Effects of cyclosporin A on active Crohn’s disease

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Summary: Seven patients with active Crohn’s disease were treated with cyclosporin A orally for 16 weeks. The initial dose was 8 mg/kg/day and the subsequent dose was adjusted to maintain the plasma concentration of cyclosporin A of approximately 200 ng/ml. The mean value of the Crohn’s disease activity index before treatment was 194.3 ± 57.4. It was gradually decreased reaching a nadir at 12 weeks (139.0 ± 45.6, p < 0.05) and one enterocutaneous fistula was closed. White blood cell counts, hemoglobin and α2-globulin did not significantly improve during treatment. Cyclosporin A could be indicated when steroids, sulfasalazine or azathioprine are not effective or not tolerated. Gastroenterol Jpn 1989;24:12-15

Key words: Crohn’s disease, Crohn’s disease activity index, Cyclosporin A

Introduction

Therapeutic effects of steroid, sulfasalazine and azathioprine have not always been satisfactory for patients with active Crohn’s disease. Poor response to medical therapy has remained as one of the major reasons for operative indications in Crohn’s disease. Recently, favorable results in inflammatory bowel disease by cyclosporin A were reported. The authors attempted a clinical trial to treat patients with active Crohn’s disease with cyclosporin A and evaluated the effects of this agent.

Methods

Patients

A diagnosis of Crohn’s disease was confirmed radiologically, endoscopically and histologically. Seven patients with active Crohn’s disease were treated with cyclosporin A. Their age ranged from 17 to 39 years, with a mean of 27 years. They were 6 males and 1 female. Their intestinal involvements were ileum and colon (6) and colon (1). The mean duration from the onset of Crohn’s disease until the present study was 8 ± 7 years (mean ± 1sd). Five of the patients had received more than one operation for Crohn’s disease previously.

Two patients had complications of intestinal fistulae. Steroid and sulfasalazine were discontinued, but elemental diet, 800-1200 Kcal/day at night was continued during cyclosporin A therapy (Table 1).

Cyclosporin A was given orally at an initial dose of 8 mg/kg/day adjusted thereafter every two weeks to maintain the plasma concentration of cyclosporin A at approximately 200 ng/ml. The plasma concentration of cyclosporin A was measured by high performance liquid chromatography. It was given for 16 weeks in 4 patients, 23 weeks in 1 patient and 30 weeks in 1 patient. Informed Consent for cyclosporin A therapy was obtained from all the patients.

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Table 1 Patients with Crohn’s disease entered cyclosporin A trial

<table>
<thead>
<tr>
<th>Patients</th>
<th>sex</th>
<th>age</th>
<th>site of lesion</th>
<th>duration of the disease</th>
<th>before CDAI</th>
<th>16 weeks CDAI</th>
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<td>M</td>
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<td>ileum, colon</td>
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<td>235</td>
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<tr>
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<td>F</td>
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<tr>
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<td>M</td>
<td>29</td>
<td>colon</td>
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<td>156</td>
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<td>M</td>
<td>30</td>
<td>ileum, colon</td>
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<td>228</td>
<td>144</td>
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<tr>
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<td>144</td>
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<tr>
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<td>M</td>
<td>29</td>
<td>ileum, colon</td>
<td>12</td>
<td>(197)</td>
<td></td>
</tr>
<tr>
<td>mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>194.3±57.4</td>
<td>169.8±37.7</td>
</tr>
</tbody>
</table>

CDAI

Fig. 1 Changes of Crohn’s disease activity index (CDAI) before and during cyclosporin A therapy.

Clinical assessment

Therapeutic effects of cyclosporin A were evaluated from clinical symptoms, Crohn’s disease activity index, white blood cell counts, alpha two globulin and hemoglobin every 2 weeks. Immunological studies, including peripheral T cell, B cell and T cell subsets, were performed before and 2 weeks after cyclosporin A therapy. Statistical significance was analyzed using Students’ t-test.

Results

All the patients except one completed this trial. One patient dropped out because of nausea, abdominal pain and diarrhea soon after commencement of cyclosporin A therapy. Renal function was maintained within normal limit throughout the trial in all cases. One patient developed upper respiratory infection associated with clinical relapse at 15 weeks but recovered soon. Symptomatically, marked improvement with a sense of well was experienced. Decreased bowel movements were noted in 2 patients and one enterocutaneous fistula was closed 3 weeks after starting cyclosporin A and remained closed for 5 months on one patient. His enterocutaneous fistula from the ileocolic anastomosis developed on March 1985, when elemental diet (1200Kcal/day) at night by per nasal intubation and a supplemental small amount of diet day were started. The fistula remained open for 18 months with treatment, then cyclosporin A was started, maintaining the same dose of elemental diet.

Crohn’s disease activity index (CDAI)

Changes of CDAI are shown in Figure 1. The CDAI value before cyclosporin A treatment was 195.3±57.3 (mean±1sd), which gradually decreased to 150.2±22.9 (4 weeks), 159.2±45.2 (8 weeks), 139.0±45.6 (12 weeks) and slightly increase at 16 weeks (169.8±37.7). The decrease in CDAI value at 12 weeks was statistically significant compared to the value before treatment (p<0.05). Patients whose CDAI values were higher than 200 seemed to respond well compared to those less than 200.

White blood cell counts

White blood cell counts before cyclosporin A therapy were 10,340±3,859/mm³ (mean±1sd) and gradually decreased to 9,975±4,927 (4 weeks), 8,675±3206 (8 weeks), 6,983±1766 (12 weeks) and 7,340±3766 (16 weeks). However