Case reports

Effective intravenous cyclosporin therapy in a patient with severe Crohn’s disease on parenteral nutrition

B F ALLAM, JANET E TILLMAN, T J THOMSON, F T CROSSLING, AND LORNA M GILBERT

From the Departments of Biochemistry and Pharmacy and Divisions of Medicine and Surgery, Stobhill General Hospital, Glasgow

SUMMARY We report a patient with severe Crohn’s disease and the short bowel syndrome on parenteral feeding who was not responding to conventional therapy and underwent treatment with cyclosporin (CyA) given initially intravenously and subsequently orally in each of two courses. Plasma drug concentrations were largely kept within the therapeutic range but wide variability was observed on oral therapy. Improvement both clinically and by objective assessment, was observed on intravenous CyA therapy, but was not sustained when the drug was given orally for several months. None of the side effects observed resisted treatment or was severe enough to warrant discontinuation of therapy. These findings suggest that there may be a place for intravenous CyA therapy in patients with severe Crohn’s disease who do not respond to conventional therapy or to oral treatment with CyA.

A 40 year old housewife in whom the diagnosis of Crohn’s disease was established eight years earlier, was admitted in an exacerbation presenting with abdominal pain and markedly increased frequency of diarrhoea with mucus and blood which did not respond to metronidazole and azathioprine. Radiological studies showed disease in the small bowel and extensively in the colon. In the previous eight years she had received several courses of conventional therapy, including prednisolone, and underwent four operations for resection of segments of terminal ileum and ascending colon affected by disease, recurrence or obstruction. Her remaining small bowel was estimated to be about 100 cm in length. Deterioration in her nutrition could not be reversed on enteral feeding (Isocal, Mead Johnson), but responded to total parenteral nutrition (TPN) and at the time of admission she had regained her usual weight after 18 months on cyclic (overnight) home TPN.

Two brief case reports published at that time described favourable response of Crohn’s disease to short courses of therapy with oral cyclosporin (CyA). It was decided to try this form of therapy as the sole treatment, but to administer the drug intravenously. Cyclosporin 5 mg/kg weight was given as a two hour infusion before the start of the TPN infusion. Cyclosporin dose was adjusted as appropriate in accordance with plasma concentrations which were monitored twice weekly (Radioimmunoassay, Sandoz). At the end of three weeks the patient found it difficult to cope with the extra infusion and the drug was administered orally. After six weeks on oral therapy, however, with absence of progress, the patient agreed to restart intravenous infusions which continued for a further seven weeks. Clinical improvement as well as a drop in the stool frequency, Crohn’s Disease Activity Index (CDAI), alcoholic 1-acid glycoprotein (AAG; Orsomucoid) and C-reactive protein (CRP) were observed largely on intravenous therapy with the drug (Figs 1 and 2). Serum albumin rose, despite a tendency to fluid retention, reflecting an improved nutritional status which allowed reduction in levels of parenteral nutrients provided. Although the patient discon- tinued therapy, her general health continued to improve and there was a further slight fall in stool frequency, the CDAI falling into the quiescent range within three weeks.

Address for correspondence: Dr B F Allam, Biochemistry Department, Stobhill General Hospital, Glasgow G21 3UW.
Received for publication 8 January 1987.
Effective intravenous cyclosporin therapy in a patient with severe Crohn's disease on parenteral nutrition

1167

Fig. 1 Changes in CDAI, stool frequency, weight, and serum albumin during the two courses of CyA therapy. Interrupted line represents CDAI calculated to include a score for the pain caused by an incisional hernia which was diagnosed before the second CyA course. Trough therapeutic range for plasma CyA: 50–400 ng/ml (hatched area).
After stopping CyA therapy for approximately two months gradual reversal started to take place with recurrence of abdominal pain and increased frequency of stools which, after a further four months, was consistently in excess of 20 per day with increasing amounts of mucus and blood. An incisional hernia was diagnosed at this stage and caused further pain. The patient by that time had lost 5 kg in weight and her serum albumin had fallen to 26 g/l. By then CDAI, AAG, and CRP were markedly raised (Figs 1 and 2).

