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Alimentary Tract

Predictive factors of efficacy of leukocytapheresis for steroid-resistant ulcerative colitis patients

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Abstract

Background. The effectiveness of leukocytapheresis against ulcerative colitis has been reported. However, the efficacy of this therapy for steroid-resistant ulcerative colitis patients has hardly been examined.

Aims. The aims of this study are to evaluate the efficacy of leukocytapheresis for steroid-resistant ulcerative colitis patients and to identify clinical factors that predict the efficacy of this therapy for these patients.

Methods. Clinical factors of 71 steroid-resistant ulcerative colitis patients who underwent leukocytapheresis analysed.

Results. Of those analysed, 53 (75%) patients showed an initial response to leukocytapheresis. Among cases with initial response, however, only 19 (27%) patients maintained remission for more than 6 months. Steroid-dependent course (Odds ratio = 5.53, 95% confidence interval; 1.24–24.73) and a high C-reactive protein degree (Odds ratio = 1.6, confidence interval; 1.09–2.35) were predictors of initial response to leukocytapheresis. Rapid response, which means remission induction within three leukocytapheresis sessions, was the only predictor of maintenance of remission for more than 6 months after successful leukocytapheresis therapy (odds ratio = 8.01, confidence interval; 1.08–59.37).

Conclusions. Leukocytapheresis was effective for steroid-resistant ulcerative colitis patients. However, relapse was frequently observed within short periods after the initial response to this therapy. Patients without a rapid response should be treated with alternative or additional therapies.

Keywords: Leukocytapheresis; Steroid-resistant ulcerative colitis

1. Introduction

Ulcerative colitis (UC) is a chronic inflammatory bowel disease characterized by periods of remission and episodes of clinical relapse due to intestinal inflammation. Patients with UC require a long-term therapy targeted towards both induction of remission in the active disease and prevention of relapse.

Despite the recent progress in medical therapy, corticosteroids are still the mainstay of remission induction therapy against UC. However, a significant portion of UC patients suffer from a steroid-resistant course of their disease. For these patients, even high-dose corticosteroids cannot induce remission (a steroid-refractory course), or the drug cannot be tapered off due to a relapse (a steroid-dependent course). Moreover, these patients are often afflicted with the adverse effects of corticosteroids, such as osteoporosis, pathologic fracture, glaucoma, or diabetes, accompanied by impairment of quality of life. Although the efficacy of cyclosporine or infliximab has recently been reported for steroid-resistant patients [1–5], a medical therapy for these patients has not

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yet been established. In addition, it was reported that steroid-resistant UC patients are at high risk for receiving colectomy [6–8].

Leukocytapheresis is a method of therapeutic apheresis to remove the patient's peripheral leukocytes by extracorporeal circulation [9]. This therapy against UC was developed in Japan, and several previous reports demonstrated its effectiveness in 60–80% of UC patients [9–13]. Moreover, this therapy was characterized by a low incidence of adverse effects. Thus, leukocytapheresis could be a promising therapy for steroid-resistant UC patients. However, most previous reports examined the efficacy of this therapy for UC patients regardless of their clinical characteristics, and failed to indicate the efficacy for steroid-resistant patients, who seem to be the most suitable target of this therapy. Moreover, clinical factors that predict the efficacy of leukocytapheresis have scarcely been reported.

In this study, we examined clinical factors of steroid-resistant UC patients who received leukocytapheresis. After evaluation of the efficacy and limitations of this therapy for steroid-resistant patients, we identified clinical factors that predict the efficacy of this therapy. Our findings may help physicians set up a strategy for the treatment of steroid-resistant UC patients, with leukocytapheresis as one of the therapeutic options.

2. Materials and methods

2.1. Patients

From November 2001 to July 2005, a total of 78 UC patients received leukocytapheresis at Okayama University hospital and its 11 affiliated hospitals. Of these patients, 7 patients were steroid naïve cases, while the other 71 cases had been distressed with a steroid-resistant course. In the current study, clinical records of the latter 71 patients were reviewed and analysed in order to identify the factors predicting the efficacy of leukocytapheresis in steroid-resistant patients. In patients who underwent two or more leukocytapheresis treatment courses during the study period, the data on only the initial course were included in the analysis.

2.2. Clinical parameters

Clinical parameters, including demographic data, disease status, and medication, were collected and analysed. In addition, varieties of detailed leukocytapheresis procedures were included in the analysis. Demographic data included patient gender, age at time of leukocytapheresis, age at onset of UC, duration of disease, body mass index, smoking and drinking habits, family history of inflammatory bowel disease, and history of appendectomy. The parameters regarding disease status included extent of disease (left-sided colitis or total colitis), severity of disease according to the Truelove and Witts' criteria (moderate or severe) [14], clinical course (steroid-dependent or -refractory), and presence or absence of extraintestinal manifestations, including primary sclerosing cholangitis, pyoderma gangrenosum, etc. The steroid-dependent course was defined as the impossibility of completely withdrawing systemic steroids because of disease relapse or the occurrence of at least two flare-ups requiring systemic steroid therapy in a 6-month period. The steroid-refractory patients presented no or little improvement after 2 weeks of intravenous steroid therapy (at least 40 mg prednisolone daily). The following degrees at the beginning of apheresis therapy were included in the analysis as the disease status parameters: Lichtiger's clinical activity index (CAI) score [1], Matts endoscopic index [15], and laboratory data including white blood cell (WBC) count and C-reactive protein (CRP). The collected information regarding medication was as follows: corticosteroid dosage at the beginning of leukocytapheresis, total amount of corticosteroids administered before leukocytapheresis, 5-aminosalicylates, and immunosuppressants (azathioprine or 6-mercaptopurine) before and after leukocytapheresis. The amount of corticosteroids was calculated as the dosage of prednisolone. The parameters regarding varieties of the leukocytapheresis procedures included the period between disease relapse and the beginning of leukocytapheresis, the total number of apheresis sessions, and the number of sessions performed a week. In the analysis of the long-term effect of leukocytapheresis, the presence or absence of rapid response, which was defined as successful remission induction within three leukocytapheresis sessions or less, was also included.

2.3. Procedure for leukocytapheresis therapy

The leukocytapheresis treatment procedure was carried out using a leukocyte removal column, Cellsorba (Asahikasei Medical, Tokyo, Japan). The column contains a polyester nonwoven fabric that traps leukocytes from whole blood. The filter mainly traps monocytes and granulocytes (more than 95%), partially traps lymphocytes and platelets (30–90%), and does not trap erythrocytes (less than 10%) [10]. Nafamostat mesilate (Torii Pharmaceutical, Tokyo, Japan) was used as an anticoagulant. Venous blood was obtained continuously from an antecubital vein and passed through the column at a flow rate of 30–50 ml/min. Approximately 2–3 l of whole blood was processed during each roughly 60 min session. This procedure was performed once or twice a week for 2–10 consecutive weeks. One course of the leukocytapheresis treatment was composed of 4–10 sessions of the apheresis procedure.

For at least 2 weeks before the beginning of apheresis therapy, we did not increase the dosages of corticosteroids, 5-aminosalicylates, and immunosuppressants for the 71 steroid-resistant patients that we analysed. In addition, these agents were not newly prescribed during the same period. The dosages of these medications could be decreased if patient symptoms were improved during or after the course of apheresis therapy.