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GENDER DIFFERENCES IN RHEUMATOID ARTHRITIS: EFFECT OF ANTI-TUMOR NECROSIS FACTOR THERAPY

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Background: Rheumatoid arthritis (RA) is more prevalent in women than men (F:M=4:1), due to hormonal, genetic and environment factors. Women present higher disease activity markers as Disease Activity Score-28 (DAS28) and Health Assessment Questionnaire (HAQ), at the onset and after c-DMARDs therapy, without correlation with radiographic damage.

Objectives: The purpose of this study was to assess gender differences in RA patients after anti-tumor necrosis factor (TNF) α treatment.

Methods: Ninety-six patients were enrolled at the beginning of anti-TNF α therapy (etanercept and adalimumab). All patients satisfied 1987 and 2010 ACR criteria for RA. They underwent to clinical and clinimetric evaluation at baseline (T0) and after three (T3) and six (T6) months of therapy with: tender and swollen joints, Visual Analogue Scale (VAS) pain, VAS patient and physician, DAS28, Clinical/Simplified clinical disease activity index (CDAI/SDAI) and HAQ. The evaluation of erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), Rheumatoid Factor (RF) and anti-citrullinated protein antibody (ACPA) was performed in all patients.

Results: Among these patients, 70 were women and 26 men; 81 patients (58 female, 23 male) started etanercept and 15 adalimumab (12 female, 3 male). They presented a mean age of 56.4 ± 14.5 years (women 55.2 ± 15.4 , men 60 ± 11.2) and mean disease duration of 11 ± 6.8 years (woman 11.51 ± 6.3 , men 9.6 ± 8.1). Both women and men had a DAS28 reduction after 3 and 6 months therapy ($p < 0.05$) but DAS28 in women was higher than men at T0, T3 and T6 ($p < 0.05$). Women presented higher number of tender joints in all evaluations, and more swollen joints than men at T0 and T6 ($p < 0.05$). Women felt more active disease at T6 (VAS patient) ($p < 0.05$). CDAI was higher in woman after 3 and 6 months ($p < 0.05$). There were no differences about physician evaluation, inflammation markers, RF and ACPA titles.

Conclusion: In this study, both women and men had a good response to anti-TNF treatment but women presented worse clinical response. Female gender resulted the only variable associated with DAS28 reduction differences. We could hypothesize that beyond to biological factors, also social context, daily life and work activity could explain a worse impact of disease on women.

Table 1.

Patients clinical characteristics (n=96)									
	T0			T3			T6		
	F (n=70)	M (n=26)	p	F (n=70)	M (n=26)	p	F (n=70)	M (n=26)	p
TJ (mean; CI)	12.16 (10.2-14.2)	8.44 (5.08-11.8)	0.0025	4.86 (3.65-6.06)	2.64 (0.68-4.6)	0.0046	4.75 (3.49-6.02)	2.16 (0.98-3.34)	0.0106
SJ (mean; CI)	5.32 (4.22-6.42)	3.56 (1.8-5.32)	0.0046	2.29 (1.59-2.98)	1.36 (0.45-2.27)	ns	2.12 (1.40-2.83)	0.6 (0.22-0.98)	0.032
CDAI (mean; CI)	27.73 (24.57-30.89)	23.63 (16.32-30.95)	ns	14.28 (12.02-16.54)	10.99 (5.11-16.87)	0.0098	12.95 (10.46-15.45)	6.78 (4.21-9.36)	0.0037
DAS28 (mean; CI)	5.25 (4.99-5.51)	4.38 (3.76-5.01)	0.0162	3.89 (3.62-4.16)	3.19 (2.6-3.77)	0.0176	3.74 (3.45-4.03)	3.00 (2.47-3.52)	0.0156
VAS pain (mean; CI)	5.55 (5.01-6.09)	5.23 (4.13-6.33)	ns	3.56 (2.85-4.28)	2.37 (1.60-3.13)	ns	3.47 (2.85-4.09)	2.84 (1.21-4.47)	ns
VAS patient (mean; CI)	5.61 (5.16-6.07)	5.22 (4.19-6.25)	ns	3.50 (2.98-4.02)	2.79 (1.74-3.84)	ns	3.32 (2.76-3.89)	1.98 (1.21-2.74)	0.017
VAS physician (mean; CI)	4.49 (3.96-5.02)	4.27 (3.29-5.26)	ns	2.78 (2.38-3.19)	2.1 (1.27-2.94)	ns	2.52 (2.05-2.99)	1.67 (1.01-2.32)	ns
ESR (mean; CI)	25.84 (21.51-30.17)	24.64 (17.41-31.87)	ns	15.99 (13.05-18.92)	16.48 (6.54-24.42)	ns	16.36 (13.25-19.48)	15.12 (8.98-21.26)	ns
CRP (mean; CI)	12.26 (7.45-17.07)	11.86 (5.55-18.16)	ns	6.36 (2.19-10.53)	9.75 (2.82-16.68)	ns	3.7074 (1.9065-5.5083)	6.1912 (2.3178-10.0649)	ns

