education, and higher fatigue, whereas older age and greater pain were associ-
ated with persistent disease activity in men. Smoking cessation in men and weight
reduction in women, and optimising MTX use may facilitate rapid reduction of
inflammation, an essential goal of treatment in early RA.

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Fat and fatty acids: targets for therapy?

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Background: Adipocytokines are implicated in the development of fibrosis,
vasculopathy and immune abnormalities through a variety of biological effects, but
their role in systemic sclerosis (SSc) is not fully investigated. Chemerin is impli-
cated in chemotaxis of immune cells, in promoting angiogenesis and it is involved
in inflammation. Adiponectin (APN) has metabolic actions and anti-inflammatory
properties, while Leptin (LEP) mediates actions in endothelial cells, such as
angiogenesis, vasodilation, NO production and upregulates various mediators of
vascular inflammation.

Objectives: In this study we investigated Chemerin, LEP and APN levels in SSc
patients according to disease subtypes and clinical characteristics.

Methods: Chemerin, LEP and APN levels were evaluated in 100 SSc patients and
in sex, age and BMI matched healthy controls. Clinical and demographical
characteristics were available for all patients.

Results: Chemerin, APN and LEP levels were lower in SSc patients compared to healthy controls (Chemerin: 58.7±27.6 ng/ml vs 74.0±29.0 ng/ml, p<0.004; APN: 19.6±18.3 ng/ml vs 28.5±23.8 ng/ml, p=0.03; LEP: 6.5±3.9 pg/ml vs 12.8 ±6.0 pg/ml, p<0.001)

Chemerin levels were lower in patients with anti-topoisomerase antibodies (50.2 ±22.7 ng/ml) respect to patients with other autoantibodies (64.6±29.7 ng/ml), p=0.018.

Regarding capillaroscopic damage, Chemerin levels were lower in patients with late pattern (44.8±18.9 ng/ml) compared to patients with early pattern (64.3±28.5 ng/ml) and active pattern (71.7±29.9 ng/ml), p<0.001. LEP levels inversely correlate with IL-6 levels (R=-0.4, p<0.001), while directly correlate with capillary density (R=0.3, p=0.03). Patients with avascular areas presented lower levels of APN (5.3 ±3.9 pg/ml) compared to patients without avascular areas (7.3±3.4 pg/ml), p=0.005. LEP levels directly correlate with vascular density on nailfold capillaro-
scopy (R=0.3, p=0.02), confirming the role of LEP in endothelial homeostasis.

Furthermore, patients with avascular areas presented lower LEP levels (15.5 ±13.0 ng/ml) compared to patients without avascular areas (31.1±28.4 ng/ml), p=0.003. LEP levels were lower in patients with active digital ulcers (9.3±6.6 ng/ ml) compared to patients without ulcers (9.3±6.6 ng/ml), p=0.01. The anti- inflamm-
atory and endothelium protective role of APN emerged also when we consid-
ered the lung involvement: in fact patients with DLCO <50% presented higher
levels of APN (7.0±3.9 pg/ml) compared to patients with DLCO >50% (5.8 ±3.8 pg/ml), p=0.05.

Considering the cardiopulmonary involvement, LEP levels inversely correlate with
PAPs on echocardiography (R=-0.24, p=0.02). Finally LEP levels inversely corre-
late with skin score (R=-0.3, p=0.009) and patients with early disease presented
lower LEP levels (15.1±13.2 ng/ml) compared to patients with long lasting dis-
ease (29.9±28.7 ng/ml), p=0.006.

Conclusions: Our data suggest an imbalance of the levels of adipocytokines in
SSc, their downregulation in patients with a more aggressive pattern on nailfold
videocapillaroscopy and organ damage, suggesting a possible role of Chemerin,
LEP and APN in the impaired angiogenesis and in the development of vasculop-
athy of SSc patients.

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Biologics in RA. Improving and maintaining the response.

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Background: B-cell depletion is a fundamental effect of rituximab (RTX). The speed/depth of initial B-cell depletion is associated with clinical response, and non-responders largely having incomplete depletion.1 however, some patients with incomplete depletion still show clinical improvement (ID-R). Little is known about factors associated with complete depletion; the long-term outcome of the two responder groups according to their level of depletion has not been studied yet.

