Journal of Crohn's and Colitis (2013) 7, e49–e54

Available online at www.sciencedirect.com

SciVerse ScienceDirect

Long-term prognosis of patients with ulcerative colitis treated with cytapheresis therapy

Tetsuro Takayama [a,b], Takanaori Kanai [a], Katsuyoshi Matsuoka [a], Susumu Okamoto [a], Tomohisa Sujino [a], Yohei Mikami [a], Tadakazu Hisamatsu [a], Tomoharu Yajima [a], Yasushi Iwao [c], Haruhiko Ogata [c], Toshifumi Hibi [a,*]

[a] *Division of Gastroenterology and Hepatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan*
[b] *Department of Internal Medicine, Saiseikai Central Hospital, Tokyo, Japan*
[c] *Center for Diagnostic and Therapeutic Endoscopy, Keio University Hospital, Tokyo, Japan*

Received 6 January 2012; received in revised form 2 April 2012; accepted 4 May 2012

KEYWORDS
Inflammatory bowel disease;
Ulcerative colitis;
Cytapheresis therapy;
Long-term prognosis

Abstract

Background: Although accumulating studies in Japan show that cytapheresis (CAP) therapy is safe and effective for the induction of remission of moderate or severe ulcerative colitis (UC), the long-term prognosis of UC patients treated with CAP is unknown. The aim of this study was to determine the long-term prognosis of UC patients treated with CAP.
Methods: Ninety patients treated previously with CAP and followed for more than 3 years were evaluated. The rates of operation, readmission, and use or dose-up of corticosteroid were analyzed as long-term prognosis.
Results: Following the first course of CAP treatment, 64% of patients showed clinical improvement (>4-point decrease in the clinical activity index (CAI)), and 49% of patients achieved clinical remission (CAI ≤4). Longer disease duration and lower age at the first CAP treatment correlated significantly with the therapeutic effects of CAP ($p=0.003$ and 0.035, respectively). The rates of operation and readmission were significantly lower in patients who showed previous clinical effects of CAP than in those who did not respond to CAP. The rates of operation and readmission were also significantly lower in patients whose treatment was combined with immunomodulators after the initiation of CAP than in patients who did not use immunomodulators. Importantly, the second course of CAP was also effective in most of the patients who showed a clinical response to the first CAP.

* Corresponding author at: Division of Gastroenterology and Hepatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo 180–8582, Japan. Fax: +81 3 3341 3631.
E-mail address: thibi@sc.itc.keio.ac.jp (T. Hibi).

1873-9946/$ - see front matter
doi:10.1016/j.crohns.2012.05.005

Conclusions: Patients who achieve remission after the first CAP therapy may have a good long-term prognosis and a good response to a second CAP therapy even after relapse.

1. Introduction

Ulcerative colitis (UC) is a chronic and recurrent inflammatory disease of the colon that impairs the quality of life (QOL). Several treatments for UC have been developed.[1–3] For instance, prednisolone (PSL) is used in induction therapy with great efficacy but has several severe side effects.[4] Immunomodulators (IM) such as 6-mercaptopurine (6-MP) and azathioprine (AZA) are effective agents for the maintenance of remission.[5] However, IM also have severe side effects such as myelosuppression and the development of lymphoma.[4] Recent advances include the use of biologics, such as infliximab, for the induction therapy and maintenance of severe UC, but the long-term safety of this medication is not known.[1,2]

In most patients, UC can be controlled by these medications without any complications, although some patients require an operation. Nearly all UC patients prefer to avoid colectomy, even for severe symptoms, although QOL is usually improved after an operation.[6] Chronic inflammation elevates the risk of developing colitic cancer, which severely impairs QOL and threatens the patient's life.[7] Therefore, it is important to choose therapies that can effectively avoid recurrences and that have the fewest side effects. Therefore, it is very critical to know the long-term prognosis by specific treatment with predicted life of each patient.

UC is often associated with an increase in peripheral blood granulocytes and monocytes.[8] Accordingly, cytapheresis (CAP) therapy is used widely in Japan in UC patients with moderate to severe activity. Several studies have shown the efficacy and safety of CAP, with most demonstrating that about 60% of patients have a clinical response to CAP therapy.[9–19] However, there are few reports on the long-term prognosis of UC patients treated with CAP therapy and the number of patients is relatively small.[20] Although some UC patients receive multiple courses of CAP therapy throughout their life, the efficacy of a second course of CAP therapy has not been reported. Therefore we here analyzed the long-term prognosis of UC patients treated with CAP therapy and assessed the efficacy of multiple courses of CAP.

2. Materials and methods

2.1. Patients

Retrospective data were collected for 114 patients with active UC who were treated with CAP by granulocytapheresis (GCAP; JIMRO Co. Ltd., Takasaki, Japan) and/or leukocytapheresis (LCAP; Asahi Kasei Kuraray Medical Co. Ltd., Tokyo, Japan) and who could be followed up for >3 years (including seven lost patients). Ninety patients (55 men, 35 women; mean age, 36.4 years) with full clinical records were enrolled for further analysis that included information about their background, medication, and long-term prognosis. The average observation period was 4.6 years. Clinical efficacy was evaluated using the clinical activity index (CAI) according to Rachmilewitz's criteria applied to information collected from questionnaires completed by the patients.[21] We defined a CAI of ≤4 points as remission and a decrease in CAI of >4 points as effective treatment, as reported previously.[22] To determine the long-term prognosis, we evaluated the rates of operation, readmission, and use or dose-up of steroid. This historical cohort study was conducted at Keio University Hospital and the study was approved by the Keio University School of Medicine review board and the permission was obtained. All patients who underwent CAP for UC with moderate to severe activity between 2001 and 2006 were enrolled. Written or oral informed consent was obtained from all patients and/or the parents of patients younger than 20 years of age.

The questionnaire was designed to collect demographic data including age, gender, disease extent, disease duration, clinical type, CAI before the first course of CAP, and medication (use of PSL and/or IM). Outcomes (rates of operation: total colectomy, readmission, and use or dose-up of PSL) were obtained from the hospital medical records.

2.1.1. Inclusion and exclusion criteria

The inclusion criteria were age between 14 and 77 years; an endoscopic and histological diagnosis of UC but not indeterminate colitis; and a CAI score>5 for patients with colonic involvement. The exclusion criteria were evidence of toxic megacolon; malignancy with serious concomitant cerebral, pulmonary, cardiac, hepatic, or renal disease; and a history of hypersensitivity reaction during apheresis.

2.2. Cytapheresis

Patients with moderately active disease were treated in our outpatient clinic, and those with severe disease were hospitalized and treated. Each patient received five or 10 GCAP or LCAP once or twice per week, respectively. Each GCAP session time was 60 min at 30 ml/min and each LCAP session time was 60 min at 30–50 ml/min. In patients who were receiving PSL at entry, the dose of PSL was tapered or discontinued according to clinical improvement during the CAP.

2.3. Data analysis

Multiple logistic regression analysis was performed using JMP version 7.0.1 (SAS Institute Japan, Co., Ltd, Tokyo, Japan) and GraphPad Prism software version 4.0 (GraphPad Software Inc., San Diego, CA). Differences at $p<0.05$ were considered significant. The log-rank test was used to compare the Kaplan–Meier survival curves. The data are expressed as mean ± SEM where appropriate.