Gastroentérologie Clinique et Biologique (2010) 34, 682—686

ORIGINAL ARTICLE

Feasibility and safety of granulocytapheresis in Crohn's disease: A prospective cohort study

Faisabilité et sécurité des granulocytaphérèse dans la maladie de Crohn : une étude prospective de cohorte

G. Bresci[a,*], A. Romano[a], A. Mazzoni[b], F. Scatena[b], E. Altomare[c], A. Capria[a], R. Sacco[a,c]

[a] *U.O. di Gastroenterologia e Malattie Ricambio, Azienda Ospedaliera-Universitaria Pisana, A. Della Spina, 11, 56124 Pisa, Italy*
[b] *U.O. di Immunoematologia, Azienda Ospedaliera-Universitaria Pisana, Pisa, Italy*
[c] *Istituto di Medicina Interna, Universita' di Foggia, Italy*

Available online 13 November 2010

Summary
Background and objective. — This study evaluated the feasibility and safety of granulocytapheresis (GCAP) in inducing and maintaining remission in refractory Crohn's disease. The relationship between the clinical outcomes and the location (ileal or ileocolonic) of disease was also assessed.
Patients. — We evaluated 16 patients with ileal location (group A), 14 with ileocolonic location (group B). The patients underwent five sessions (1 session/wk) of GCAP (Adacolumn™). CDAI was measured at the end of the GCAP, at 6, 9 and 12 months.
Results and conclusions. — No major complications were observed. At the end of GCAP, 19 (63.3%) patients showed a clinical remission: 10 (62.5%) in group A versus 9 (64.2%) in group B. At 6 months, 16 (53.3%) of the cases had maintained remission: 9 (56.2%) in group A versus 7 (50.0%) in group B. At 9 months, 13 (43.3%) patients had maintained remission: 7 (43.7%) in group A versus 6 (42.8%) in group B. At 12 months, 12 (40%) patients were still in clinical remission: 7 (43.7%) in group A versus 5 (35.7%) in group B. Risk of relapse was not related to disease location. The procedure was well tolerated and feasible in an important percentage of Crohn's disease patients.

Introduction

The definition ''inflammatory bowel diseases (IBD)'' usually includes two similar but distinct chronic diseases of the gut,

* Corresponding author.
E-mail address: gbresci@libero.it (G. Bresci).

0399-8320/$ – see front matter © 2010 Elsevier Masson SAS. All rights reserved.
doi:10.1016/j.gcb.2010.09.009

ulcerative colitis and Crohn's disease, that are both characterised by episodes of remission and exacerbation with systemic complications [1—4].

During the last 20 years, the treatment of IBD has greatly improved; however, it is still empirical, due to the unknown aetiology of such diseases [5—8]. Both ulcerative colitis and Crohn's disease are supposed to have a multifactorial aetiology; however, regardless the cause, the final pathway leading to tissue damage in IBDs is mediated by the cellular immune response, through white blood cells, in the intestinal mucosa.

Corticosteroids are a mainstay of acute therapy for moderate to severe ulcerative colitis or Crohn's disease; however, up to 40% of patients do not respond to high-dose steroid therapy [9]. Preliminary results suggested that aminosalylates, e.g. melasazine, can be safe in the treatment of active Crohn's disease, but the clinical efficacy of mesalazine is currently under debate [9]. Classic immunosuppressant drugs, such as azathioprine or mercaptopurine, need some weeks to exert their full activity, and are therefore of limited use during the acute phases of the diseases. Newer immunosuppressants like cyclosporine and/or biological agents (e.g. anti-Tumor Necrosis Factor agents) have become available in the therapeutic armamentarium for the treatment of IBD. Unfortunately, many patients show often serious side effects after the administration of these drugs or are unresponsive to these medications [10].

Therefore, new therapeutic approaches are needed to improve the clinical outcome in active steroid-refractory IBDs. In recent years, some trials have suggested that granulocytapheresis (GCAP), a technique that selectively sequestrates granulocyte and monocyte subpopulations, can be a useful and safe option to induce clinical remission in patients with IBD [11—16]. However, these studies mainly involved patients affected from ulcerative colitis, while fewer data are currently available on the use of GCAP in the treatment of patients with Crohn's disease.

In the present study, we report our experience using GCAP when treating patients with Crohn's disease who failed to respond to conventional treatment.

The primary objective of this trial was to evaluate the safety and feasibility of GCAP in inducing and maintaining remission in patients with Crohn's disease who were refractory to conventional treatment with steroids and melasazine. A secondary objective was to assess a possible relationship between the efficacy of GCAP and the location (ileal or ileocolonic) of the disease.

Patients and methods

The study protocol conformed to the ethical guidelines of the 2008 Declaration of Helsinki and was approved by the Ethical Committee of our hospital. Written informed consents were obtained before GCAP from all patients.

Consecutive patients with active Crohn's disease (Crohn's Disease Activity Index [CDAI] > 150) who were refractory to steroid and mesalazine therapy were eligible to this study. These subjects were defined as refractory if they did not achieve disease remission (CDAI < 150) after the administration of metylprednisolone 1 mg/kg/day and of oral mesalazine 2.4 g/day, during the 8 weeks prior to GCAP initiation. We selected this time period in order to evaluate the response to first-line steroids for a longer period than the one usually considered in the standard definition of refractory patient (i.e. 4 weeks).

Exclusion criteria were: pregnancy, allergy to heparin, serious cardiovascular diseases, extraintestinal manifestations, structuring or penetrating (fistulising) disease, perianal disease, actual treatment with immunosuppressant drugs or biological therapy, steroid-dependence.

The activity of the disease was evaluated by CDAI, the main index of disease activity used in clinical trials [17,18].

From September 1st 2005 to December 31st 2009 we have identified 30 consecutive patients with active Crohn's disease who were refractory to steroid therapy and were visited at our Center. These patients were divided in two groups according to disease location: group A, 16 patients, with ileal location of disease, while group B, 14 patients, with ileocolonic location of disease. Patients were classified

Table 1 Characteristics of patients at baseline.

Characteristic	Total	A	B	*P*-value
Number patients	30	16	14	NS
Age (years ± SD)	36.5 ± 5	36 ± 6	37 ± 4	NS
Male/Female	17/13	9/7	8/6	NS
Smokers	10	6	4	NS
Previous surgical therapy	0	0	0	NS
Extraintestinal complications	0	0	0	NS
Disease duration(years ± SD)	6.5 ± 3.5	7.0 ± 4.0	6.0 ± 3.0	NS
Months of remission before study entry	4.5 ± 2.0	5.0 ± 2.0	4.0 ± 2.0	NS
Steroids use (days ± SD)	58	56 ± 2.0	56 ± 2.0	NS
Non-stricturing/non penetrating	30	16	14	NS
Presence of granulomas	14	8	6	NS
CDAI (mean ± SD)	235 ± 35	240 ± 30	230 ± 40	NS
CRP(mean ± SD)	35 ± 15	40 ± 20	30 ± 10	NS
ESR(mean ± SD)	85 ± 9	80 ± 10	90 ± 8	NS

NS: not significant. SD: standard deviation.