Objectives: To assess factors that are associated with complete depletion and clinical response (CD-R) and compare the 3 year RTX retention between the two RTX responder groups (CD-R vs ID-R), with a view to inform practice on the optimal use of RTX in RA.

Methods: A prospective observational study was conducted in patients with RA who were treated with RTX in Leeds. Each initial cycle of RTX consisted of 2 x 1000 mg infusions, repeated either on clinical relapse or fixed 6 monthly

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retreatment strategy. B-cells were measured at 0, 2 weeks and every 6 months using highly sensitive flow cytometry (as previously described). Complete depletion was defined as total B cell count <0.0001×10^9/L at week 2. Patients were classified into 4 groups based on B cell depletion (CD=complete,) and EULAR response (R=good/moderate, NR=no response). Multiple imputation was used for missing data. Factors for predicting CD-R in cycle 1 (C1) were tested using logistic regression analyses. In the survival analysis, an event was defined as RTX cessation either due to death, safety or switching to other biologics.

Results: A total of 693 patients were treated with RTX in Leeds. Of these, 624 had clinical data at 6 months and were included in the analysis. Total follow-up was 2826 patient-years. In cycle 1, 418/624 (67%) had EULAR response. Of these, 242/418 (58%) had CD-R. In univariable analysis, age, concomitant MTX/LEF, non-smoker, pre-RTX lower naïve, memory B-cell and plasmablasts were associated with CD-R in C1. However, in a multivariable analysis, only concomitant MTX/LEF (OR 2.1; 95% CI: 1.3 to 3.5), non-smoker (1.6; 1.2 to 2.6) increased the odds while lower plasmablasts (0.89; 0.83 to 0.95) decreased the odds of CD-R. After adjusting for confounders including age, gender, concomitant MTX/LEF and previous exposure to TNF-i, there was a trend to longer maintenance on RTX (surrrogate for response) in the CD-R vs ID-R groups; HR 0.70 (95% CI: 0.46 to 1.05); p=0.058 (figure 1).

Conclusions: Among patients with good initial clinical response to RTX, we observed differences in immunological response. This had important long term consequences: in patients with early complete B-cell depletion accompanied by good clinical response, RTX treatment was sustained over 3 years numerically, and RTX treatment was associated with a decrease of 1.5 microgram/ml in the serum TCZ concentrations (95% CI: 0.8 to 2.2) and every increase of 1 kg in weight was associated with a decrease of 1.5 microgram/ml in the serum TCZ concentrations (95% CI: 0.8 to 2.2) and every increase of 1 BMI unit was associated with a decrease of 2.6% (95% CI: 2% to 22%) in the CDAI score. In a multivariate model which included age, sex, visit date and both sIL6R and TCZ levels, only the associated between TCZ levels and CDAI scores remained significant. Similarly, every increase of 10 microgram/ml in the serum concentra- tion of TCZ was associated with an odds ratio of 1.35 (95% CI: 1.07 to 1.72) of being in a state of CDAI remission or low disease activity versus moderate/high disease activity state. TCZ and sIL6R serum levels were not associated with HAQ DI scores. Female sex was associated with an increase of 12.9 microgram/ml in the serum TCZ concentrations (95% CI: 5.9 to 20.0). Also, every increase of 1 BMI unit was associated with a decrease of 1.5 microgram/ml in the serum TCZ concentrations (95% CI: 0.8 to 2.2) and every increase of 1 kg in weight was associated with a decrease of 0.6 microgram/ml in the serum TCZ concentrations (95% CI: 0.3 to 0.9).

Conclusions: In the first year of TCZ treatment with a fixed dose regimen of 162 mg SC injection once a week, serum trough concentrations of TCZ are associated with clinical disease activity outcomes in RA patients. It is unknown whether serum trough levels of tocilizumab (TCZ) administered as a fixed dose subcutaneous injection, also associate with clinical disease activity responses.

Abstract OP0109 – Figure 1 Rituximab retention 3 years after the administration of the first cycle


References:

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