had the characteristic radiological appearances and clinical picture of Crohn's disease. All the patients had abdominal pain and diarrhoea, accompanied by weight loss in 17. Eight patients had had a fever of 38°C for one week. All had a sedimentation rate greater than 20 mm in the first hour, 12 had a haemoglobin concentration of less than 12·5 g/dl (men) or 10·5 g/dl (women), and 13 had a serum albumin concentration of less than 35 g/l.

*Treatment*—After initial inpatient assessment the patients were allocated at random to one of two treatment groups. Ten were treated with prednisolone 0·75 mg/kg body weight daily for two weeks and then with reduced dosages as clinically appropriate. Eleven were treated with an elemental diet whereby all food except tea and coffee (without milk) was withdrawn and replaced with Vivonex, supplying 150-250 kJ (40-60 kcal)/kg body weight and 8-12 g of nitrogen daily. The concentration of the elemental diet was gradually increased from

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**Northwick Park Hospital and Clinical Research Centre, Harrow, Middlesex HA1 3UJ**
C Ó'MORÁIN, MD, MRCPI, honorary senior registrar
A J LEVI, MD, FRCP, consultant gastroenterologist

**Department of Haematology, Faculty of Clinical Sciences, University College, London WC1**
A W SEGAL, PHD, MRCP, senior lecturer

Correspondence to: Dr A J Levi.

one third to the full recommended strength over three days to reduce side effects such as diarrhoea and abdominal colic, which occui because the preparation is hyperosmolar (600 mmol). After four weeks normal food was gradually reintroduced, its consistency being increased from fluid to solid over three days. Treatment was instituted in hospital but all the patients were allowed home once they had improved clinically.

TABLE I—*Clinical details of patients and results of randomisation and treatment*

| Case No | Sex and age | Main clinical features* | Site of disease | Outcome at three months |
|---|---|---|---|---|
| | | | *Steroids* | |
| 1 | M 34 | WL, AP, D | Ileocaecal | Improved |
| 5 | M 20 | AP, D | Ileocaecal | Relapse at six weeks |
| 6 | F 25 | WL, AP, D | Large bowel | Improved |
| 8 | F 43 | WL, AP, D | Large bowel | Improved |
| 12 | M 68 | WL, AP, D | Large bowel | Improved |
| 13 | F 42 | WL, AP, D | Large bowel | Withdrawn |
| 16 | M 65 | AP, D | Ileocaecal | Improved |
| 18 | F 19 | WL, AP, D | Large and small bowel | Withdrawn |
| 19 | M 34 | WL, AP, D | Large and small bowel | Improved |
| 20 | F 36 | WL, AP, D | Small bowel | Improved |
| | | | *Elemental diet* | |
| 2 | M 16 | WL, AP, D | Large and small bowel | Withdrawn |
| 3 | M 60 | WL, AP, D | Ileocaecal | Improved |
| 4 | M 24 | WL, AP, D | Large and small bowel | Withdrawn |
| 7 | M 29 | WL, AP, D | Ileocaecal | Relapse at five weeks |
| 9 | M 15 | WL, AP, D | Small bowel | Improved |
| 10 | M 48 | WL, AP, D | Small bowel | Improved |
| 11 | M 17 | WL, AP, D | Ileocaecal | Improved |
| 14 | M 40 | AP, D | Large and small bowel | Improved |
| 15 | M 29 | WL, AP, D | Large bowel | Improved |
| 17 | F 15 | AP, D | Large bowel | Improved |
| 21 | F 58 | WL, AP, D | Large bowel | Improved |

*WL = Weight loss. AP = Abdominal pain. D = Diarrhoea.

*Assessment*—Clinical symptoms and laboratory values were assessed before treatment and at weekly intervals for four weeks and then at three months. Clinical severity was quantified using a prearranged scoring system based on the five items of the "simple activity index."[2] General wellbeing was noted as excellent, fair with no limitation of activity, poor with some limitation of activity, or very poor with considerable limitation of activity and assigned corresponding scores of zero to three. Numbers of liquid stools were recorded as fewer than three, three to five, and more than five a day and assigned corresponding scores of zero to two. Abdominal mass was noted as absent, dubious, or definite and scored zero to two. Abdominal tenderness was also looked for and scored as mild (one), moderate (two), or severe (three). Complications affecting eyes, joints, skin, or fistulas were scored as one per item. The sum of these scores was called the clinical score. The higher the score the more active was the disease, and negative changes meant clinical improvement. Subsequent values were compared with baseline using Student's $t$ test for each group. The changes in values obtained for both groups were compared with one another by one way analysis of variance.

