

MATERIAL AND METHODS: 12 patients (5 females, 7 males, mean age 49 years, range 33-71 years), with mild-moderate UC dependent/refractory upon steroids were enrolled. Each patient was treated for a 5-week period with five cycles of Adacolumn. Patients were evaluated at baseline and 1 week after the last apheresis by means of Global Physician Assessment, quality of life features, laboratory tests (erythrocyte sedimentation rate, CRP, full blood count, faecal calprotectin), endoscopy and histology. **RESULTS:** At week 6 of follow-up, complete mucosal healing was observed in 3 out of 12 patients, partial mucosal healing in 8 patients and no change in 1 patient. Clinical response was complete in 8 out of 12 patients. **CONCLUSION:** These data suggest that granulocyte-monocyte-apheresis induces an improvement both in clinical and mucosal lesions in steroid-dependent/refractory ulcerative colitis. Of note, the reduction in granulocyte infiltration and the improvement in mucosal lesions are accompanied by a reduction in faecal calprotectin.

Therapeutic leukocytapheresis for inflammatory bowel disease

Saniabadi AR, Hanai H, Fukunaga K, Sawada K, Shima C, Bjarnason I, Lofberg R, Transfusion and Apheresis Science 2007; 37: 191-200

The inference that granulocytes and monocytes/macrophages (GM) are part of the immunopathogenesis of inflammatory bowel disease (IBD) and hence should be targets of therapy stems from observations of elevated, and activated GM in patients with IBD. The Adacolumn can selectively deplete GM by adsorption (GMA) and in patients with IBD, GMA has been associated with significant clinical efficacy together with sustained suppression of inflammatory cytokine profiles. Additionally, GMA depleted proinflammatory CD14(+)/CD16(+) monocytes and was followed by an increase in CD4(+) T lymphocytes including the regulatory CD4(+)/CD25(high+)/Foxp3 phenotype. Hence, GMA could be a non-pharmacologic therapy for IBD with potential to spare steroids and other unsafe pharmacologic preparations.

Clinical effectiveness of selective granulocyte, monocyte adsorptive apheresis with the Adacolumn device in ulcerative colitis ***Habermalz B, Sauerland S, Dig Dis Sci (2010) 55: 1421-1428***

Meta-analysis. Seven RCTs including 594 patients were found and six RCTs on active UC contributed to the main analyses. Homogeneous evidence from seven RCTs shows that GMA apheresis induces a clinical remission in a higher proportion of UC patients as compared to conventional medical therapy.

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IBD bibliography 2009

Granulocyte and monocyte apheresis with the G-1 column in the treatment of patients with active ulcerative colitis (Granulocyte and monocyte apheresis in patients with active ulcerative colitis – multicenter controlled study)
Shimoyama T et al., Japanese Journal of Apheresis 1999; 18 (1): 117-131

A randomized multicenter study which compares Adacolumn versus systemic treatment with steroids for active ulcerative colitis. N=105. Evaluation at week 7. Adacolumn is superior to standard steroid regimens ($p=0.045$).

Adsorptive granulocyte and monocyte apheresis versus prednisolone in patients with corticosteroid-dependent moderately severe ulcerative colitis

Hanai H et al., Digestion 2004; 70: 36-44

69 patients randomized to two treatment arms; corticosteroids or Adacolumn. Indicates the steroid sparing effect of Adacolumn and that Adacolumn can be used in patients with steroid dependent disease.

Intensive granulocyte and monocyte apheresis versus intravenous prednisolone in patients with severe ulcerative colitis: a multicentre randomized controlled study

Hanai H et al., Gut 2006; 55 (suppl V): A40

Compared the efficacy and safety of intensive GMA with intensive intravenous (iv) prednisolone (PSL) in patients with severe UC. 66 patients with clinical activity index CAI 10-18 were randomly assigned to intensive GMA with the Adacolumn, at 2 sessions/week in the first 3 weeks and then 1 session/week for up to 10 sessions (n=33) or iv PSL, 40-60mg/day for 5-10 days. Efficacy was assessed at weeks 2, 6, 12.

