PROSPECTIVE OPEN-LABEL PILOT STUDY TO EVALUATE THE SAFETY, TOLERABILITY AND EFFICACY OF A NOVEL ADSORPTIVE TYPE CYTAPHERESIS MODULE IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS

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INTRODUCTION

Adsorptive cytapheresis techniques, which selectively remove leukocytes from the peripheral blood, have been recognized as safe and effective treatment strategies for immunological diseases such as inflammatory bowel disease (IBD), rheumatoid arthritis, and other[1-3]. Currently, two extracorporeal blood perfusion systems are commercially available: Adacolumn® is using using cellulose acetate beads preferentially adsorbing granulocytes, monocytes, platelets but only a small fraction of lymphocytes. The Cellsorba® apheresis system consists of a column filled with polyethylenephtarate fibers and captures lymphocytes, granulocytes, monocytes, and platelets (35 % decrease).

An increase in peripheral platelets has been recognized as a common feature during the active phase of IBD, and high platelet numbers correlate with disease severity. Interestingly, the reduction of activated platelets has been shown to be a possible early predictor for a successful outcome after leukocytapheresis[4]. Therefore, the development of new adsorber materials further decreasing activated platelets as well as the number of leukocytes would be an interesting approach for the treatment of patients with IBD. Here, our aim was to evaluate the safety, tolerability and clinical efficacy of the novel adsorptive type cytapheresis module Immunopure® which particularly captures platelets in patients with active ulcerative colitis (UC).

PATIENTS AND METHODS

Demographic data:

10 patients (6 male, 4 female, mean age: 47.1 years, minimum age: 25 years, maximum age: 73 years) with moderately to severely active UC, defined by Clinical Activity Index (CAI according to Rachmilewitz[5]: 6-10), who have failed to achieve long-term remission with steroids and/or immunosuppressants or who were contraindicated or intolerant to steroids and/or immunosuppressants were recruited.

The Immunopure® (Nikkiso, Japan) device has been specifically designed to be used in a simple hemoperfusion setting for the removal of activated granulocytes, monocytes and platelets. The device is a gamma-ray sterilized single use (disposable) module filled with amorphous polyarylate resin beads of 1.0 mm diameter. The total volume is 350 ml. The void volume of the device is 139 mL.

Study design:

- 5 treatment sessions at weekly intervals (week 1-5) with a treatment duration of 60 min
- Blood flow of 30mL/min, anticoagulation by standard heparin
- Safety analyses: laboratory parameters and vital signs
- Disease activity: evaluated by assessing the CAI (baseline, week 6 and week 10) as well as the Endoscopic Index (baseline, week 10). Clinical remission in UC is defined as a CAI score of 4 or less. Clinical response is defined as CAI drop ≥ 3 or CAI ≤ 4 .

CONCLUSIONS

- The apheresis treatments with Immunopure® columns assured a high degree of safety. All measured safety parameters remained substantially unchanged, both during intra-treatment and inter-treatment periods.
- Vital parameters such as blood pressure, heart rate and body temperature were essentially stable during the apheresis sessions.
- The tolerability of the apheresis treatments with the Immunopure® device was well to very well.
- The clinical efficacy appears to be very good. The response rates are in full concordance with response rates reported for other adsorptive cytapheresis devices (Adacolumn®, Cellsorba®) in patients suffering from active ulcerative colitis.
- Controlled studies are needed to further elucidate the efficacy of the new device.

ACKNOWLEDGEMENTS

This work was supported by NIKKISO Co., Ltd., Tokyo, Japan. The authors thank the nursing staff of the Apheresis Center Rostock for excellent technical and logistic support.

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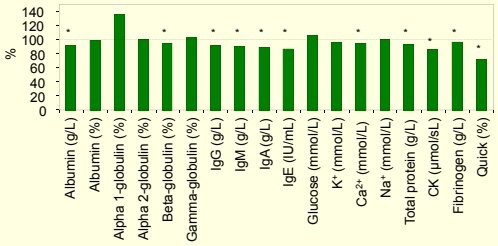
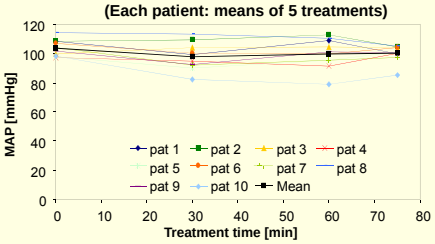
RESULTS

Safety laboratory parameters – intra-treatment impacts
Percentage change after Immunopure® treatments
0 min-value (100 %) vs. end value (n = 10, 5 treatments each)

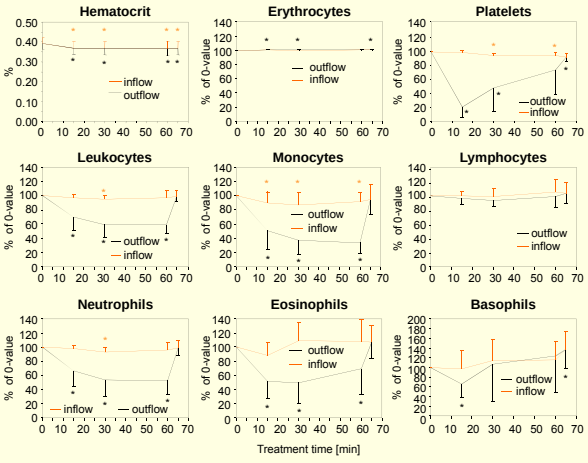


All of the 10 patients finished the study according to the suggested protocol. The observed intra-treatment and inter-treatment changes of safety parameters were within the normal range and clinically not relevant.

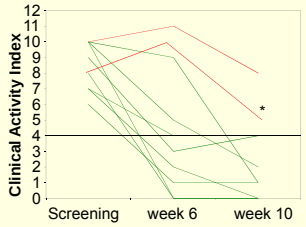
Mean Arterial Pressure during Immunopure® treatments
(Each patient: means of 5 treatments)



Vital parameters such as blood pressure, heart rate and body temperature remained essentially stable with a slight temporary reduction of the heart rate and the blood pressure during the apheresis sessions.



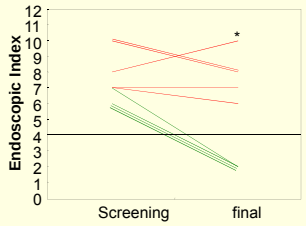
Performance data showed that especially platelets (to 20 %), monocytes (to 34 %) and neutrophil granulocytes (to 53 %) were effectively reduced during the cytapheresis treatments.



	Week 6 Number of patients	%	Week 10 Number of patients	%
Intent-to-treat population	10	100	10	100
Remission	6	60	8	80
Response	1	10	0	0
Remission + response	7	70	8	80
Non-responder	3	30	2	20

*had to receive prednisolone therapy

Remission (CAI) of the disease was achieved in 8 out of 10 patients (80 %) at week 10.



Endoscopic Score	Final evaluation Number of patients	%
Per-Protocol Population	10	
Remission	4	44.4
No endoscopic examination	1	-
Non-responder	5	55.6

*had to receive prednisolone therapy

Clinical remission was accompanied by the reduction of endoscopic index in 4 out of 9 patients (44 %) who gave consent to endoscopic examination (in 1 patient no endoscopic investigation was performed).