ACUTE REFRACTORY INFLAMMATORY BOWEL DISEASE AND CYCLOSPORIN

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SUMMARY

During the period May 1995 to March, 1997, we treated 08 patients (03 female, 05 male; 06 with crohn's disease and 02 with ulcerative colitis) with severe inflammatory bowel disease as per Truelove and Witt's criteria with Cyclosporin as a measure to avoid surgery after failure of conventional therapy, i.e. intravenous steroids, 5-aminosalicylate and elemental diet supplemented with parenteral nutrition. Six patients responded completely while two patients showed partial response and had to have proctocolectomy within three months.

INTRODUCTION

The medical community and patients of inflammatory bowel disease have eagerly awaited the development of fast acting non toxic and selective immunosuppressive agents. Various small studies have suggested that cyclosporin may fulfill these hopes. We also used the drug with encouraging results.

MATERIALS AND METHODS

As per Truelove and Witt's criteria, 08 patients (03 female, 05 male) with severe acute flare up of inflammatory bowel disease were treated conventionally with intravenous steroids, 5 aminosalicylate, elemental diet and parenteral nutrition. If there was no impairment on day 3 to 5 initiation of therapy, cyclosporin was added to the treatment at a dose of 5 mg/kg body weight daily, intravenously for the first 07 days and then orally for 04-06 weeks.

Progress was monitored by improvement in general well being decreasing frequency of stool and colonoscopic examination before and after cyclosporin therapy.

Response of the patients was analysed as follows:

Complete Response:
- No diarrhoea
- Weight gain
- Colonoscopic evidence of complete healing or marked reduction in the extent and severity of the disease.
Partial Response:
- < 03 stools/day with or without blood or mucus
- Dome endoscopic improvement.

No Response:
- > 03 stools/day with or without blood or mucus.
- No endoscopic improvement.

Assessment
(Truelove and Witt's criteria)

- Intravenous Hydrocortisone
- Oral 5-Amino Salicylic Acid
  - Element Diet
- Parenteral Nutrition

Intravenous Cyclosporin 5 mg/kg
When no improvement by day 03 to 05.

Oral Cyclosporin continued for 4-6 weeks

Side effects: One patient had oral candidiasis and generalized tremors which responded to anti-fungal treatment and reduction in the dose of cyclosporin respectively.

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\begin{aligned}
\text{Patients} & \quad 08 \\
\text{Acute Phase: Complete Response} & \quad 06 \\
\text{Partial response} & \quad 02 \\
\text{No response} & \quad 0 \\
\text{Chronic Phase: Surgery Avoided} & \quad 05 \\
\text{Surgery within 6 months} & \quad 01 \\
\text{Surgery with 3 months} & \quad 02
\end{aligned}
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DISCUSSION

Inflammatory bowel disease is a chronic relapsing and remitting disease with evidence of immune activation. It is therefore thought that some antigen (endotoxin derived peptide) forms a complex with the antigen presenting cells. T-helper cells recognize this complex, are activated and start producing cytokines, e.g. IL-1, IL-2, IL-6, IL-8, gamma interferon and TNFα.

Immunosuppressive agents such as azathioprine and 6-mercaptopurine have been shown to be effective in IBD with a response rate of 60-70% but their optimal effects in only reached after 3-4 months. Hence they are not useful in acute phase of the disease.

Cyclosporin prevent the production of IL-2 by blocking the IL-1 mediated action of macrophages on T-helper cells without interfering with the action or development of T-suppressor cells and without producing myelosuppression.

Our small study shows that cyclosporin is effective in 75% cases in the acute stage. This figure is quite close to those previously reported 76%, 83% and 82%. On average, patients responded clinically within a week.
which is also comparable to previous reports — 7 days$^9$ and$^9$ days$^{7,10}$. Endoscopically, they responded within 4-6 weeks.

There are reports that clinical response does not correlate with whole blood or intestinal tissue cyclosporin concentration in patients treated with high dose cyclosporin$^14$. We used an average, fixed dose of 5 mg/kg body weight daily with the aim to reach serum cyclosporin levels between 50 and 130 ug/L. We did not give maintenance cyclosporin therapy as to date there is no evidence to suggest that it can prevent a relapse.

It is widely accepted that a patient with I.B.D. not responding to i.v. steroids within 07 days should undergo colectomy or be referred for investigational therapy$^1$. We introduced cyclosporin a little earlier, i.e. on day 3 to 5 of conventional therapy which is probably the reason for our good results despite using a relatively low dose of cyclosporin. In our study, Short term colectomy rate (within 6 months) was 37.5% compared to the reported rate of 70%.

We conclude that until the role of cyclosporin for routine use in acute I.B.D. is established, appropriate recipients of such treatment would be patients with recently diagnosed disease who are not yet psychologically prepared for colectomy and those who would be high risk candidates for surgery.

REFERENCES

3. Van Hozegand RA. Medical management of patients with difficult to treat inflammatory bowel disease. (review); Netherlands Journal of Medicine; 1994; 45 (2): 55.