Results: 4 patients in the PSL group withdrew within the first 5 days, while all 33 patients in the GMA group completed their treatment course. At weeks 2, 6 and 12 the remission (CAI = or <4) rates (%) in the GMA group were 9.1, 54.5, 75.8, respectively. The corresponding values in the PSL group were 21.2, 45.5 and 39.4. In the GMA group, flushing and light-headedness were observed in four patients vs. typical steroid side effects in 43% of the PSL group.

Adacolumn for selective leukocytapheresis as a non-pharmacological treatment for patients with disorders of the immune system: an adjunct or an alternative to drug therapy?

Saniabadi A, Hanai H, Beretta A, Bjarnason I, Löfberg R et al., Journal of Clinical Apheresis 2005; 20 (3): 171-184

A comprehensive review of the logics and mechanisms of action.

Positions of selective leukocytapheresis in the medical therapy of ulcerative colitis

Hanai H, World J Gastroenterol 2006; 12: 7568-7577

IBD is perpetuated by inflammatory cytokines like TNF-alpha, interleukin (IL)-1beta, IL-6 and IL-8. The development of biologicals to intercept tumor necrosis factor (TNF)-alpha represents therapeutic progress, albeit major concern about side effects and a lack of long-term safety and efficacy profiles. As sources for pro-inflammatory cytokines, activated peripheral granulocytes and monocytes/macrophages (GM) are the target in selective granulocyte-monocyte adsorptive apheresis (GMA) with Adacolumn. Current clinical data in patients with steroid dependent or steroid refractory UC show up to 85% efficacy and tapering or discontinuation of steroids. GMA has an excellent safety profile.

Open label trial of granulocyte apheresis suggests therapeutic efficacy in chronically active steroid refractory ulcerative colitis
Kruis W, Dignass A, Steinhagen-Thiessen E, Morgenstern J, Mössner J, Schreiber S, Vecchi M, Malesci A, Reinshagen M, Löfberg R, World Journal of Gastroenterology 2005; 11 (44): 7001-7006

An open label multicenter study (n= 39) with active ulcerative colitis (CAI 6-8) despite continuous use of steroids (a minimum total dose of 400 mg prednisone within the last 4 wk). Five apheresis using Adacolumn. Assessments at wk 6 and during follow-up until 4 month comprised clinical (CAI) and endoscopic (EI) activity index, histology, quality of life (IBDQ) and laboratory tests. RESULTS: 35 out of 39 patients were qualified for intent-to-treat analysis. After the apheresis treatment at wk 6, 13/35 (37.1%) patients achieved clinical remission and 10/35 (28.6%) patients had endoscopic remission (CAI<4, EI<4). Quality of life (IBDQ) increased significantly (24 points, $P<0.01$) at wk 6. Apheresis could be performed in all but one patient. Apheresis was well tolerated.

CONCLUSION: In patients with steroid refractory ulcerative colitis, five apheresis with a granulocyte/monocyte depleting filter show potential short-term efficacy. Tolerability and technical feasibility of the procedure are excellent.

Granulocyteapheresis in steroid-dependent inflammatory bowel disease: a prospective, open, pilot study

Domènech E, Hinojosa J, Esteve-Comas M, Gomollón F, Herrera JM et al. (GETECCU), Alimentary Pharmacology & Therapeutics 2004; 20: 1347-1352

Uncontrolled multi-center study in active steroid dependent inflammatory bowel disease. All patients were started on 60 mg/day of prednisone; after 1 week, a five session programme of granulocyte apheresis (once per week) was started. The steroid dose was tapered weekly if there was clinical improvement. Remission was defined as an inactive clinical activity index together with complete withdrawal of steroids at week 6. The patients were followed up for at least 6 months or until disease relapse. RESULTS: 26 patients (14 UC, 12 CD) were included. More than a half had been previously treated with immunomodulators. Remission was achieved in 62 and 70% of ulcerative colitis and Crohn's disease, respectively. During a median follow up of 12.6 months, six of eight ulcerative colitis patients maintained their clinical remission; however, only one Crohn's disease patient remained in remission after the first 6 months of follow up.

