Reduction of monocyte activation by bowel cleanse and one week fasting suggests permanent pathogenetic triggering from the gut in rheumatoid arthritis


1Rheumatology, 2Internal and Complementary Medicine, Charité, 3Deutsches Rheuma Forschungszentrum, Berlin, Germany

Background:
Fasting can improve clinical disease activity in rheumatoid arthritis (RA) [1]. Recently, we demonstrated that monocytes in RA express transcriptome patterns characteristic for increased myelopoiesis, premature egress from bone marrow and reduced blood circulation time as indicators of permanent innate immune activation [2].

Objective:
We investigated the influence of bowel cleanse and fasting on monocyte subpopulations in the blood to determine the extent of microbiota and gut immunity related triggering of chronic inflammation in RA on this early stage of monocyte activation.

Methods:
RA patients (n=22; table 1) and controls (n=12, mostly metabolic syndrome patients), who presented at the Charité University hospital for fasting according to Dr. Buchinger, were analyzed for DAS28, CrP, differential blood count and high resolution cytometric immune phenotyping at baseline, day 3, day 7 (end of fasting) and day 10 (3 days after fasting), which was analyzed using the immunoclust pipeline (fig. 5).

Results:
Disease activity was decreasing after fasting in 21 of the 22 RA patients (median DAS28 from 4.44 to 3.17, p<0.000007) with significant reduction already after 3 days (p<0.01). This was accompanied by a significant decline of CrP and ESR after fasting (fig. 1). Differential blood count revealed a slight decrease in the total leukocytes and significant reduction of lymphocytes and eosinophils in RA. However, these changes were also observed but on a lower level in the controls. The most dominant effect of fasting and only observed in RA was a significant reduction of total monocytes when compared to baseline or to controls at day 10. Flow-cytometric analysis of classical (CD14+CD16–), intermediate (CD14++CD16+) and non-classical (CD14+CD16+) monocytes prior to fasting identified a decreased number of non-classical and intermediate monocytes in RA compared to controls, which confirmed our previous results [2]. Bowel cleanse and fasting induced a significant decrease of these two blood monocyte subpopulations by absolute numbers and even more by percentage of total monocyte count (fig. 2, 3). This indicates reduced recruitment to inflamed tissue and prolonged circulation with more cells differentiating from classical to non-classical monocytes in the blood [3]. The decrease of lymphocyte counts in RA patients after fasting (fig. 4) was characterized by a dominant reduction of naïve T-, B-cells and CD16 NK-cells along with a relative increase in memory lymphocytes and CD16+ NK-cells. These effects were also observed but less pronounced in controls.

Conclusion:
Bowel cleanse and fasting in RA induces a reduction of inflammation related to monocyte activation and turnover immediately within few days. Changes in the monocyte compartment were specific for RA compared to controls and dominated the immunological changes, indicating that innate triggering mechanisms from gut and its microbiota are etiologically relevant in RA.

Figure 1: Change of RA disease activity upon bowel cleanse and one week fasting. A ΔDAS28: change of disease activity score based on 28 joints and DAS28 reduction already after 3 days (p<0.01).

Figure 2: Change of RA non-classical monocyte count and frequency upon bowel cleanse and fasting.

Figure 3: No change of non-classical monocyte count and frequency in metabolic syndrome patients.

Figure 4: Change of CD4+ T-cell count upon fasting in RA and metabolic syndrome (Met Syn).

Table 1: Patient characteristics.


Contact: Thomas Häupl  
Department of Rheumatology and Clinical Immunology  
Charité Universitätsmedizin Berlin  
Charitéplatz 1; 10117 Berlin; Germany  
thomas.haeupl@charite.de  
www.charite-bioinformatik.de