REDUCTION OF MONOCYTE ACTIVATION BY BOWEL CLEANSE AND ONE WEEK FASTING SUGGESTS PERMANENT PATHOGENETIC TRIGGERING FROM THE GUT IN RHEUMATOID ARTHRITIS

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Background and objective:
Fasting can improve clinical disease activity in rheumatoid arthritis (RA) [1], but the mechanism involved are not clear. Recently, we demonstrated that monocytes in RA express transcriptome patterns of increased myelopoiesis, premature egress from bone marrow and reduced blood circulation time as indicators of permanent activation of the innate immune response [2]. Objectives: 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.

Materials and Methods:
RA patients (n=22) and controls (n=12, metabolic syndrome), who presented for fasting according to the Buchinger procedure (bowel cleanse with colonoscopy fluid), were analyzed for DAS28, CrP, differential blood count and high resolution cytometric pheno-typing at baseline, day 3, day 7 (end of fasting) and day 10. ImmunoClust was applied by automated cell clustering [3].

Results:
Disease activity was strikingly decreased after fasting in virtually all RA patients (DAS28 from 4.24 to 3.17, p<0.00005) with significant reduction already after 3 days (p<0.01). This was accompanied by a significant decline of CrP and ESR. Differential blood count revealed a slight decrease in total leukocytes and significant reduction of lymphocytes and eosinophils in RA. However, these blood changes were also observed but on a lower level in the metabolic controls. The most dominant and RA specific effect was a significant reduction of total monocytes when compared to RA baseline or to controls at day 10. Deep profiling of the monocyte compartment revealed reduced non-classical (CD14+CD16+) and intermediate (CD14++CD16+) monocytes prior to fasting in RA compared to controls and confirmed previous results [2]. Bowel cleanse and fasting induced a significant increase of these two monocyte subpopulations by absolute counts and even more by frequency of total monocytes. This indicates reduced recruitment to inflamed tissue and prolonged circulation with more cells differentiating from classical to non-classical monocytes in the blood [4]. The decrease of lymphocytes in RA patients after fasting was characterized by a dominant reduction of naive 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.

Conclusions:
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, suggesting that innate triggering mechanisms from gut and its microbiota are etiologically relevant in RA.

References:
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