CI (confidence interval); TJ (tender joints); SJ (swollen joints); CDAI (Clinical Disease Activity Index); DAS28 (Disease Activity Score 28); VAS (Visual Analogue Scale); ESR (erythrocyte sedimentation rate); CRP (C-reactive protein)

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AB0380

ISTHERE AN EFFECT OF TOCILIZUMAB IN SERUM AUTOANTIBODIES LEVELS IN RHEUMATOID ARTHRITIS?

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Background: Interleukin 6 (IL-6) plays a role on B cell differentiation and antibody production. However, few information is available considering the effect of tocilizumab (TCZ) on rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPAs) levels in Rheumatoid Arthritis.

Objectives: To compare serum levels of RF and ACPAs on RA patients at the beginning of therapy with TCZ and at 6 and 12 months under TCZ, assessing if its variations correlate with the several disease activity scores.

Methods: Longitudinal retrospective study of RA patients ever treated with TCZ at a Rheumatology Department. Serum levels of RF and ACPAs at 0, 6 and 12 months after starting anti-IL6 treatment were collected, as well as DAS28, DAS28 CRP, CDAI, SDAI, HAQ, ESR, CRP, patient's global assessment (PGA), physician's global assessment (PhGA), swollen joint count (SJC) and tender joint count (TJC). Demographic and clinical data were collected. SPSS statistics 22.0 was used for statistical analysis; p values under 0.05 were considered significant.

Results: 75 patients were included, 93.3% female (N=70), with a median (min-max) age of 58 (33-80) years and median disease duration at TCZ initiation of 10.7 years (1.0-43.3); 33.3% were on TCZ monotherapy (N=25). At baseline, forty-two (56.0%) were RF positive (≥ 30 UI/ml) and 47 (62.7%) were ACPAs positive (≥ 10 UI/ml). Median serum RF levels were 255.0 UI/mL (37.20-5560.00), 193.5 UI/mL (9.80-5270.00) and 131.0 UI/mL (9.40-6260.00) at 0, 6 and 12 months respectively; serum RF levels were only statistically different ($p=0.006$) between 0 and 6 months. Median serum ACPAs levels were 278.5 UI/mL (17.00-9300.00), 348.0 UI/mL (19.00-4720.00) and 277.0 UI/mL (16.00-4400.00) at 0, 6 and 12 months respectively, without any statistically significant differences. Considering the autoantibodies levels variation, Δ RF at 6 months correlated positively with Δ HAQ ($r=0.482$; $p=0.009$) and Δ CPR ($r=0.413$; $p=0.026$). After one year, Δ RF correlated positively with ESR ($r=0.426$; $p=0.019$) and DAS28 ($r=0.428$; $p=0.018$). As for ACPAs at 6 months, it correlated positively with PhGA ($r=0.461$; $p=0.035$). At 12 months, there was a positive correlation between Δ ACPAs and Δ CDAI ($r=0.385$; $p=0.036$) and between Δ ACPAs and Δ SJC ($r=0.469$; $p=0.002$).

Conclusion: In our RA sample, serum RF levels showed a significant titre difference past 6 months of treatment with TCZ. Moreover, a moderately strong correlation was found between Δ ACPAs/ Δ RF at 12 months months and the variations in several disease activity scores. Thus, this study reinforces the evidence of an impact of IL-6 inhibition on autoantibodies production in RA patients, as well as a relation between autoantibodies titre variation and clinical response. These findings need to be assessed in larger, prospective studies.

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