Infliximab in the treatment of severe ulcerative colitis: a follow-up study

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Abstract. – Conventional treatment options for patients with severe steroid-refractory ulcerative colitis (UC) include intravenous cyclosporine, which is frequently burdened by toxicity, or colectomy. Preliminary data suggest a benefit of anti-tumor necrosis factor alpha (Infliximab) therapy in patients with steroid refractory UC. Thirteen patients with severe UC, refractory to therapy with methyl-prednisolone, 60 mg IV daily were treated with a single intravenous infusion of Infliximab 5 mg/kg. Ten out of 13 patients (77%) had a clinical response to therapy defined by a CAI ≤ 10 on two consecutive days. Two patients (15%) underwent total colectomy because of clinical worsening; one patient refused surgery and was lost to follow-up. Infusion with Infliximab produced no significant adverse events. The mean time of follow-up was 25.6 months (range 17-24); in this period of time 8 out of 10 patients (80%) maintained clinical remission and were able to discontinue corticosteroids therapy. Infliximab appears to be an effective agent for inducing long standing remission in refractory patients with severe UC.

Key Words:
Ulcerative colitis, Infliximab, Anti-TNF-α monoclonal antibody.

Introduction

Approximately 15% patients with ulcerative colitis have a severe attack requiring hospital admission at some time during their illness. Lack of response to intravenous corticosteroid therapy accounts for about 30-40% of severe attacks of ulcerative colitis and requires cyclosporine administration or colectomy. Continuous intravenous infusion of cyclosporine induces a remission of the acute episode in 70-80% of patients with steroid-resistant ulcerative colitis1,2 and avoids emergency colectomy. However, 19% to 36% of patients may fail to respond to cyclosporine1,2 and serious toxicity has been reported, mainly due to infectious problems3, with high rates of relapsed discontinuation.

Up to now the efficacy of Infliximab, an anti-TNF-α chimerical monoclonal antibody, for the treatment of ulcerative colitis, has not been assessed in a controlled fashion. The first and only double blind placebo controlled trial was sponsored by an industry and was interrupt because of slow accrual after enrolment of 8 Infliximab patients receiving either 5, 10, 20 mg/kg IV and 3 placebo patients4. Preliminary data from open studies suggest a benefit of Infliximab therapy in patients with steroid-refractory ulcerative colitis although some conflicting results are reported probably owing to differences among groups of patients5-8.

In this study we report the clinical outcome of 13 patients with severe steroid-refractory ulcerative colitis treated with Infliximab and the results of long term follow-up.

Methods

A n open study has been carried out on 13 patients5, ranging from 12 to 62 years of age, admitted to S. Camillo Hospital in Rome (No = 7) or to Mauriziano Hospital in Torino (No = 6) with severe ulcerative colitis refractory to intravenous corticosteroid therapy (methyl prednisolone 60 mg daily) performed for seven or more days. The severity of disease was established according to the Truelove and...
Witts classification. Abdominal complications were ruled out by plain abdominal X-ray film and disease activity was evaluated by flexible proctosigmoidoscopy. A chest x-ray was obtained to exclude respiratory tract infections. All patients received a single intravenous infusion of Infliximab at a dose of 5 mg/kg; four patients who responded to the first infusion received a second infusion of Infliximab, after 2 weeks due to the severity of endoscopic lesions. Clinical activity was assessed by means of a Clinical Activity Index (CAI) for the evaluation of patients with Ulcerative Colitis; the patients were included if the CAI score was > 10.

All concomitant medications were continued and oral food intake was permitted at the discretion of the gastroenterologist. Patients whose condition worsened or whose CAI score did not fall below 10 for two consecutive days, within 7 days after infusion of Infliximab, were considered to have no response to treatment and underwent colectomy.

After hospital discharge all patients were followed with serial clinical evaluation at 6, 12 and 24 months and clinical activity was evaluated using CAI.

Results

Ten of the 13 patients (77%) had a clinical response to therapy as defined by a CAI ≤ 10 on two consecutive days; nine patients (69%) showed a dramatic clinical improvement after the first 48-72 hours, one of ten responded after 6 days (Figure 1). Two patients (15%) underwent total colectomy within 3 days because of clinical worsening; one patient, with no evidence of clinical response after 7 days, refused surgery and was lost to follow-up. Four patients who responded to the first infusion were retreated after 2 weeks. Nine out of 10 patients (90%) who reached remission were discharged on immune modifier treatment with Azathioprine or 6-MP alone or in combination with sulfasalazine or 5-acetylsalicylate.

All patients who responded to treatment (10/13) were followed and 80% (8/10) maintained remission off steroids at a mean of 25.6 months (range, 17-24 months). One patient, on treatment with azathioprine 2 mg/kg of body weight, relapsed after 17 months and underwent elective colectomy; 1 patient, on treatment with azathioprine and sulfasalazine, relapsed after 5 and 20 months requiring steroids in this last occasion, for 8 wks, with good clinical outcome (Figure 2).

As a whole 77% of patients with severe refractory colitis treated with a single infusion of Infliximab 5 mg/kg, repeated in few cases a second time, avoided colectomy. In these patients Infliximab acted as a “bridge therapy” to immunomodifiers and, after 24 months, 62% of patients were still on remission without steroids.
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References