## Results

Table II shows the comparability of the two groups for age, sex, site of disease, and parameters of disease activity. Of the 21 patients, seven were women, of whom five were randomised to receive steroid treatment. Two patients in each treatment group were withdrawn from the study (table I). One of these (case 13) developed a steroid psychosis,

TABLE II—*Comparison of treatment groups on initial randomisation*

| | Steroids (n = 10) | Elemental diet (n = 11) |
|---|---|---|
| Mean age in years (range) | 38·6 (19-68) | 31·9 (15-60) |
| Sex { M | 5 | 9 |
| { F | 5 | 2 |
| Site of disease: | | |
| Small bowel | 1 | 2 |
| Ileocaecal | 3 | 3 |
| Large bowel | 4 | 3 |
| Large and small bowel | 2 | 3 |
| Mean pretrial values (SEM): | | |
| Clinical score | 7·8 (2·2) | 8·3 (2·2) |
| Weight (kg) | 55·8 (9·5) | 47·7 (9·8) |
| Haemoglobin (g/dl) | 11·9 (1·7) | 11·2 (1·5) |
| Erythrocyte sedimentation rate (mm in 1st h) | 62·2 (29·0) | 54·1 (29·0) |
| Albumin (g/l) | 36·0 (6·0) | 33·0 (5·0) |

and another (case 18) failed to improve clinically and developed toxic megacolon. In cases 2 and 4 the patients could not tolerate the elemental diet by mouth. Case 4 was withdrawn and the other patient fed through a nasogastric tube and treated with steroids. All four patients were withdrawn in the first 10 days of treatment.

Eight of the 10 steroid treated and nine of the 11 dietetically treated patients were considered to be in remission at four weeks. At three months one patient in each group was considered to be a treatment failure. Of these, the patient in the steroid treated group
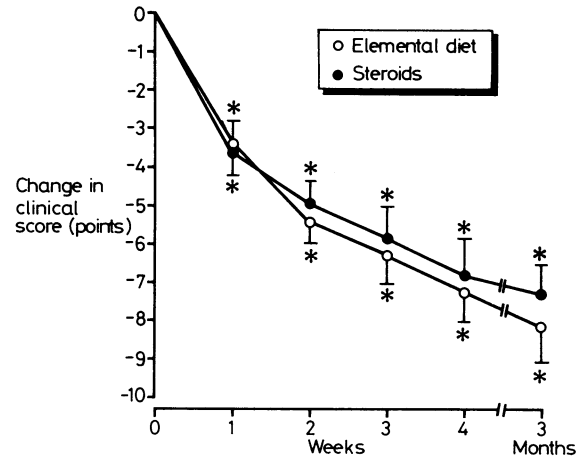


FIG 1—Mean changes in clinical score (points) from pretrial value, arbitrarily taken as zero. Bars are SEM.
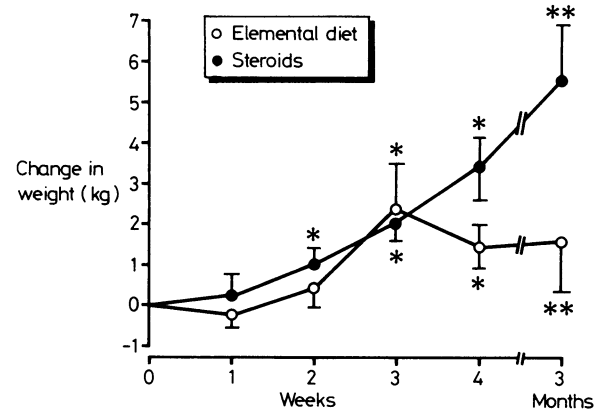*Significantly different from zero at $p < 0.05$.



FIG 2—Mean changes in weight from pretrial value, arbitrarily taken as zero. Bars are SEM.
*Significantly different from zero at $p < 0.05$. **Significant difference between both groups at $p < 0.05$.

(case 5) relapsed with symptoms as severe as on first entry to the trial and was successfully treated with an elemental diet. The other patient (case 7) presented with symptoms of a free perforation two days after returning to whole food.

Both groups showed similar highly significant reductions in their average clinical scores within a week, and this improvement continued throughout (fig 1). There were no significant differences in the rate or degree of improvement between the two groups (fig 1). Body weight also showed a consistent upward trend for the steroid treated group, but the dietetically treated group diverged significantly ($p < 0.05$) from this pattern by the end of treatment and after three months (fig 2). At that time, however, patients in the drug treatment group were still taking 10-20 mg prednisolone daily, whereas those in the other group were receiving no specific treatment.