A second CyA course was started and the drug was given intravenously but once again and despite a remarkable response to treatment, lack of patient’s cooperation necessitated a change to oral therapy (two divided daily doses) after eight weeks. Remission took place remarkably rapidly on intravenous therapy and this was associated with parallel and striking improvement in stool frequency, CDAI, AAG, and CRP levels. Serum albumin rose along with other nutritional parameters monitored, once again allowing reduction in levels of parenteral nutrients given. These improvements were not sustained on oral therapy, which continued for three months (Figs 1 and 2). Despite frequent adjustment of the oral dose, wide fluctuation of plasma CyA concentrations was noticed on oral therapy (Fig. 1). A number of side effects of CyA therapy were seen including mild hyperaesthesia of the hands and fine hirsutism of the arms and to a lesser extent the face. There was a brief period of nausea and vomiting which responded to metoclopramide, and a transient hyperkalaemia which was controlled with oral potassium binding resin and bicarbonate therapy.
Effective intravenous cyclosporin therapy in a patient with severe Crohn’s disease on parenteral nutrition

A tendency to hypomagnesaemia caused by increased urinary magnesium output was controlled by increasing the magnesium content of the TPN regimen, the volume of which was kept low to minimise fluid retention. None of the side effects observed resisted treatment or was severe enough to warrant discontinuation of therapy. Blood pressure as well as renal and liver function tests remained satisfactory and no anaphylactic reaction to the intravenous form of therapy took place.

Discussion

Cyclosporin therapy has been found effective in various autoimmune diseases. Remission on oral CyA therapy was reported in a few patients with Crohn’s disease but not in all patients studied. The patient reported here underwent two separate courses of treatment with the drug and although not originally intended, therapy alternated between the intravenous and the oral routes of administration. Beneficial effect, quite dramatic in the second course, was seen on intravenous therapy. Although plasma CyA concentrations were largely kept within the therapeutic range, great variability in concentrations and loss of beneficial effect were seen on oral therapy. This is not surprising because the bioavailability of oral CyA is incomplete and shows wide variability, between patients and within the same patient, in time-to-reach-peak plasma concentrations and in the relationship between the dose and the peak concentration attained and is further reduced in patients with intestinal dysfunction especially in the presence of diarrhoea. From our experience in this case, therefore, we believe that in some patients with Crohn’s disease successful therapy may not be possible if the drug is administered orally. For appropriate assessment of the effectiveness of the drug in this disease we believe that controlled studies of oral CyA treatment in Crohn’s disease should be extended to evaluate intravenous therapy. If our observation is confirmed by others, the intravenous form of therapy may acquire a place in the management of patients with severe Crohn’s disease who do not respond to conventional therapy or to the oral form of treatment. Additional potential benefit of this form of therapy to patients on TPN, who constitute the largest group in the UK home TPN register, would include improvement in nutritional status on reduced levels of intravenous nutrient provision and, consequently, in some, the prospect of change to enteral feeding.

We would like to thank the staff of the Blood Transfusion Department, Glasgow Royal Infirmary, for carrying out the plasma Cyclosporin assay and Drs C W Howden, G M Fullarton, and A McKenzie for assistance in clinical follow up of this patient. We also thank members of Stobhill Nutritional Advisory Group for assistance in the management of this case and the staffs of the Biochemistry and Haematology departments in Stobhill Hospital for laboratory monitoring of this patient’s progress.

References

Effective intravenous cyclosporin therapy in a patient with severe Crohn’s disease on parenteral nutrition.
B F Allam, J E Tillman, T J Thomson, F T Crossling and L M Gilbert

*Gut* 1987 28: 1166-1169
doi: 10.1136/gut.28.9.1166

Updated information and services can be found at:
http://gut.bmj.com/content/28/9/1166

---

**Email alerting service**
Receive free email alerts when new articles cite this article.
Sign up in the box at the top right corner of the online article.

**Topic Collections**
Articles on similar topics can be found in the following collections
*Crohn's disease* (932)

---

**Notes**

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/