CONCLUSION: Granulocyte apheresis is a safe treatment option in inflammatory bowel disease. A five session programme of granulocyte apheresis seems to be efficient in the treatment of steroid dependent ulcerative colitis, but not in Crohn's disease.

Granulocyte, monocyte/macrophage apheresis for IBD in clinical practice. Clinical results from the first 100 patients treated in Scandinavia

Ljung T, Thomsen OO, Vatn M, Grip O, Karlén P, Kilander A, Gillberg R, Tysk C, Befrits R, Nilsson SU, Karlsen LN, Löfberg R, Scandinavian Journal of Gastroenterology 2007; 42: 221-227

Retrospective study on the first consecutive 100 patients treated by Adacolumn in Scandinavia at 24 centers. Clinical outcome was assessed one month after the last treatment. Remission was defined as absence/near absence of clinical symptoms, response as improvement of symptoms or tapering of steroids, and failure as no change or worsening of symptoms. RESULTS: 52 patients had UC, 44 CD and 4 IC. In 97 patients the indication for leukocyte apheresis was steroid-refractory or steroid-dependent disease. Remission/response was seen in 69 patients. The median time to first sign of clinical response was 2 weeks (range 1-12 wk) and median time to remission was 6 weeks (range 1-16 wk). Complete steroid withdrawal was achieved in 27 out of 50 patients on steroids at baseline. 12 months follow-up data were accessible in 37 out of 69 of the responding patients. UC patients achieving initial complete remission had the longest relapse-free period (median 10 months).

CONCLUSION: Granulocyte, monocyte/macrophage apheresis treatment seems to be a valuable adjuvant therapy in selected patients with refractory inflammatory bowel disease. The risk for toxicity or severe adverse events appears to be low.

Selective white cell apheresis reduces relapse rates in patients with IBD at significant risk of clinical relapse.

Maiden L. et al., Inflamm Bowel Dis. 2008 Oct; 14 (10): 1413-1418

Interim analysis of a multi-center, prospective, randomized controlled trial that assesses the efficacy of Adacolumn apheresis in preventing clinical relapse in asymptomatic IBD patients at risk of deterioration. RESULTS: 30 patients were recruited from 244 potential subjects attending the clinics. 13 (5 female; 6 with CD) received Adacolumn apheresis. 17 (10 female; 6 CD) were controls. In the Adacolumn group 8 patients (62%) maintained their remission vs 4 (24%) in the control group ($p < 0.04$, Pearson Chi squared test). In the Adacolumn group mean survival was 181 days vs 104 days in the control group ($p = 0.016$, Mantel Chi-squared test).

CONCLUSION: These studies represent a new approach to the treatment of IBD, namely targeting the inflammatory component of the disease at an asymptomatic stage. Five weekly sessions of Adacolumn apheresis significantly reduce relapse rates and prolong time to relapse in IBD patients at significant risk.

Treatment of patients with acute ulcerative colitis: conventional corticosteroid therapy (MP) versus granulocyteapheresis (GMA): a pilot study

Bresci G, Parisi G, Mazzoni A, Scatena F, Capria A, Digestive and Liver Disease 2007; 39: 430-434

Forty patients with acute ulcerative colitis were randomized to two groups of 20; one group was treated with five sessions of granulocyteapheresis, the other with methylprednisolone for 5 weeks. Complete response was defined as clinical activity index lower than 6 and endoscopic index lower than 4 after 6 weeks of follow-up. Complete clinical response was observed in 70% of patients treated with granulocyteapheresis versus 60% of patients treated with methylprednisolone. Side effects were more common (50% vs. 10%) in the group treated with methylprednisolone.

Mucosal features and granulocyte-monocyte-apheresis in steroid-dependent/refractory ulcerative colitis

D'Óvidio V, Arantari A, Viscido A, Marcheggiano A, Papi C, Capurso L, Caprilli R, Digestive and Liver Disease 2006; 38: 389-394

Assess the effects of granulocyte-monocyte-apheresis on clinical and mucosal features in patients with ulcerative colitis, dependent upon or refractory to steroids.