Haemoglobin concentration showed a small but significant rise by the fourth week of treatment, but at three months this was maintained only in patients given the elemental diet (fig 3). Both groups showed a significant rise in serum albumin concentrations (fig 4), but rises were greater in the dietetically treated group. There was a significant and comparable fall in the sedimentation rate in the two groups (fig 5).

## Discussion

This paper reports on the first controlled trial of an elemental diet in the treatment of acute Crohn's disease, and the results show that the diet was as effective as steroids in inducing a remission: $80\%$ of the patients in both groups were in remission by four weeks.

We think it unlikely that the changes in these patients resulted from a placebo effect or simply admission to hospital. It was
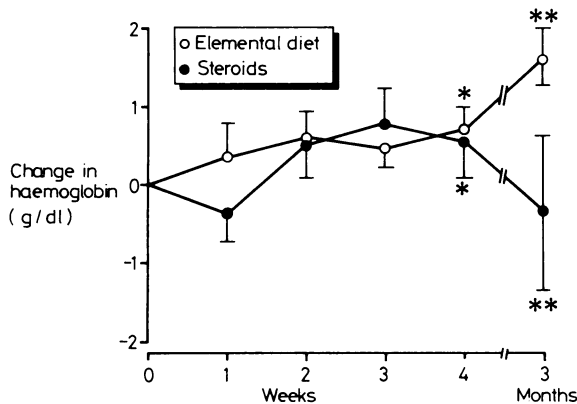


FIG 3—Mean changes in haemoglobin concentration (excluding patients transfused) from pretrial value, arbitrarily taken as zero. Bars are SEM.
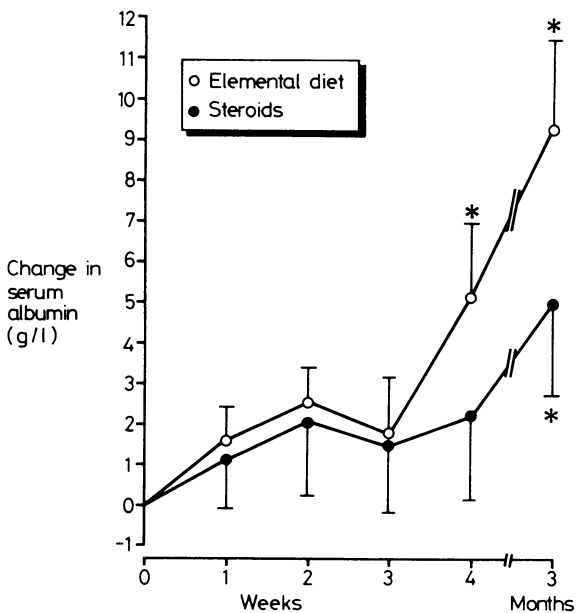*Significantly different from zero at $p < 0.05$. **Significant difference between both groups at $p < 0.05$.



FIG 4—Mean changes in serum albumin concentration from pretrial value, arbitrarily taken as zero. Bars are SEM.
*Significant difference from zero at $p < 0.05$.

thought to be inappropriate to withhold treatment from these acutely ill patients, and therefore a placebo group was not included. In the national cooperative Crohn's disease trial only $30\%$ of patients given placebo went into remission.[3] In another controlled trial the placebo treated group showed the same degree of disease activity after 16 weeks as they did at the outset.[4] It is most unlikely that the therapeutic effect observed in our series was due to bed rest alone, as the median stay in hospital for both groups after beginning treatment was 12 days.

Response to treatment was monitored by a simple activity index[2] in preference to the Crohn's disease activity index proposed by the National Cooperative Crohn's Disease Group.[5] A similar simple activity index was used in three other controlled trials.[6] [7] The Crohn's disease activity index depends largely on subjective variables such as general wellbeing and pain, each given different weightings, and includes as the sole laboratory investigation measurement of the packed cell volume, which bears little relation to disease activity.[8] Concentrations of acute phase proteins, serum albumin value, and sedimentation rate are more reliable laboratory indices of disease activity.[9] The simple index correlates well with the complex Crohn's disease activity index.[2]

Other reports of the use of elemental diet in Crohn's disease were uncontrolled and anecdotal.[10] [16] Fromm et al treated 23 consecutive patients with total parenteral nutrition or an elemental diet[10]; the patients, however, received drugs as well.

