Kinetics of the Soluble IL-1 Receptor Type I During Treatment with an LCAP Filter in Patients with Inflammatory Bowel Disease

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Leukocyte apheresis primarily used for treatment of inflammatory diseases such as inflammatory bowel disease (IBD). Beside an effect of the apheresis column, the plastic lines in the apheresis system might also have an effect due to interaction between the plastic surfaces and circulating leukocytes and plasma proteins. We recently reported generation of LL-37 in the plastic lines during leukocyte adsorbing apheresis. This generation might have a positive impact on the immunologic tolerance and therefore be one operational mechanism by which the apheresis treatment executes its effect. In the present study, we report a significant generation of sIL-1RI in the apheresis lines that is initially absorbed by the LCAP device. This finding, together with our previous data on IL-1Ra indicate that important members of the IL-1 family are significantly altered during the LCAP treatment of patients with IBD. Since IL-1 and its antagonists are important for regulation of inflammatory processes in IBD, we speculate that the LCAP related changes in sIL-1RI and IL-1Ra might impact the clinical outcome. These findings have to be taken into consideration when designing new apheresis techniques as well as sham-controlled studies. J. Clin. Apheresis 27:61–63, 2012.   © 2012 Wiley Periodicals, Inc.

Key words: sIL-1RI; IL-1Ra; leukocyte apheresis; apheresis lines; IBD

INTRODUCTION

Leukocyte apheresis primarily used for treatment of inflammatory diseases such as inflammatory bowel disease (IBD). Beside an effect of the apheresis column, the plastic lines in the apheresis system might also have an effect due to interaction between the plastic surfaces and circulating leukocytes and plasma proteins [1,2]. We recently reported generation of LL-37 in the plastic lines during leukocyte adsorbing apheresis (LCAP) using ACD-A in patients with ulcerative colitis (UC) [3]. This generation might have a positive impact on the immunologic tolerance and therefore be one operational mechanism by which the apheresis treatment executes its effect.

In addition, we reported a significant decrease of the IL-1 receptor antagonist (IL-1Ra) in the apheresis plastic lines during the LCAP session [3]. IL-1 and its antagonists are important in the regulation of inflammatory processes such as IBD [4]. The IL-1 axis is regulated by several factors such as soluble IL-1 receptor type I (sIL-1RI) and soluble IL-1 receptor type II (sIL-1RII), IL-1Ra and the IL-1 receptor accessory protein. IL-1RI and IL-1RII become soluble after shedding and retain there affinity to IL-1Ra, with high and low affinity, respectively [5–7]. IL-1Ra is regarded as an anti-inflammatory molecule and has recently been registered as a pharmaceutical drug in rheumatoid arthritis (Anakinra®) and sIL-1RI have been attributed with anti-inflammatory properties in an animal model [7]. Given the IL-1 family an important role in the pathogenesis of IBD we assessed the impact of LCAP treatment on sIL-1RI.

METHODS

Six patients with UC underwent 10 LCAP sessions each and blood samples were collected and analysed as presented in our previous publication [3]. Briefly, the samples were collected ''Before'' start and from the inlet and outlet lines of the LCAP (Cellsorba^{TM} EX) device at two occasions during a treatment session; at time of the first blood return (I), and before the rinse back (II). These samples are designated ''Before,'' ''In-I,'' ''Out-I,'' ''In-II,'' and ''Out-II,'' respectively. The samples were collected at first and then treatment sessions. Four of six patients were responders out of which two reached remission 8 weeks after the last session. ACD-A (citrate) was used as an anticoagulant during the LCAP session. The sIL-1RI was analyzed by a commercial ELISA according to manufacturers instructions (USCN Life Science, Wuhan, China).

Statistics

Statistical analyses were assessed by the Wilcoxon nonparametric tests. P-values <0.05 were considered significant.

RESULTS

The sIL-1RI increased significantly in the apheresis lines ($P = 0.0033$) and decreased initially over the filter ($P = 0.0025$, between In-I and Out-I). There were no significant differences between In-I and In-II or Out-II. The difference between ''Before'' versus Out-II was significant ($P = 0.0034$) (Fig. 1).

DISCUSSION

In this study, we report a significant generation of sIL-1RI in the apheresis lines that is initially absorbed by the LCAP device. This finding, together with our previous data on IL-1Ra [3], indicate that important members of the IL-1 family are significantly altered during the LCAP treatment of patients with IBD. The generation of sIL-1RI could be a consequence of complement activation in the lines and the subsequent degranulation of neutrophil granulae, thereby releasing elastase, which mediates a quick shedding of cell surface receptors. The LCAP-device contains a polyester filter, and initially the sIL-1RI concentration diminished over the filter probably due to filer binding, however, sIL-1RI increases again at the end of the treatment session. Potentially, at the end of the apheresis session, the filter could have been saturated and therefore did not absorb newly generated sIL-1RI.

The excess of sIL-1RI generated during the apheresis could have the potential to bind IL-1 and thereby neutralize its biological effect. IL-1 is important in amplification of mucosal inflammation and the expression is enhanced in IBD [8]. Both sIL-1RI and IL-
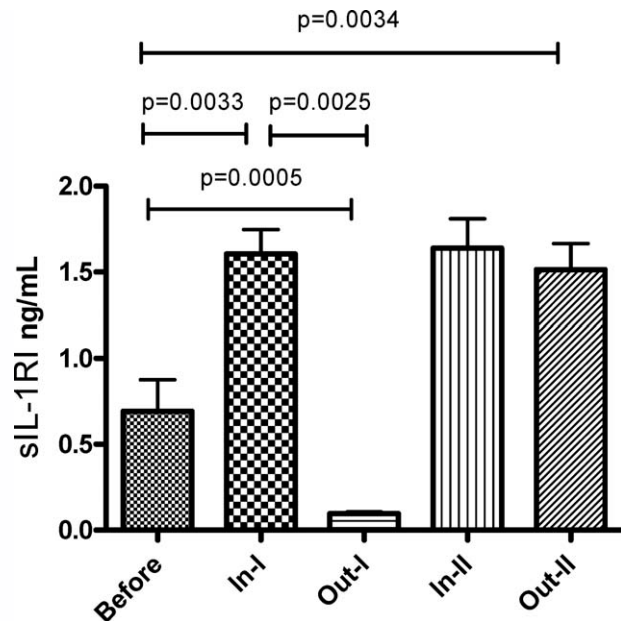

Fig. 1. The concentration of sIL-1RI during the LCAP session ($n = 12$). The bars represent mean and SEM.

1Ra are regarded as anti-inflammatory. They have high affinity to each other and can form a complex, which dissipates their anti-inflammatory properties [6]. Some part of newly generated sIL-1RI binds IL-1Ra but is still in surplus and can bind to and neutralize IL-1. However, the integrated outcome of the LCAP related changes in these molecules are not fully understood.

In this article, we demonstrate that soluble regulators of the proinflammatory cytokine IL-1 are altered by the apheresis lines and the LCAP filter. Since IL-1 and its antagonists are important for regulation of inflammatory processes in IBD, we speculate that the LCAP-related changes in sIL-1RI and IL-1Ra might impact the clinical outcome. These findings have to be taken into consideration when designing new apheresis techniques as well sham-controlled studies.

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