THU0219

BENEFICIAL EFFECT OF ANTI-IL-6 BLOCKADE ON INSULIN RESISTANCE AND INSULIN SENSITIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Systemic inflammation, insulin resistance (IR), and endothelial dysfunction have been implicated in the development of cardiovascular disease in rheumatoid arthritis (RA).¹⁻³ In this regard, it has been described that the blockade of IL-6, a cytokine involved in the pathogenesis of both RA and atherosclerosis, yields a rapid improvement of endothelial function in RA.⁴ However, there are no studies on the role of anti-IL-6 treatment on IR in patients with RA.

Objectives: To assess whether IL-6 blockade may result in a reduction of insulin serum levels and an improvement of IR in patients with RA.

Methods: 50 Spanish patients on treatment with anti-IL-6 monoclonal antibody-Tocilizumab who fulfilled the 2010 classification criteria for RA⁵ were recruited. Patients with diabetes mellitus or plasma glucose >110 mg/dl were excluded. Fasting blood samples were taken for determination of plasma glucose and serum insulin levels immediately prior to (time 0) and after (time 60 min) Tocilizumab infusion. IR was assessed by the homeostasis model assessment (HOMA) and insulin sensitivity was evaluated by the quantitative insulin sensitivity check index (QUICKI).

Results: A marked reduction in the serum insulin levels was observed following Tocilizumab infusion (mean ± standard deviation (SD): 10.60±5.80 µU/ml versus 7.61±5.08 µU/ml, p<0.0001). In addition, a decrease in the insulin/glucose index was observed in patients with RA after Tocilizumab dose (mean ±SD: 0.12 ±0.06 versus 0.08±0.05, p<0.0001). Finally, our results disclosed a significant improvement of insulin resistance (HOMA: mean ±SD: 2.61±2.05 versus 1.65 ±1.14, p=0.0003) and insulin sensitivity (QUICKI: mean ±SD: 0.34±0.003 versus 0.37±0.04, p<0.0001) following Tocilizumab infusion.

Conclusions: Our study confirms a rapid beneficial effect of Tocilizumab on IR and insulin sensitivity in RA patients treated with this drug. It may support the long-term use of drugs that act blocking IL-6 function to reduce the mechanisms implicated in the development of atherosclerosis in RA patients.

REFERENCES:

- Am J Med 2003;114:647–652.
- Autoimmun Rev 2016;15:1013–1030.
- Autoimmun Rev 2004; 3:301–304.
- Atherosclerosis 2011;219:734–736.
- Arthritis Rheum 2010;62:2569–2581.

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THU0220

DISCONTINUATION OF BIOLOGIC DMARDS IN A REAL-LIFE POPULATION OF PATIENTS IN REMISSION: OUTCOME AND PREDICTORS

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Background: Data from randomised controlled trials have shown that in patients with sustained remission discontinuation of bDMARD therapy is feasible. However, the criteria for selecting patients that will successfully remain in remission after bDMARD discontinuation remain to be defined.

Objectives: To assess the rate of loss of remission after discontinuation of bDMARDs in a real life setting and to identify predictors in a large cohort of patients.

Methods: Adult RA patients in bDMARD-free remission from the Swiss clinical quality management in rheumatic diseases registry (SCQM) were included. bDMARD-free remission was defined as a discontinuation of the bDMARD and a DAS28 ≤2.6 at a clinical visit within 90 days prior to 30 days after the bDMARD discontinuation. Loss of remission was defined as a DAS28 >2.6 or restart of a bDMARD. Patients treated with rituximab were excluded. Kaplan-Meier methods were applied and cox regression was used for multivariable analyses (adjusted for sex, anti-CCP, RF, DAS28, bDMARD Type, CDAI, therapy with conventional DMARDs, number of previous bDMARDs). Missing data were imputed using multiple imputation.

Results: Between 1997 and 2017, 318 patients achieved a bDMARD-free remission (table1). Median observation time was 2.8 years (IQR 1.2–4.9). 241 patients lost remission (76%), 54% of those re-started a bDMARD, 34% experienced a DAS28 flare and 12% did both. The median time to loss of remission was 0.9 years (95% CI 0.7–1.0). 76% discontinued a TNFα-inhibitor, 6% stopped abatacept, 14% tocilizumab and 4% tofacitinib. Women lost remission faster than men (figure 1A; p=0.005); this was also seen in multivariable analysis (HR 1.4, p=0.03). Longer disease duration was associated with a faster loss of remission (figure 1B; p=0.03) also in multivariable analysis (HR[4–8 years] 1.6, p=0.03, HR [8–13 years] 1.6, p=0.01, HR[>13 years] 1.5, p=0.035 vs 0–4 years disease duration). Remission was lost faster by patients who discontinued tofacitinib compared to those who stopped a TNFα-inhibitor (HR 2.3, p=0.01) also after adjustment (HR 2.0, p=0.047). There was a trend for a faster loss of remission in patients with a higher disease activity as measured by the CDAI at baseline (figure 1C; p=0.7); this association was significant in multivariable analysis (HR[CDAI low disease activity] 1.6, p=0.03, HR[CDAI moderate/high disease activity] 2.5, p=0.003, both vs CDAI remission). Patients who received MTX/leflunomide during the observation period lost remission less rapidly (figure 1D; p=0.006) also in multivariable analysis (HR 0.8, p=0.046).

Abstract THU0220 – Table 1. Baseline demographic and disease characteristics of patients with bDMARD-free remission

Characteristics	% or median (IQR)
Male sex	26
Age	57 (46–66)
Disease duration in years	8 (4–13)
Number of previous bDMARDs	0 68 1–2 27 ≥3 5
cDMARD any time during Remission	64
Anti-CCP/RF positive	64/72
DAS28	2.0 (1.5–2.3)
HAQ	0.4 (0–1.0)
CDAI	Remission 27 Low Activity 54 Moderate-High Activity 19

Abstract THU0220 – Figure 1. Kaplan-Meier for time in biologic-free remission according to sex (A), disease duration (B), CDAI (C), conventional DMARD therapy (D)

Conclusions: In a large real-life cohort of RA patients that achieved DAS28 remission and stopped therapy with bDMARD the majority lost remission within less than a year. Predictors for loss of remission included female sex, longer disease duration, a higher CDAI score and absence of cDMARD therapy. This