The principal difficulty of using an elemental diet is its unpalatability. But with encouragement from dietetic, nursing, and medical staff the patients do adapt, particularly when they note
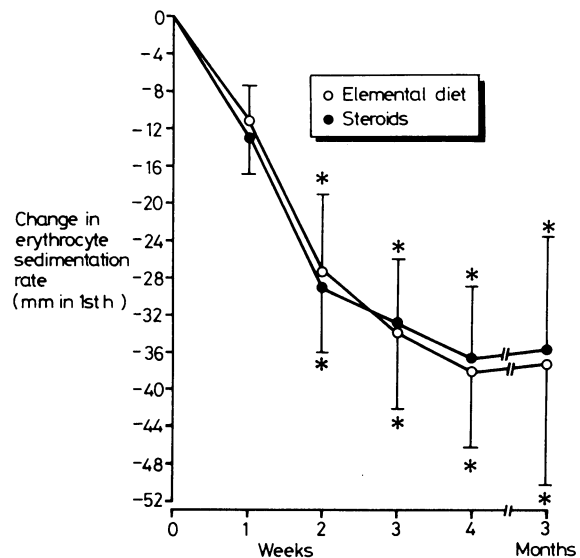


FIG 5—Mean changes in erythrocyte sedimentation rate from pretrial value, arbitrarily taken as zero. Bars are SEM.
*Significant difference from zero at $p < 0.05$.

subjective improvement, and only two of our patients were unable to tolerate the diet; one of these was given a nasogastric line. We have monitored other patients receiving an elemental diet for six to 12 months. Although the products cost between £9 and £13 a day, the clinical improvement, greater wellbeing, and productivity of the patient provide an excellent cost:benefit ratio.

Nutritional improvements are unlikely to be responsible for alleviating the symptoms of Crohn's disease because clinical improvement starts long before positive nitrogen balance develops. Alterations in bacterial flora in the gut lumen do occur in patients taking an elemental diet, and this might have a beneficial effect.[17] [21] We have been unable to find any difference in faecal flora before and after treatment.[22] The nitrogen source of Vivonex is simple amino acids. By contrast, other liquid diets contain peptides with variable length chains, and all contain some oligopeptides, which may be allergenic. Vivonex may be beneficial in one or two ways: as the components of the diet are absorbed mainly in the upper small bowel, it may act simply as a medical bypass, preventing the dietary contents and digestive enzymes having access to the inflamed, ulcerated gut. Alternatively there may be a secondary immune reponse in Crohn's disease to exogenous protein which gains access to the gut wall through the

ulcerated mucosa. This is likely because antibodies to a wide range of foreign proteins are detectable in the serum of these patients. Possibly this inflammatory immune response to exogenous protein perpetuates chronic inflammation of areas in which the mucosa is breached by acute insults which would otherwise resolve spontaneously.

Elemental dietary treatment of acute exacerbations of Crohn's disease offers a therapeutically effective non-toxic alternative to conventional surgery and drugs. It merits serious consideration as the treatment of choice of acute Crohn's disease.

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# Body content of selenium in coeliac disease

LESLEY J HINKS,    KAREN D INWARDS,    BARBARA LLOYD,    BARBARA E CLAYTON

## Abstract

Concentrations of selenium in whole blood, plasma, and leucocytes were determined in 16 patients with coeliac disease confirmed by biopsy and 32 controls. All the patients were clinically well and receiving gluten free diets. The concentrations of selenium were significantly lower in the leucocytes, blood, and plasma of patients compared with controls, probably indicating a decrease in the body content of selenium.

A high incidence of malignancy in coeliac disease has been reported. As a protective role for selenium against cancer has been postulated, the importance of this unexpected observation of lowered tissue concentrations of selenium requires further investigation.

## Introduction

A low body content of selenium has been suggested in association with several chronic diseases in man. Studies with selenium-75 have indicated that the duodenum is the main site for absorption of selenium. In untreated coeliac disease the mucosa of the small intestine is abnormal, the duodenum and jejunum being most severely affected. The purpose of this study was to assess the body content of selenium in a group of patients with coeliac disease by determining concentrations in leucocytes, plasma, and whole blood.

## Subjects and methods

We studied 16 patients aged 23-71 (mean 50·6) years who all had coeliac disease. The mean duration of the disease from diagnosis was 7·7 (range 2-19) years. All the patients were clinically well and receiving gluten free diets.

Leucocytes were separated with a dextran sedimentation technique.[1]

University Department of Chemical Pathology and Human Metabolism, Faculty of Medicine, University of Southampton, Southampton General Hospital, Southampton SO9 4XY

LESLEY J HINKS, FIMLS, senior medical laboratory scientific officer
KAREN D INWARDS, fourth year medical student
BARBARA LLOYD, FIMLS, senior chief medical laboratory scientific officer
BARBARA E CLAYTON, FRCP, FRCPATH, professor of chemical pathology and human metabolism

Correspondence to: Miss L J Hinks.